THE DESIGN, SYNTHESIS, AND CHARACTERIZATION OF POLYDENTATE POLYPHOSPHINE LIGANDS FOR ACTINIDE AND LANTHANIDE EXTRACTION

by

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ABSTRACT

As the proliferation of nuclear facilities continues, the need for a cheap, efficient way to selectively extract and separate the elements of the lanthanide and actinide families becomes paramount. "Wastes" from these facilities often contain long-lived radioactive particles (which must be safely removed and isolated from the environment) along with elements of great commercial or scientific value. Separation schemes exist, but better methods must be developed which offer the selectivity necessary to obtain useful, pure materials. These methods must be safe, easy to use, and cost effective.

A series of triphosphine oxide compounds with a tripodal structure have been synthesized for this purpose. These ligands should be ideal for the chelation of lanthanide and actinide ions. They allow for tridentate coordination and should separate radionuclides into small groups of like characteristics on the basis of size. By using tripods of increasing bite-size in series, it is should be possible to obtain effective separation of cations on the basis of size. Further selectivity should be provided by the substitution of either electron-withdrawing or electron-donating groups on the phosphorus atom. Electron-withdrawing groups cause the phosphine oxide to be a harder ligand while, conversely, electron-donating groups cause the phosphine oxide to become a softer ligand.

The synthesis, characterization and properties of this family of tripodal triphosphine oxides will be examined.

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ABBREVIATIONS

X	halogen
R	organic group
t-Bu	tertiary butyl
Me	methyl
Et	ethyl
Ph	phenyl
Bz	benzyl
THF	tetrahydrofuran
py	pyridine
IR	infrared
NMR	nuclear magnetic resonance
HLW	high level nuclear waste
NEA	Nuclear Energy Agency
LANL	Los Alamos National Laboratory

Key for infrared spectra:

vw: very weak, w: weak, m: medium, s: strong

vs: very strong, sh: sholder, br: broad

Key for nuclear magnetic resonance spectra:

s: singlet, d: doublet, t: triplet, q: quartet, p: pentet

sex: sextet, sep: septet, m: multiplet

CHAPTER I

INTRODUCTION

1.1 The Problem

Since the first observed nuclear reactions in Becquerel's laboratory, the transmutatory processes of nuclear fission and fusion have fascinated and terrified both scientists and laymen alike. In many respects nuclear synthesis represents the first realization of the alchemist's dream, that of transforming one element into another. The enormous amounts of energy released from such a transformation had never before been within the reach of mankind. Advances in the field of nuclear research were quickly progressed through the experiments of the late 1940's and early 1950's, when vast quantities of human and monetary resources were devoted to the development of an atomic weapon. Scientists sought to harness the energy contained within the atom to put an end to the war. During the Manhattan Project and the following Cold War years, priority was placed on the production of ^{239}Pu to ensure national security. Commercial development of nuclear technology did not occur until after the end of World War II. Nuclear reactors were hailed as a near limitless alternative to rapidly depleting fossil fuels for the production of energy, but little thought was given to the issue of nuclear waste management. It was thought that by the time the problem of nuclear waste became acute, improving technology would have provided a solution to the problem.[1] The United States, as well as many other modern industrialized nations, is currently in the process of cleaning up and containing large stockpiles of nuclear waste accumulated throughout the past half century.

1.2 The History of the Atomic Age

At the beginning of the twentieth century, scientists realized that a great deal of energy was contained within the nucleus of the atom, but it was not until the discovery of nuclear fission by Hahn and Strassmann in December of 1938 that the potential of atomic energy was realized. Hahn and Strassmann observed that uranium had only marginal stability and that it could divide upon the capture of a neutron into nuclei of roughly equal size, liberating a relatively large amount of energy in the process. In 1939, Niels Bohr successfully predicted that ^{238}U would be incapable of sustaining a nuclear chain reaction because it required very fast high energy neutrons to undergo fission; however, he also predicted that ^{235}U would undergo nuclear fission following a collision with any neutron. His theory was proved experimentally in 1940 by John Dunning and his co-workers at Columbia University.[2]

On the evening of December 4, 1940, Glenn T. Seaborg and his graduate student A. H. Wahl bombarded uranium oxide with 16-MeV deuterons to produce the synthetic transuranium element, ^{238}Pu.

$$^{238}_{92}U + {}^{2}_{1}H \longrightarrow {}^{238}_{93}Np + 2n$$

$$^{238}_{93}Np \xrightarrow{-\beta} {}^{238}_{94}Pu \quad (2.1 \text{ days}).$$

The discovery of ^{239}Pu followed three days later and its possibilities as a nuclear energy source were established in the Spring of 1941.

$$^{238}_{92}U + n \longrightarrow {}^{239}_{92}U + \gamma$$

$$^{239}_{92}U \xrightarrow{-\beta} {}^{239}_{93}Np \quad (23.5 \text{ min.})$$

$$^{239}_{93}Np \xrightarrow{-\beta} {}^{239}_{94}Pu \quad (2.33 \text{ days}).$$

All news of the discovery remained unpublished until after WW II due to self-imposed wartime secrecy.[3]

The first artificial nuclear reactor was constructed on December 2, 1942, under the West Stands of Stagg Field at the University of Chicago. The reactor, assembled by

Enrico Fermi, served as the predecessor to today's reactors. The production of ^{239}Pu was accomplished by developing chain-reacting units (piles) utilizing the neutron-induced fission reaction of ^{235}U in naturally occurring uranium. The extra neutrons, beyond those required to perpetuate the chain reaction, were absorbed to form ^{239}Pu.[4] Fermi's technology was quickly scaled up at Clinton Laboratories in Oak Ridge, Tennessee, where the first gram quantity of plutonium was produced.[5]

The early investigations of plutonium were carried out with unweighable amounts on a tracer scale. Even though no one had actually seen any plutonium, the exigencies of war made it necessary to begin designing separation plants immediately so that construction of these facilities could occur simultaneously with the construction of the chain-reacting piles. On August 20, 1942, Burris B. Cunningham, his student Louis B. Werner, and research associate Michael Cefola isolated approximately one μg of plutonium fluoride. This was the first visible amount of a chemical compound containing a man-made element. On September 10, 1942, in room 405 of the Jones Laboratory at the University of Chicago, Cunningham and Werner performed the first weighing of plutonium (2.77 μg PuO_2). A separation scheme was developed based on the unique coprecipitation characteristics of bismuth phosphate.[4] The discovery that $BiPO_4$ would carry down Pu(IV) but not Pu(VI), combined with the crystallinity and ease of dissolution of the bismuth phosphate precipitates resulted in the selection of this procedure in a time when speed was more important than economic considerations. Although obsolete by today's standards, the Bismuth Phosphate Process had many advantages over other technologies in use at the time. The engineering experience necessary for plant scale utilization was well established and the process was easily adapted to remote operation.[6]

Nuclear processing and production sites were built in 1942 near Hanford, Washington to produce ^{239}Pu for the nation's first atomic weapons. Within twenty-nine months of breaking ground at the site, the project had delivered the plutonium used in the

bomb dropped on Nagasaki, Japan (August 9, 1945).[7] This was truly the largest successful scale up ever attempted, a factor of 10^6.[3]

Secrecy surrounding the nuclear weapons program continued throughout the Cold War years, concealing the fact that for decades, hazardous and radioactive wastes were discharged to the ground, water, and air at Hanford. Documents describing the construction, operation, and maintenance of the Hanford facilities were not declassified until 1986.

Today plutonium is produced in much larger quantities than any other synthetic element. During the past four decades plants at Savannah River, South Carolina and Hanford, Washington have produced some one hundred metric tons of plutonium.[4]

1.3 Commercial Waste

The privatization of nuclear energy was accelerated by events in 1953 and 1954. In the spring of 1953, electricity was produced for the first time from nuclear power using a small government reactor at the Idaho National Engineering Laboratory. Eisenhower's "Atoms for Peace" speech in December 1953 emphasized an international program for civilian uses of atomic energy, especially reactors to produce power for fuel hungry Europe. Government sought to promote the peaceful uses of nuclear energy as the nation's economy swiched over from a war to a peacetime economy.

In December of the same year, the Atomic Energy Commission selected the Duquesne Light and Power Company, a Pittsburgh utility, to join in a three-way partnership with the federal government and the Westinghouse Corporation. Under the agreement, Duquesne would provide the land and about $300 million. It would also operate and maintain the plant after construction. Westinghouse and the government would be responsible for manufacturing the facility.

In the summer of 1954, Congress amended the Atomic Energy Act of 1946, thereby encouraging further private nuclear reactor development. The new legislation gave the Atomic Energy Commission the authority to license private corporations to build and operate nuclear-fueled power plants. The Commission would continue to fund research and development, but the act prohibited the construction of power "reactors for the purpose of selling or distributing electricity." Free enterprise would provide the impetus for civilian nuclear power. Congress believed that, "The goal of atomic power at competitive prices will be reached more quickly if private enterprise, using private funds, is ... encouraged to pay a far larger role in the development of atomic power ..."(cited in Williams, 1984, p. 293).

In December of 1954, the Atomic Energy Commission asked private industry to submit proposals for the construction of new facilities as part of the Power Demonstration Reactor Program. Five proposals were submitted. In May 1956, the commission granted the first public power permit to the Consolidated Edison Company of New York to build a pressurized water reactor at Indian Point. Indian Point was located just thirty-five miles up the Hudson River from New York City. Government reactors had always been located in remote areas, but to make nuclear energy feasible, power companies sought to locate plants near their customers and existing power grids. This created a new regulatory concern and the commission was forced to draw up new siting plans, and radiation standards to ensure the public's health and safety.

The Atomic Energy Act of 1954 gave the Atomic Energy Commission responsibility for regulating and licensing power reactors. It also charged the commission with the task of promoting the use of nuclear power. Congress later split the commission into the Nuclear Regulatory Commission and the Energy Research and Development Administration in 1974. The Nuclear Regulatory Commission retained responsibility for the regulation of nuclear power; however, the responsibility for the promotion of nuclear

power was assumed by the Energy Research and Development Administration (later renamed the Department of Energy).[8]

Nuclear power made its first significant contribution to the U.S. energy supply in 1960, showing rapid growth thereafter until 1978. Original Nuclear Energy Agency (NEA) estimates proposed that by the year 2000, the U.S. capacity for generating nuclear power would reach 600 gigawatts of electricity. The generation of one gigawatt of electrical power results in 6 m^3 of high-level nuclear waste (HLW) in vitrified form, and an additional 50 m^3 of intermediate-level radioactive waste containing α emitters. Therefore, the resulting discharge from this production would result in ~15,000 metric tons of spent fuel annually. Subsequent reprocessing would bring the total waste production to 750 m^3 high level waste per year. Output from nuclear plants has, however, declined slightly each year since 1978 as shown in Figure 1.1.[9]

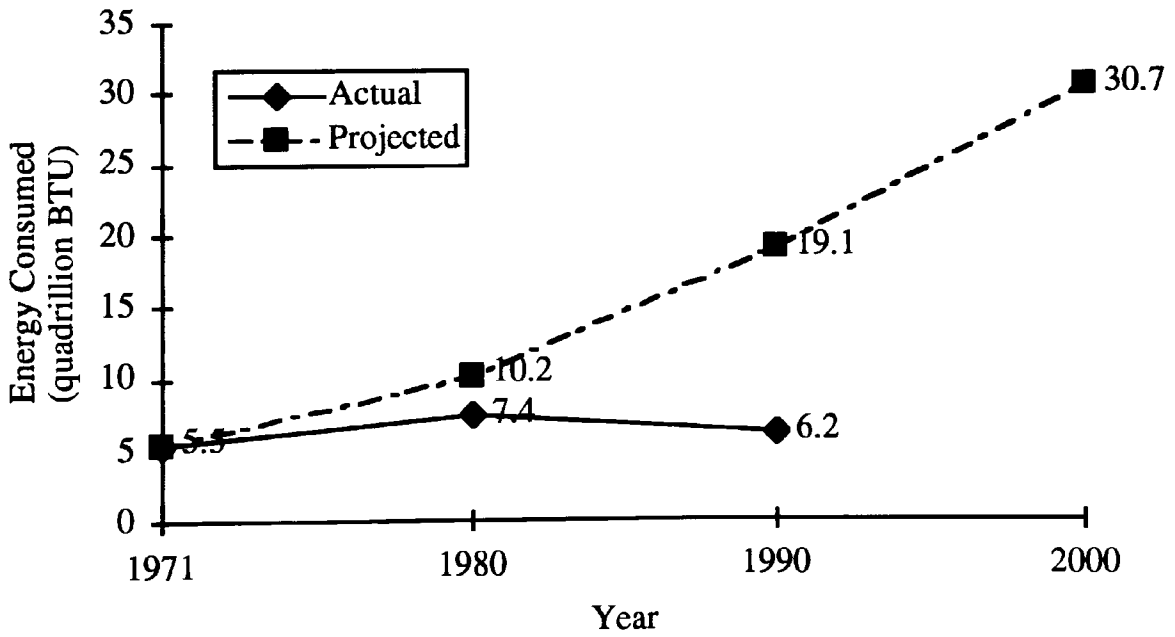


Figure 1.1.

NRC projection of U.S. nuclear energy consumption.[9,10]

The decline in the usage of atomic energy was, in part, due to a change in the public's perception of nuclear power. In the late 1970's, the general public began to have serious doubts about the safety and environmental soundness of atomic energy used for the production of electricity. These doubts were compounded by the Three Mile Island incident in 1979 which received unprecedented press coverage. In 1980, nuclear power plants only accounted for 11 percent of electrical generation in the U.S.[9] This is 18 percent lower than originally predicted by the Nuclear Regulatory Commission in 1974. Projections for 1992 were even further off.[10] Utilities turned from nuclear plants to coal plants because the nuclear plants were no longer economically feasible. Because of costs associated with the interim storage, processing and disposal of nuclear waste, the production and construction expenses for nuclear plants rose higher than those for coal plants.[9] Older reactor sites were no longer able to compete because their short-term storage pools were nearing capacity.

By 2010 the number of nuclear plants that will have exceeded their storage pool capacities is expected to increase by ~80. The amount of fuel that is beyond their capacity to store is projected to increase from ~150 metric tons currently to over 12,000 metric tons (see Figure 1.2).[11]

Congress passed the Nuclear Waste Policy Act (P.L. 97-425) in December 1982. President Ronald Reagan later signed the bill into law on January 7, 1983. The act "provided for the development of repositories for the disposal of high-level radioactive waste and spent nuclear fuel" by establishing "a program of research, development, and demonstration regarding the disposal of high-level radioactive waste and spent nuclear fuel ...."(96 Stat. 2207).[12] The act mandated that a permanent repository for high-level

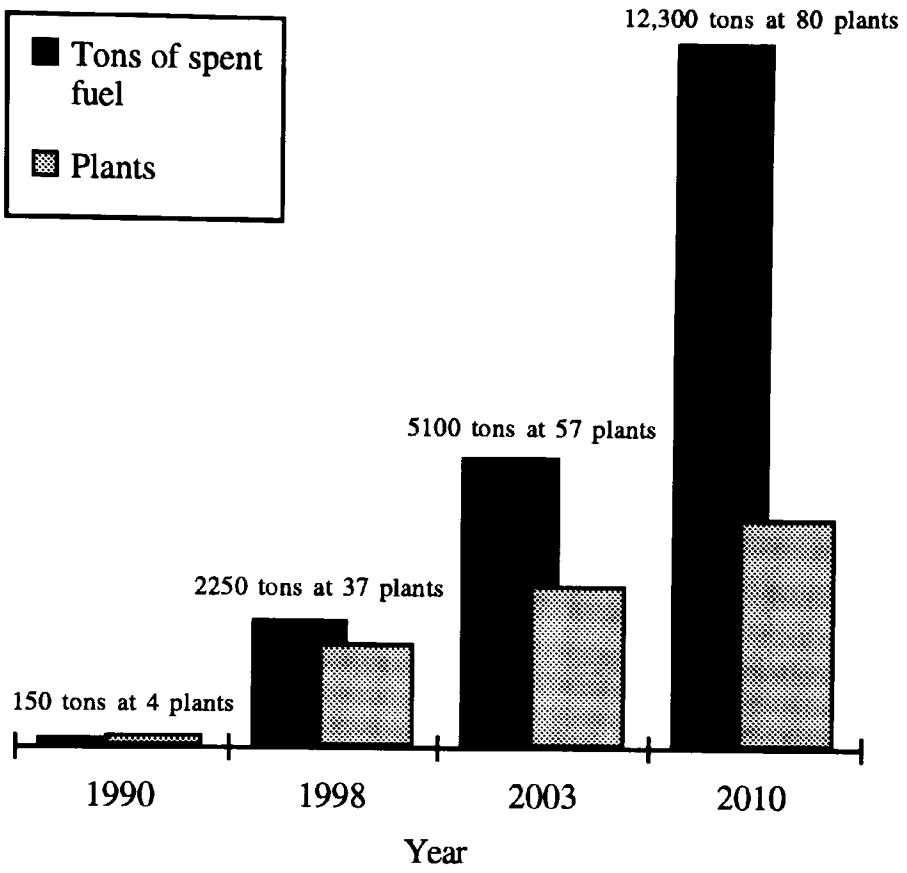


Figure 1.2.

Projected number of nuclear plants with fuel that cannot be accommodated in storage pools and corresponding waste requiring storage or processing.[11]

radioactive waste would be in operation by the year 1998. It also specified that funding for the repository would come from an energy tax (1).[12]

Since 1983, electricity customers have paid a one-tenth-of-a-cent fee on every nuclear-generated kilowatt-hour of electricity to pay for eventual waste disposal, but because of political, legal, and technical delays the opening date for a permanent,

government-operated repository will be delayed until at least 2010.[13-17] Governments in Japan, Canada, and Europe face similar problems (see Table 1.1).

1.4 Military Waste

Although, the overall amount of waste generated by commercial reactors outweighs that produced by the military, the major constituents of some military refuse are highly radioactive. Programs such as weapons and submarine-propulsion programs have produced approximately 380,000 cubic meters of high-level waste, whereas, commercial reactors have produced 8000 cubic meters, including spent fuel rods.[18] The Hanford site occupies 560 square miles of desert in southeastern Washington State. It was shut down as a production facility in 1991[19], but still contains over 1.4 billion cubic meters of hazardous or radioactive waste along with nine decommissioned nuclear reactors and the old reprocessing plants that await decommissioning. The 1,377 waste sites contained within the reservation consist of trenches, tanks, ponds, cribs, and soil burial sites. Hanford contains over one-third of the Department of Energy's waste sites, one-half of all of its transuranic waste, and two-thirds of its high-level waste.

Liquefied effluents: 11 million cubic meters.

Nuclear materials: 6900 metric tons

- 4100 metric tons are uranium
- 15 metric tons are cesium-strontium capsules
- other

Waste in storage tanks: 770,000 metric tons.

Contaminated soils and ground water: over one billion metric tons.

Total Radioactivity: 446 million Curies.

Table 1.1.

Storage of commercial spent fuel and high-level waste in nine countries.

Country	Nuclear capacity, gigawatts (proportion of electrically generated)[a]	Number of reactors[a]	Reprocessing (where)	Interim storage			Institutional responsibility[g]	Repository schedule
				Locations	Methods	Duration, yr.		
Canada	12.2 (15.6%)	18	No[b]	Reactor sites	Wet pools perhaps dry casks[d] at Pickering, Ont.	> 50	Utilities	> 2010
France	52.6 (74.6%)	55	Yes	Reactor sites	Wet pools	~ 1	EDF	> 2010
				Reprocessing plants	SF-wet pools HLW-dry vaults	~ 2 > 20	Cogéma	
West Germany	22.7 (34.3%)	24	Yes (WG, FR, UK)	Reactor sites	Wet pools	3-10	Utilities	~ 2008
				Independent facility[c] (Gorleben, Ahaus)	SF-dry casks[e] HLW-dry casks[e]	Undecided > 10	Utilities (through BLG)	
Japan	29.3 (27.8%)	39	Yes (FR, JA, UK)	Reactor sites	Wet pools[e]	2-3	Utilities	> 2030
				Reprocessing plants	SF-wet pools HLW-undecided	~ 4 30-50	Utilities (through JNFS)	
Spain	7.54 (38.4%)	10	No	Reactor sites	Wet pools	40	Utilities	~ 2020
				Independent facility (not sited)	Pools and/or dry cask[f]	40	Government corporation (Enresa)	
Sweden	9.82 (45.1%)	12	No	Reactor sites	Wet pools	~ 1	Utilities	> 2020
				Independent facility (CLAB, at Oscarshman reactor site)	Wet pools	15-40	Utilities (through SKB)	

Table 1.1.

Continued.

Country	Nuclear capacity, gigawatts (proportion of electrically generated)	Number of reactors	Reprocessing (where)	Interim storage			Institutional responsibility	Repository schedule
				Locations	Methods	Duration, yr.		
Switzerland	2.95 (21.7%)	39	Yes	Reactor sites	Wet pools	< 12	Utilities	> 2025
				Independent facility (Würenlingen)	SF, HLW-dry casks [e]	~ 40	Utilities (through Zwischenlager Gesellschaft)	
United Kingdom	11.2 (12.2%)	39	Yes	Reactor sites	Wet pools	~ 1	Utilities	> 2040
				Independent facility for AGR fuel (at Heysham reactor site)	SF-dry vault	Undecided	Utilities (joint venture)	
				Reprocessing plant	SF-wet pools HLW-dry storage	Few > 50	BNFL	
United States	98.3 (19.1%)	110	No	Reactor sites	Wet pools, dry modules	Undecided	Utilities	> 2010

KEY

AGR = advanced gas cooled reactor
BLG = subsidiary of DWK, which is owned by FRG nuclear utilities
BNFL = British Nuclear Fuels PLC
CLAB = central storage for spent fuel
Cogéma = Compagnie Générale des Matiéres Nucléaires
EDF = Electricité de France
Enresa = Empresa Nacional de Residuos Radiactivos SA
HLW = high-level wastes
JNFS = Japan Nuclear Fuel Services Company
SF = spent fuel
SKB = Svensk Kärnbränslehantering AB

[a]As of Dec. 31, 1989.
[b]No decision about future reprocessing has been made.
[c]A storage facility that does not affect the safety of a nuclear-power or fuel-reprocessing plant.
[d]Transportable storage casks are being investigated for buffer storage.
[e]Transportable storage casks have been selected for the storage facility.
[f]Transportable storage casks are under development for storage.
[g]May be private, government, or joint industry-government entities.

Wastes at the site are commingled and often contain a potpourri of organic wastes, heavy metals, fission products and transuranics. The waste burial trenches used from 1944 to 1970 contain mixtures which include solid sodium, plutonium, pyrophorics, munitions, and other wastes in close proximity to each other.[7]

1.5 High-Level Waste Reprocessing

General schemes for the reprocessing of nuclear waste at nearly every site, world-wide, have the same fundamental steps. This is mainly because they were all derived from methods developed at Savanna River, South Carolina, and other government facilities in the United States.[18] A schematic of the process used at Los Alamos National Laboratory is presented in Figure 1.3. Typically, bulk wastes, along with any packing material, are dissolved in a concentrated nitric acid solution. The highly acidic, aqueous solution is then extracted with an organic solution containing one of several organophosphorus ligands.[20-23] The organic and aqueous phases are mixed in ion exchange vessels until a pseudo-equilibrium is achieved and the organic phase is back-extracted to retrieve the uranium and plutonium.The plutonium is precipitated using oxalate and finally reduced with calcium to produce plutonium oxide.

The aqueous phase from the initial ion exchange, which contains most of the high-level waste, is heated in an evaporator. The distillate is condensed and transferred to a low-level waste site. The solids or "bottoms" are milled and either mixed with cement, as at Los Alamos, or vitrified in borosilicate glass prior to sealing in 55-gallon barrels for storage. These solids account for approximately 98 percent of the radioactivity found in the original bulk waste material.[18]

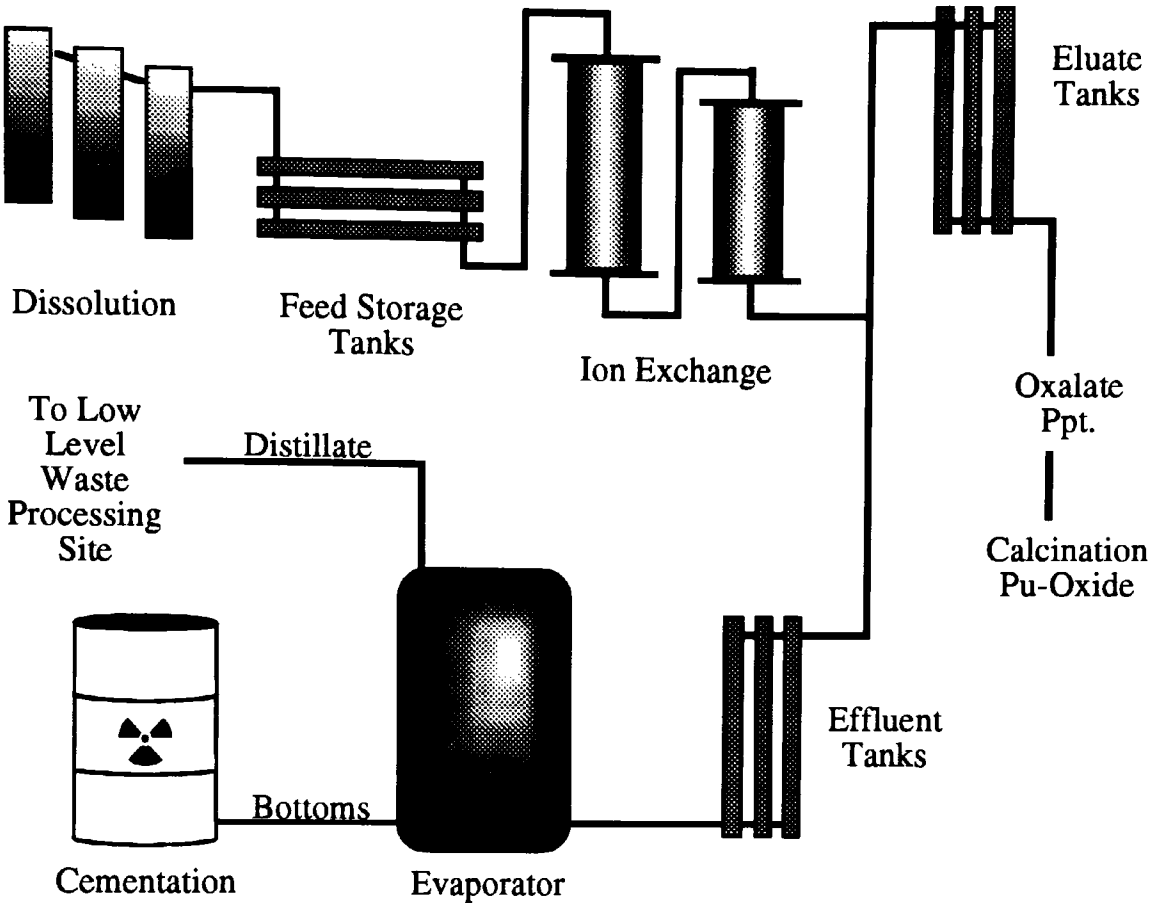


Figure 1.3.

Scheme for high level waste reprocessing at Los Alamos National Laboratory.[24]

Nuclear wastes contain substantial amounts of radioisotopes with short (less than one year), long (one to 30 years), or very long half-lives (greater than 30 years) as shown in Figures 1.4 and 1.5.[25] These highly contaminated and long-lived wastes must be isolated from the environment for tens of thousands of years. Although short on a geological time scale, this period of time is longer than the normal lifetime of any currently known human organization. It is also beyond the viability of any manmade structure built to serve as a permanent repository.

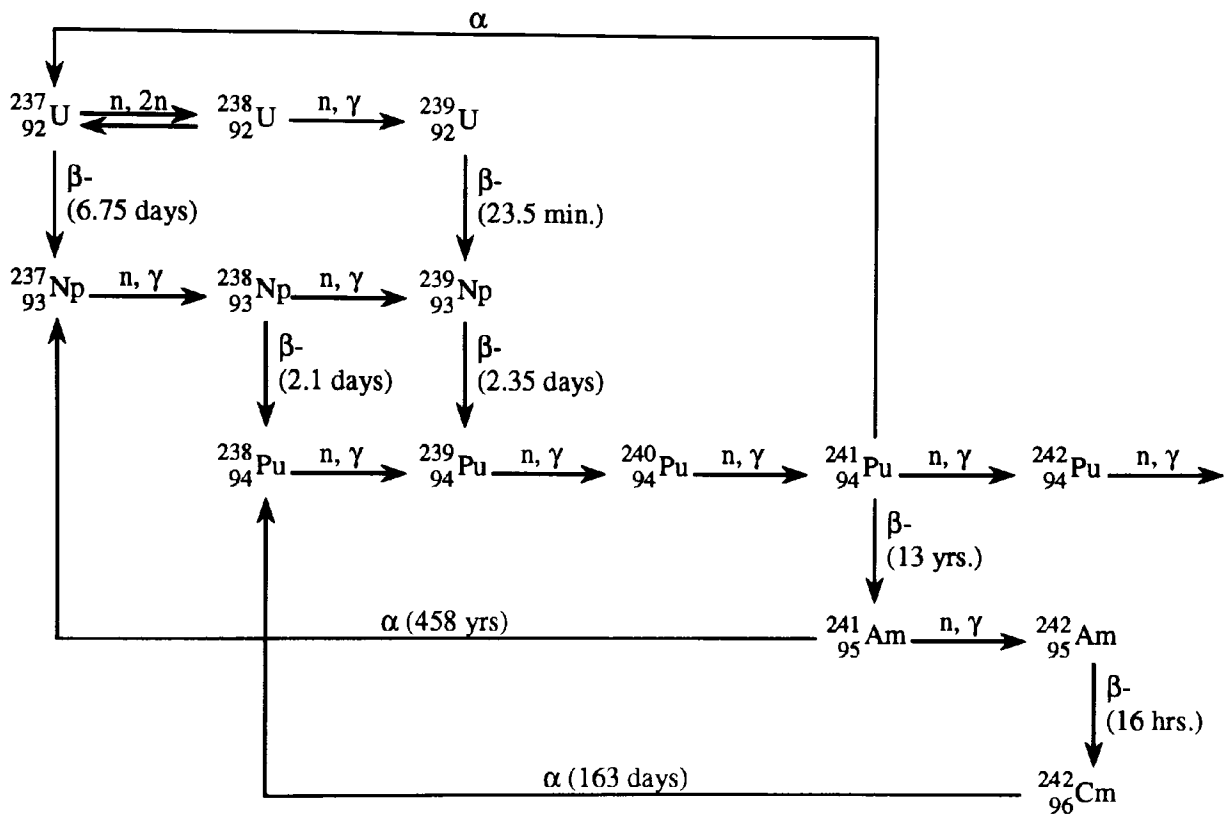


Figure 1.4.

Formation of plutonium radionuclides and daughters.[26]

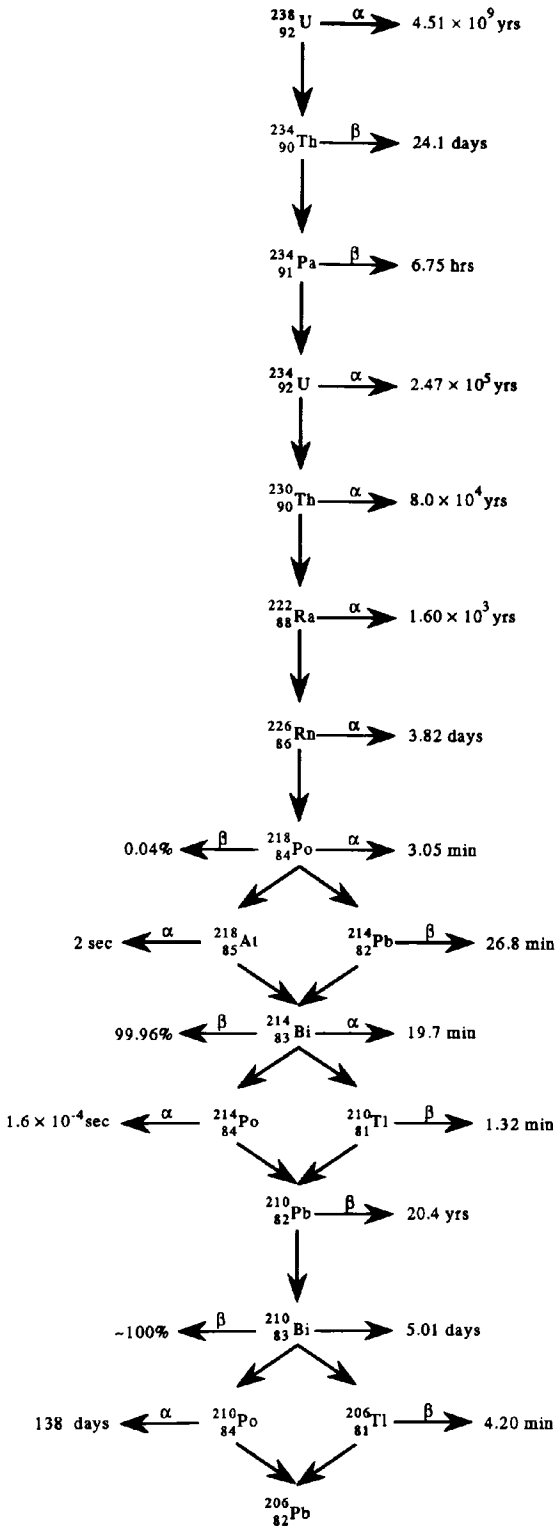
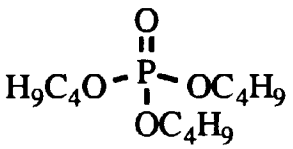


Figure 1.5.

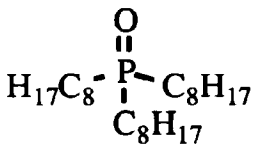
Uranium decay series.[27]

Many of the radioisotopes leftover after reprocessing are of great commercial or scientific value. Others, such as ^{237}Np, ^{241}Am, ^{234}Am, and ^{241}Cm, are excellent candidates for muon-induced fission[28], as a means of disposal, but they must be isolated from each other to facilitate processing. A cheap, efficient way to selectively extract and separate the elements of the lanthanide and actinide families is needed

The organophosphorus ligands which have previously been developed generally can be classified in one of six categories: phosphonates, phosphine oxides, diphosphine oxides, diphosphonates, carbamoylphosphonates, and carbamoylphosphine oxides. Phosphonates, such as TBP, and phosphine oxides, such as TOPO, are monodentate, neutral ligands (see Scheme 1.1).[29-32]



Tributylphosphonate
(TBP)



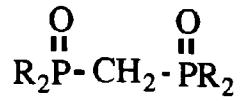
Trioctylphosphine oxide
(TOPO)

Scheme 1.1.

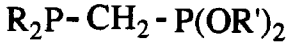
The diphosphine oxides (DPO), diphosphonates (DP), carbamoylphosphonates (CMP), and carbamoylphosphine oxides (CMPO) are all neutral bidentate ligands (see Scheme 1.2).[33-37]

TBP is the most common extractant (the PUREX process). It effectively extracts U(VI), Np(IV), and Pu(IV) from highly acidic solutions; however, it does not extract Am(III), Cm(III) or other actinides under these conditions.[30-32] The bifunctional organophosphorus extractants offer some hope, but their limited solubility in the organic diluents used in biphasal separations restrict their usefulness. CMP was found to extract

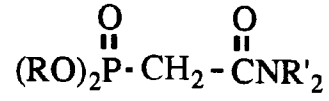
Ln(III) ions, An(III) ions, Th(IV), and U(VI) effectively from highly acidic (>2M) nitric acid solutions.[22,38-44] Substitution of alkyl or phenyl groups for the OR groups, as in



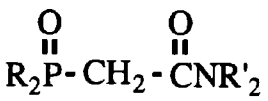
Diphosphine oxide
(DPO)



Diphosphonate
(DP)



Carbamoylphosphonate
(CMP)



Carbamoylphosphine oxide
(CMPO)

Scheme 1.2.

CMPO, was found to increase the extractant's capacity, but decreased its selectablity and solubility in the organic phase.[45,46] Carbamoylmethylphosphine oxides of the type $R(Ph)P(O)CH_2C(O)NR'_2$ were found to be the most effective extractants and led to the first implementation of the TRUEX process for the extraction of generic actinides.

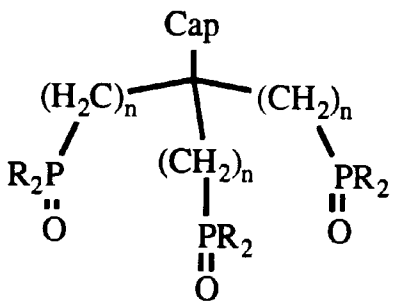
As promising and effective as these extractants are, they fail to offer the ability to selectively extract one or two Ln/An ions in a series. They also involve biphasal liquid-liquid separations which are labor intensive and require large volumes of organic solvents.

The ideal extractant should coordinate in a tridentate fashion to take maximum advantage of the chelation effect. It should also be able to separate radionuclides into small groups of like characteristics, and contain a mechanism to fine tune the ligand's chelating ability so that, preferentially, only one radionuclide is targeted at a time. The extraction process should also allow for the maximum amount of automation so that human exposure to radiation would be limited. This could be accomplished by attaching the ligand to a solid support such as polystyrene through a covalently bonded alkyl tether so that effluent flows

could be directed through a series of heterogeneous extraction columns. Attaching the ligand to a solid support would eliminate the need for the tedious and expensive back-extractions involved in biphasal liquid-liquid separations.

1.6 The Solution

In an attempt to provide a new series of ligands to meet the above criteria (based on derivative chemistry), a series of tripodal, triphosphine oxides with the structure, as depicted in Scheme 1.3, have been developed.



Scheme 1.3.

The ligands are tridentate to allow for coordination with lanthanides and actinides. The length of the legs can also be varied so that the ligand's bite-size can be changed to match to the size of the species being extracted. Ligands can be attached to a solid support by substituting an organic tether group in place of the cap. It is hoped that by using tripods of increasing bite-size in series, it will be possible to obtain effective separation of cations on the basis of size (see Figure 1.6). Analogs were synthesized with n values of one, two, and three corresponding to methyl, ethyl, and propyl legs, respectively. Lanthanide and actinide cations are characteristically hard acids; however, they do vary slightly with respect to hardness and softness. By substituting either electron-withdrawing or electron-donating

CHAPTER II

PROTOTYPE ONE:

1,1,1-TRIS(DIPHENYLPHOSPHORYLMETHYL)ETHANE

2.1 Introduction

The first tripodal triphosphine oxide in the proposed synthetic series is 1,1,1-tris(diphenylphosphorylmethyl)ethane. Hewertson and Watson first synthesized 1,1,1-Tris(diphenylphosphorylmethyl)ethane in 1962.[47] In the preparation they reacted 1,1,1-tris(hydroxy-methyl)ethane with thionyl chloride or phosphorus tribromide to generate the corresponding trichloro- or tribromo-tripod, respectively (see Scheme 2.1).

$$CH_3C(CH_2OH)_3 + 3\,SOCl_2 \xrightarrow[[N_2]]{0°C,\ pyridine} \xrightarrow[50°C]{oil\ bath} CH_3C(CH_2Cl)_3$$

$$CH_3C(CH_2OH)_3 + PBr_3 \xrightarrow[[N_2]]{170°C} CH_3C(CH_2Br)_3$$

Scheme 2.1.

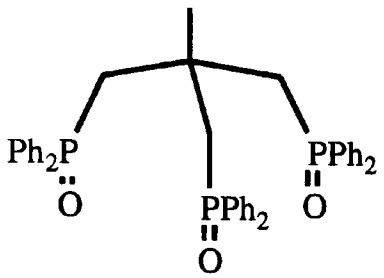
The resulting halogenated compound was then reacted with lithium diphenylphosphide to produce the tripod triphosphine, compound **1** in Scheme 2.2.

$$CH_3C(CH_2X)_3 + 3\,LiPPh_2 \xrightarrow{[N_2]} \underset{\mathbf{1}}{CH_3C(CH_2PPh_2)_3} + 3\,LiX$$

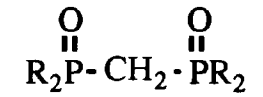
Scheme 2.2.

Compound **1**, known commercially as triphos, is now readily available and has become one of today's most popular tridentate ligands for the chelation of transition metals. This is revealed in Cotton and Hong's recent review of polydentate phosphines.[48] Very little

research has been reported with regards to the chelating ability of 1,1,1-tris(diphenyl-phosphorylmethyl)ethane. Phosphine oxides are typically hard bases and are, therefore, poor choices for the chelation of transition metals. Oxides, however, are a good choice for the chelation of the transuranics (refer to Section 1.5). The compound, 1,1,1-Tris(diphenylphosphoryl-methyl)ethane, shows remarkable similarities to other phosphine oxides currently in use as extractants (Scheme 2.3).



1,1,1-Tris(diphenylphosphorylmethyl)ethane



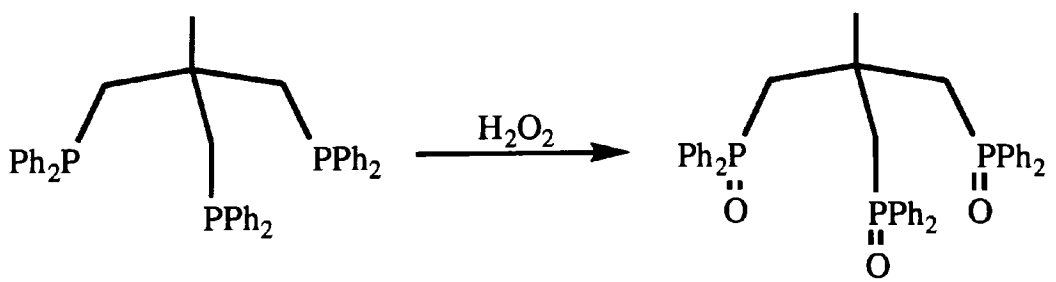
Diphosphine oxide
(DPO)

Scheme 2.3.

The fact that it would chelate in a tridentate fashion instead of in a bidentate fashion should only enhance its chelating ability.

2.2 Results

Triphos, compound **1**, was oxidized in an aqueous solution of hydrogen peroxide to produce 1,1,1-tris(diphenylphosphorylmethyl)ethane, compound **2**, in near quantitative yield (Scheme 2.4).



1 **2**

Scheme 2.4.

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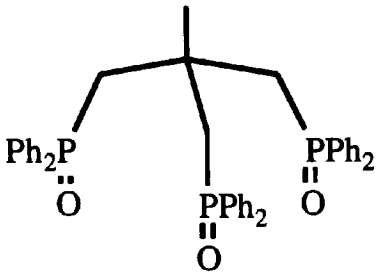
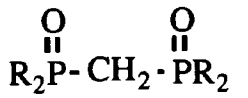


1,1,1-Tris(diphenylphosphorylmethyl)ethane



Diphosphine oxide
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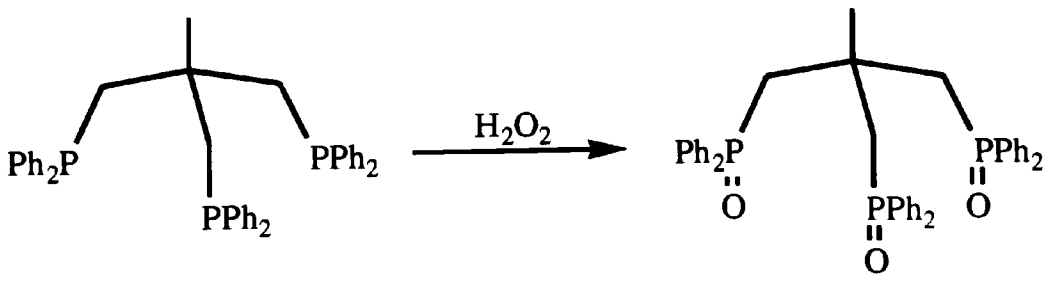


1 **2**

Scheme 2.4.

Samples of **2** were then submitted to Los Alamos National Laboratory for testing. Surprisingly the ligand was not found to effectively chelate any of the trivalent actinides or lanthanides, even at significant concentration levels (3 M ligand). This was a very unexpected result, because bis(diphenylphosphoryl)methane has been found to be very effective at coordinating lanthanide and actinide ions under similar conditions.

2.3 Discussion

Computer simulations of compound **2** both at Texas Tech and at Los Alamos suggested that the cause for the lack of coordination of compound **2** was steric in nature.[49] It was felt that the bite-size of the ligand was too small to provide optimum binding conditions, because the legs of the ligand were too short to wrap around the metal ion.

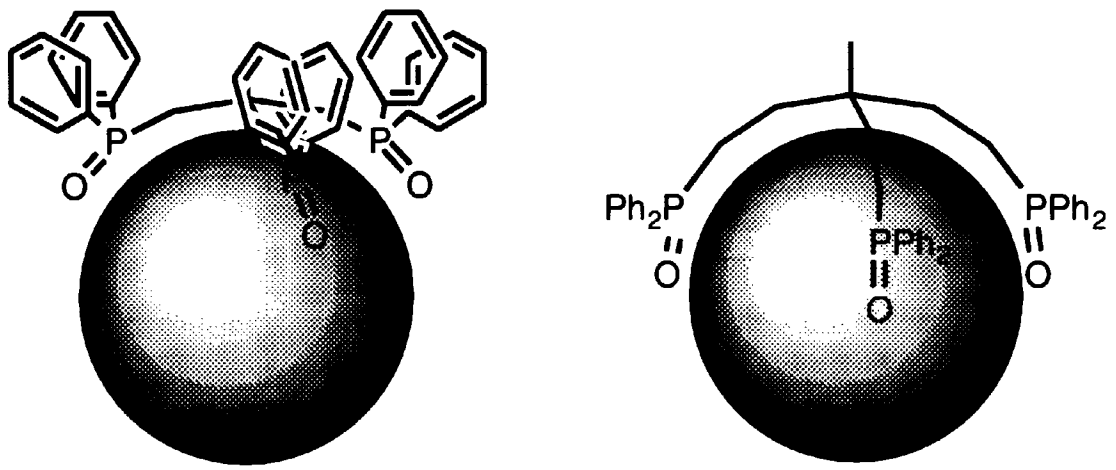
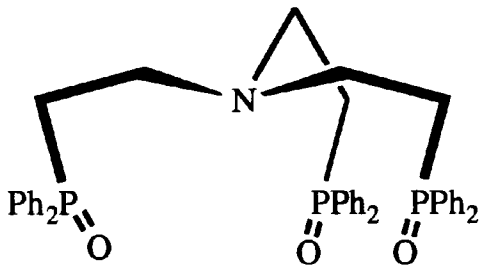


Figure 2.1.

Depiction of bite-size for (a) 1,1,1-tris(diphenylphosphorylmethyl)ethane and (b) 1,1,1-tris-(diphenylphosphorylethyl)ethane.

Similar studies with 1,1,1-tris-(diphenylphosphorylethyl)ethane, the next prototype in the synthetic series, indicated that it should be able to effectively coordinate to the metal ion (see Figure 2.1).

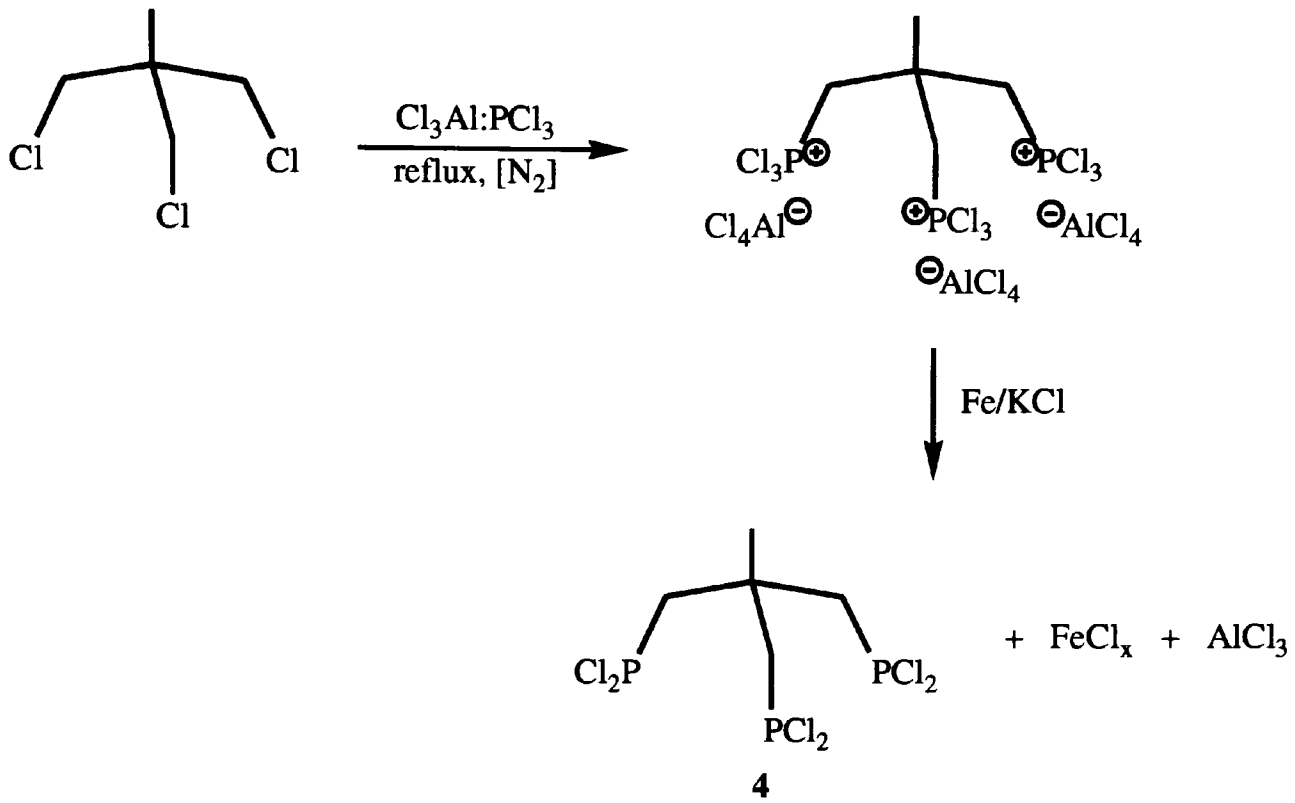
The amine analog to 1,1,1-tris(diphenylphosphorylethyl)ethane, tris(diphenyl-phosphorylethyl)amine (Scheme 2.5) was synthesized at Los Alamos and performed well in extraction studies; however, the substitution of nitrogen for carbon at the apical position presented new synthetic challenges with respect to attachment to a solid support.



3

Scheme 2.5.

In an attempt to develop a method for the attachment of different R groups to the phosphorus of compound **1**, a synthetic route employing the substitution of dichlorophosphinogroups was attempted, as depicted in Scheme 2.6.[50]
The desired product could then be reacted with any of a series of lithioalkyl salts, where R=Me, Et, or Bu (see Scheme 2.7). The trisubstituted product, **4**, however, was never observed. Only mono- and di-substituted products resulted. This was presumably due to a build-up of positive charge on the intermediate in Scheme 2.6. The synthesis was abandoned after compound **2** was found to be ineffective as a chelating reagent for lanthanide and actinide ions.



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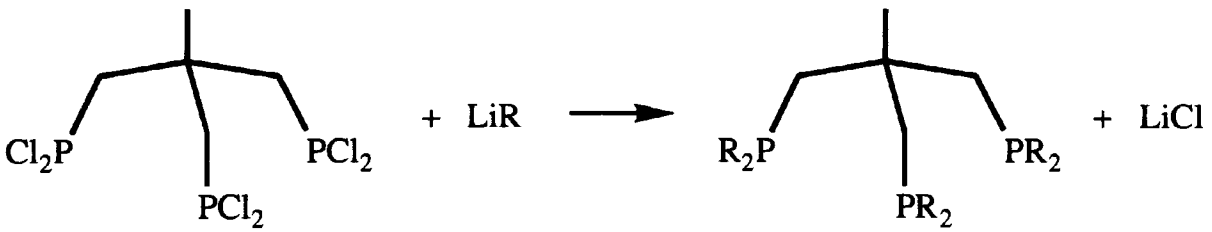
Scheme 2.6.



Scheme 2.7.

2.4 Experimental Procedure

2.4.1 General Methods

All reactions involving air sensitive compounds were carried out under inert atmospheres using standard Schlenk line techniques or under argon in a dry box. Glassware was dried in an oven at 130°C and then dried under vacuum before use. Unless otherwise noted, all commercially available starting materials were used as received. Tetrahydrofuran (THF) and diethyl ether (ether) were distilled under nitrogen from a dark

blue solution containing the sodium ketyl of benzophenone immediately before use. Quinoline and pyridine were distilled under nitrogen prior to use. Benzene was distilled from P_2O_5, and stored over molecular sieves (4 Å). Dichloromethane was distilled from CaH and stored under nitrogen. The literature method[51] was used to prepare 1,1,1-tris(chloromethyl)ethane and 1,1,1-tris(bromomethyl)ethane. Nitrogen gas was provided by Big Three Industries and was passed through a chromic oxide drying column prior to use.

NMR spectra were obtained on either an IBM AF-200 (200 MHz for proton, 50 MHz for carbon) or an IBM AF-300 (300 MHz for proton, 75 MHz for carbon, 121 MHz for phosphorus) instrument. Unless otherwise noted, all spectra were obtained in deutereochloroform ($CDCl_3$) solvent, with ether residual chloroform or tetramethylsilane (TMS) as an internal reference. Spectra are reported as follows: peak position (δ) (number of protons, multiplicity, coupling constant[s]). The peak position (δ) is in parts per million (ppm). The coupling constant (J) is in Hertz (Hz).

Infrared (IR) spectra were measured on a Perkin Elmer 1600 series FT-IR. Liquid samples were neat samples or concentrated chloroform solutions between KBr plates.

Elemental analysis were performed by Desert Analytics of Tucson, Arizona. High Resolution mass spectral analysis were performed by the Midwest Center for Mass Spectrometry, Lincoln, Nebraska.

2.4.1 Starting Materials

The compound, 1,1,1-Tris(diphenylphosphinomethyl)ethane was purchased from Strem Chemical Company and used without further purification. Aluminum chloride was purchased from Fisher Scientific Company, and was sublimed prior to use.

2.4.2 Preparation of $CH_3C(CH_2P(O)Ph_2)_3$, (**2**)

Compound **1** (1.013 g, 1.621 mmol) was placed in round bottom flask along with a magnetic stirbar. Methylene chloride (~100 mL) was added to the flask as solvent and stirring was initiated. An aqueous solution of hydrogen peroxide(mL of 3% H_2O_2: mol) was added dropwise to the solution. A white precipitate was observed to form. The precipitate was filtered from the solution and washed with diethyl ether. The white solid was then dried with gentle heating under reduced pressure.

$$C^aH_3C^b(C^cH_2P(O)Ph^{d\text{-}g}{}_2)_3$$

^1H (300 MHz, $CDCl_3$): H^a(δ0.88, 3H, s); H^c(δ3.16, 6H, d); $H^{e,f}$(δ7.39, 24H, m); H^g(δ7.75, 6H, m).

^{13}C (75 MHz, $CDCl_3$): C^a(δ28.7); C^b(δ39.2); C^c(δ40.6, J_{PC}=69.4 Hz); C^d(δ134.7, J_{PC}=98.1 Hz); C^e(δ128.6, $J_{PC}{}^2$=11.7 Hz); C^f(δ130.5, $J_{PC}{}^3$=9.4 Hz); C^g(δ131.3).

^{31}P (121 MHz, $CDCl_3$): P(δ29.78) with an external H_3PO_4 standard.

2.4.3 Extraction studies of $CH_3C(CH_2P(O)Ph_2)_3$, (**2**), and $N(CH_2CH_2P(O)Ph_2)_3$, (**3**)

(All extraction studies were done at Los Alamos National Laboratory by B.F. Smith, M.M. Jones, G.D. Jarvinen.) The solutions of the extractant ligands were prepared by dissolving weighed samples in reagent grade chloroform or toluene. The aqueous phases were prepared using $NaNO_3$ to control the ionic strength at 0.1 and sulfanilic acid as a buffer at 0.01 M when necessary. Nitric acid was used to adjust the acidity. The aqueous solutions were spiked with the appropriate tracers. All chemicals used were reagent grade or better.

The distribution coefficients, D, of the metal ions are defined as the $[M]_{org}/[M]_{aq}$. The distribution studies of Eu(III) and Am(III) were performed using carrier-free

radioisotopes (~10^8 M) ^{152}Eu and ^{241}Am (New England Nuclear). A batch equilibrium method was used to obtain the distribution data. Duplicate extractions were performed with equal volumes of pre-equilibrated aqueous and organic phases that were contacted at room temperature (22-24°C) by using a mechanical shaker for 30 minutes or a vortex mixer for 15 minutes. The samples were then centrifuged and 1 mL aliquots were taken from each phase for gamma counting. The pH of the aqueous phase was determined after extraction if necessary. The use of sulfanilic acid under these conditions does not require correction for metal binding in the aqueous phase.[49]

2.4.4 Attempted preparation of $CH_3C(CH_2PCl_2)_3$[50], (**4**)

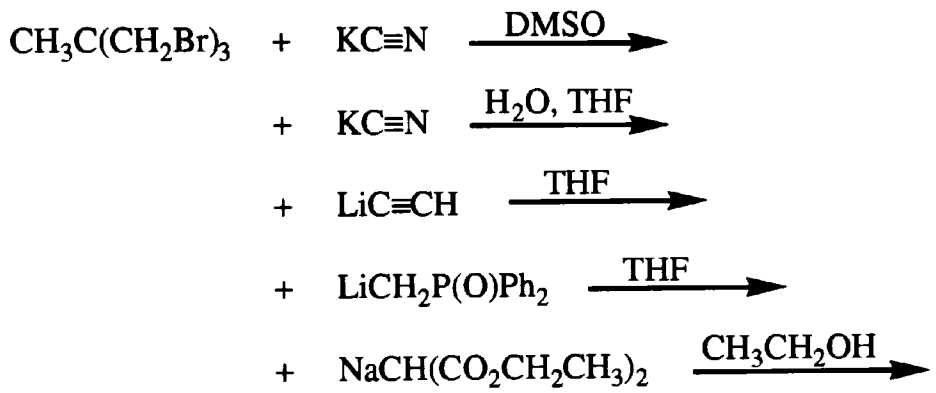
A Schlenk flask was dried in the oven and flushed with nitrogen. A magnetic stirbar, PCl_3 (12.4 mL, 85.5 mmol), and anhydrous $AlCl_3$ (11.4 g, 85.5 mmol) were added to the flask under flow of nitrogen. The mixture was heated at 75°C until an adduct was observed to form (~35 minutes). The reaction pot was lowered into an ice bath and 1,1,1-tris(chloromethyl)ethane (4.09 mL, 28.5 mmol) was added to the flask via syringe. A gray sludge began to form in the bottom of the flask which became liquid enough for the stirrer to spin after approximately 5 minutes. The mixture was removed from the ice bath and heated for three days. The flask contained a black solid. Iron powder (1.591 g, 28.5 mmol) and dry KCl (2.124 g, 28.5 mmol) were mixed together and added to the flask. The flask was warmed with a heating mantle until the black mass began to boil. The mixture was refluxed for 12 hours. ^{31}P NMR revealed that only partial substitution had taken place. Evidence was found for $CH_3C(CH_2PCl_2)(CH_2Cl)_2$ and $CH_3C(CH_2PCl_2)_2(CH_2Cl)$. Evidence for the trisubstituted species was not found.

CHAPTER III

HOMOLOGATION REACTIONS

3.1 Introduction

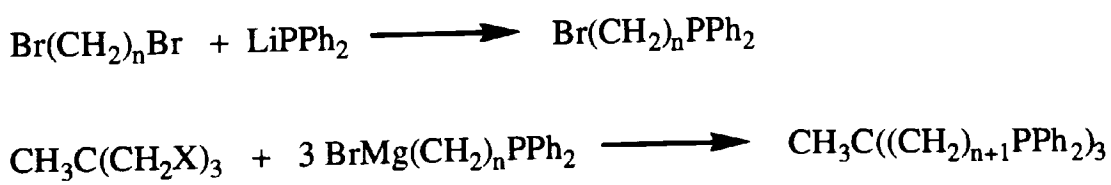
Upon first inspection of the compound, 1,1,1-Tris(diphenylphosphorylmethyl)-ethane, it would seem that the easiest route to lengthening the tripodal legs would be a simple homologation reaction. Several reactions were tried including:



Scheme 3.1.

However, none were successful.

An attempt was also made to synthesize the legs of the tripod first and then attach them to a preexisting backbone via a Grignard reaction, Scheme 3.2. The legs were synthesized, but were never attached (parallel studies indicated that their attachment was



where n = 2,3 or 4

Scheme 3.2.

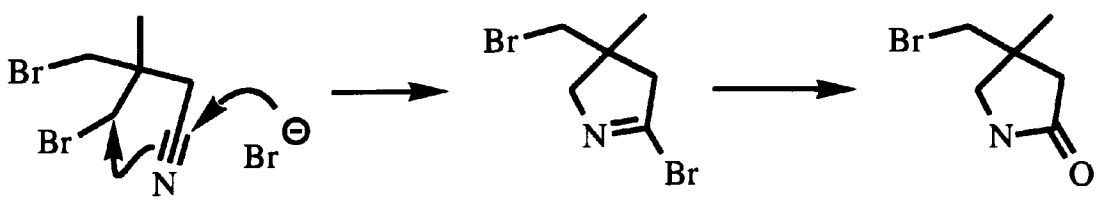
prevented by a build-up of positive charge at the apical carbon of the proposed neopentyl center). The synthesis of the precursor halofunctionalized alkylphosphines may, however, prove to be of interest to other investigators, since these were previously undescribed compounds.

3.2 Results and Discussion

As alluded to in the introduction, several attempts were made toward the direct cyanation of 1,1,1-tris(bromomethyl)ethane. Permutations of the experimental procedure included: time, temperature, and the addition of a phase transfer catalyst. Under mild conditions, only partial substitution, on one leg of the tribromo tripod took place (see Scheme 3.3). Under more harsh conditions (extended time, and heating) a side reaction

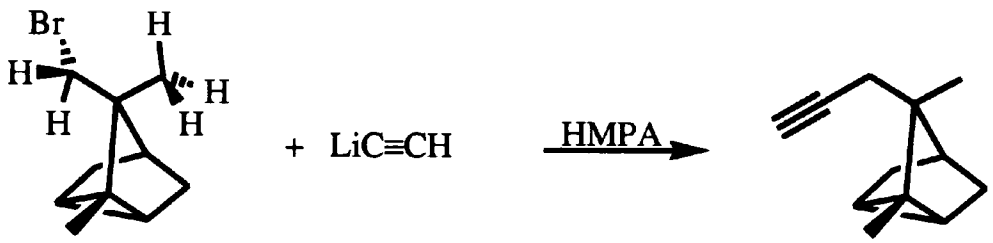
Scheme 3.3.

took place producing several cyclic by-products, as indicated by ^{1}H NMR. A suggested mechanism for the major side reaction is shown in Scheme 3.4.



Scheme 3.4.

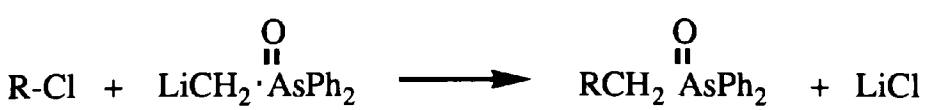
Lewis, Gustafson, and Erman reported in 1967 that they were able to overcome the neopentyl effect by reacting lithium acetylide-ethylenediamine complex with a bromo substituted, bicyclic precursor to seqcis-α-santalol (derivable from sandalwood oil) in either DMSO or HMPA. Although displacement of the bromide ion was anticipated to be difficult, rapid displacement to give the desired product was readily achieved (see Scheme 3.5).[52]



Scheme 3.5.

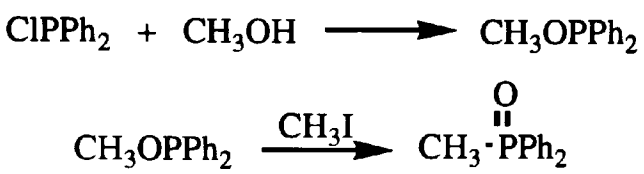
Attempts to parallel their work substituting 1,1,1-tris(bromomethyl)ethane for the bicyclo compound were not effective. Analysis by ^1H NMR revealed that no reaction took place.

A more direct approach to the synthesis of 1,1,1-tris(diphenylphosphorylethyl)-ethane would be to couple the nucleophilic species with the trihalogenated tripod via a second order substitution (S_N2) reaction. Kauffmann, et al., reported the coupling of lithiomethyldiphenylarsine oxide with a series of haloalkanes (see Scheme 3.6).[53] Since phosphorus is a member of the same periodic group as arsenic, it was hoped that an analogous reaction would occur.



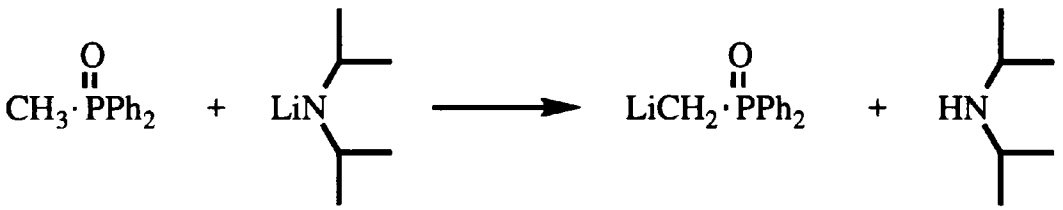
Scheme 3.6.

Methyldiphenylphosphine oxide was prepared by the Arbuzov method (see Scheme 3.7).[54] Chlorodiphenylphosphine was reacted with methanol to yield methoxy-



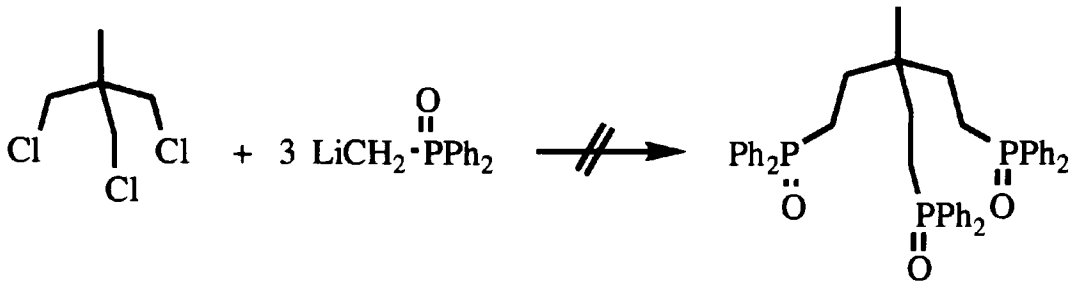
Scheme 3.7.

(diphenyl)phosphine. Methoxy(diphenyl)phosphine then undergoes a rearrangement reaction in the presence of methyl iodide to form the corresponding oxide. Methyldiphenylphosphine oxide is then reacted with lithium diisopropyl amine to produce lithiomethyldiphenylphosphine oxide as shown in Scheme 3.8.



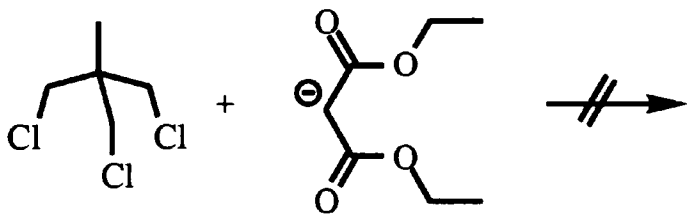
Scheme 3.8.

The formation of lithiomethyldiphenylphosphine oxide was confirmed by reacting the lithium salt with both deuterium oxide and methyl iodide to form deteriomethyl-diphenylphosphine oxide and ethyldiphenylphosphine oxide, respectively. Reaction of lithiomethyldiphenylphosphine oxide with 1,1,1-tris(chloromethyl)ethane, however, did not produce the desired product (see Scheme 3.9). Annalysis by ^{1}H NMR revealed that only mono-substitution occured. It appears that the methyldiphenyl-phosphine oxide anion is too hard to react with the neopentyl center of the trichloro tripod.



Scheme 3.9.

To see whether the trihalo tripod would react with a softer nucleophile, 1,1,1-tris(chloromethyl)ethane was reacted with the sodium salt of diethylmalonate (see Scheme 3.10). Again there was no reaction. Homologation was therefore abandoned as a means of synthesizing further prototypes in the extraction series.



Scheme 3.10.

3.3 Experimental Procedure

3.3.1 Starting Materials

Literature method[51] was used to prepare 1,1,1-tris(tribromomethyl)ethane and 1,1,1-tris(trichloromethyl)ethane. All other materials were purchased from Aldrich Chemical Company and were used without further purification.

3.3.2 First attempted preparation of $CH_3C(CH_2C{\equiv}N)_3$, (**5**)

potassium cyanide (2.397 g, 36.81 mmol) was added to an Erlenmeyer flask along with 1,1,1-Tris(tribromomethyl)ethane (3.430 g, 11.11 mmol), and DMSO (~30 mL),

with stirring. The potassium cyanide did not go into solution. The mixture was stirred overnight at room temperature. The solution darkened in color slightly, but remained clear, with the potassium cyanide undisolved. Heating at 65 - 70°C for 22 hours only caused the solution to become slightly darker. The mixture was washed into a separatory funnel with water and extracted with three separate aliquots of diethyl ether. The ether extracts were combined and washed with water until the aqueous wash tested neutral to pH paper. The solvent was removed on the rotary evaporator. ^{1}H NMR, mass spectometry, and IR revealed the product of substitution on one leg of the tripod.

$$C^qH_3C^r(C^sH_2C^t{\equiv}N)(C^uH_2Br)_2$$

^{1}H (200 MHz, $CDCl_3$): H^q(δ1.29, 3H, s); H^r(δ3.63, 6H, s); H^q(δ1.36, 2H, s); H^u(δ3.66, 2H, s); H^t(δ3.66, 2H, s).

3.3.3 Second attempted preparation of $CH_3C(CH_2C{\equiv}N)_3$, (**5**).

Phase transfer catalysts trials 1 - 4:

trial 1 $CH_3C(CH_2Br)_3$ + KCN $\xrightarrow[(C_4H_9)_4NBr]{\text{benzene/}H_2O}$

trial 2 $CH_3C(CH_2Br)_3$ + KCN $\xrightarrow[(C_6H_5CH_2)(CH_3)_3NBr]{\text{benzene/}H_2O}$

trial 3 $CH_3C(CH_2Cl)_3$ + KCN $\xrightarrow[(C_4H_9)_4NBr]{\text{benzene/}H_2O}$

trial 4 $CH_3C(CH_2Cl)_3$ + KCN $\xrightarrow[(C_6H_5CH_2)(CH_3)_3NBr]{\text{benzene/}H_2O}$

Scheme 3.11.

Table 3.1

Reaction conditions for the second attempted preparation of $CH_3C(CH_2C{\equiv}N)_3$, (**5**).

Trial number	Tripod mass (g)/ mmol	KCN mass (g)/ mmol	Duration of Reaction (hours)
1	3.179 / 10.29	9.60 / 147	24
2	~ 3 / ~ 10	9.60 / 147	24
3	2.522 / 14.37	9.60 / 147	24
4	2.310 / 13.16	9.60 / 147	24

In each trial the trihalogenated tripod and potassium cyanide (as indicated in Table 3.1) were added to an Erlenmeyer flask along with 30 mL of benzene and 30 mL of water. The phase transfer catalyst (~ 1 g), as indicated in Scheme 3.11, was added to each flask. The flasks were sealed with parafilm and stirred for 24 hours. Samples were taken of both the aqueous and organic phases for NMR analysis. Spectra from ^1H NMR revealed that no reaction had taken place in any of the trials. Only starting material was recovered.

3.3.4 Attempted preparation of $CH_3C(CH_2C{\equiv}CH)_3$, (**6**)

Freshly distilled, dry THF (~75 mL) was added to a Schlenk flask along with 1,1,1-Tris(tribromomethyl)ethane (5.405 g, 17.50 mmol). The flask was lowered into an ice bath and stirring was initiated. After the flask was allowed to cool, lithium acetylide diamine (1.710 g, 18.57 mmol) was added to the solution. The lithium acetylide diamine complex was not soluble in the solution and no reaction was observed. The ice bath was removed and the rest of the lithium acetylide diamine complex (3.124 g, 33.93 mmol; for a total of 4.833 g, 52.49 mmol) was added to the solution. The flask was sealed with a rubber stopper (still open to the nitrogen line/Hg bubbler). By the following morning, all

of the lithium acetylide diamine complex had gone into solution. There was only a small amount of black-brown precipitate in the bottom of the flask. The flask was cooled in an ice bath and small slivers of ice were added to the solution until bubbling ceased. The solution was diluted with water and extracted twice with diethyl ether. The ether fractions were combined and dried over $MgSO_4$, solvent was removed on the rotary evaporator. ^1H NMR analysis revealed that no reaction had taken place.

3.3.5 Preparation of $CH_3P(O)Ph_2$, (7)

Methyldiphenylphosphine (10 mL) was poured into an open beaker. Water (50 mL), diethyl ether (30 mL) and a magnetic stirbar were added to the beaker. Stirring was initiated. Hydrogen peroxide (~5 mL of 30%) was added to the flask dropwise. The clear yellow solution slowly changed to cloudy and white. The mixture was washed into a separatory funnel with water and extracted twice with diethyl ether. The ether phases were then combined, dried over $MgSO_4$, and filtered. The solvent was removed on a rotary evaporator at 40°C. The phosphine oxide was observed as a powdery white solid.

$$C^aH_3P(O)Ph^{b\text{-}e}{}_2$$

^1H (300 MHz, $CDCl_3$): H^a(δ2.00, 3H, d; $^2J_{PH}$=13.1 Hz); $H^{b\text{-}e}$(δ3.63, 10H, m).

^{13}C (75 MHz, $CDCl_3$): C^a(δ16.6, $^1J_{PC}$=74 Hz); C^b(δ135, $^1J_{PC}$=168 Hz); C^c(δ131); C^d(δ130); C^e(δ124).

^{31}P (121 MHz, THF): P(δ29.5) with an external H_3PO_4 standard.

Alternatively, methyldiphenylphosphine oxide was produced by Arbuzov's original method[54] when reserves of methyldiphenyl phosphide were exausted. Arbuzov's

preparation resulted in high yields of the oxide (**7**) with only a small amount of methyl iodide as an impurity.

3.3.6 Preparation of $DCH_2P(O)Ph_2$, (**8**)

Dry, freshly distilled THF (~75 mL) and methyldiphenylphosphine oxide (0.084 g, 0.39 mmol) were added to the Schlenk flask along with constant stirring. Lithium diisopropyl amide (0.19 mL of 2.0 M LDA in heptane/THF/ethyl benzene, 0.39 mmol) was added to the solution via syringe. The solution quickly changed color to deep yellow-orange. Deuterium oxide (1 mL) was injected into the flask. The solution changed to light yellow. Solvent was removed on the rotary evaporator.

$$DC^{a}H_2P(O)Ph^{b\text{-}e}{}_2$$

^1H (200 MHz, $CDCl_3$): H^a(δ2.00, 3H, d; $^2J_{PH}$=13.1 Hz); $H^{b\text{-}e}$(δ3.63, 10H, m).

3.3.7 Attempted preparation of $CH_3C(CH_2CH_2P(O)Ph_2)_3$[53], (**9**)

A methyldiphenylphosphine oxide (0.623 g, 2.88 mmol) was added to a Schlenk flask. The flask was sealed with a rubber septum and dry freshly distilled THF (~100 mL) was added via canula. Stirring was initiated and lithium diisopropyl amide (1.5 mL of 2.0 M LDA in heptane/THF/ethyl benzene, 3.0 mmol) was injected into the flask. The solution became light yellow and all of the methyldiphenylphosphine oxide dissolved. Upon addition of 1,1,1-tris(chloromethyl)ethane the solution changed to orange-red. The flask was sealed and left to react overnight. Two layers resulted from the addition of water (~200 mL) to the solution, an upper brown layer and a lower yellow layer. After the usual workup, the ^1H NMR spectrum revealed only partial substitution on one leg of the tripod.

3.3.8 Attempted preparation of $CH_3C[CH_2CH(CO_2CH_2CH_3)_2]_3$, (**10**)

$NaCH(CO_2CH_2CH_3)_2$ was generated by adding diethyl malonate (3.396 g, 21.22 mmol) to a flask containing sodium ethoxide solution (296.8 mL of a 0.0900 M solution, 24.3 mmol) and a magnetic stirbar. 1,1,1-Tris(tribromomethyl)ethane (4.621 g, 16.46 mmol) was added to the flask. The flask was topped with a $CaCl_2$ drying tube and left to react overnight. The solution has changed from brown to clear, with substatial NaCl precipitate. The ethanol was removed on the rotary evaporator. The residue was diluted to 500 mL with water and transferred into a separatory funnel. The solution was acidified with 5% HCl (pH 2) and extracted twice with diethyl ether, followed by a 5% $NaHCO_3$ wash and three water washes. The solution was dried over $MgSO_4$ and filtered. Solvent was removed on the rotary evaporator. ^1H and ^{13}C NMR analysis revealed that no reaction had taken place.

3.3.9 Preparation of $NaPPh_2$, (**13**)

Dry THF (250 mL) was transferred into a Schlenk flask equipped with N_2 and a magnetic stirbar. Sodium metal (4.88 g; 0.212 mol) was added to the THF with N_2 flowing over the solution. The $ClPPh_2$ (31.8 mL; 0.177 mol) was added via syringe. The clear colorless solution turned reddish-orange after 24 hours. Analysis of the solution by ^{31}P NMR revealed the formation of compound (**13**).

^{31}P (121 MHz, THF): P(δ-20.9) with an external H_3PO_4 standard.

3.3.10 Preparation of $Ph_2PCH_2CH_2CH_2Cl$, (**14**)

A Schlenk flask was sealed with a rubber and septum and 1-Bromo-3-chloro-propane (110.2 mL, 1.114 mol) was added via syringe. Dry, freshly distilled THF (~50 mL) was transferred into the flask via canula with stirring. The reaction flask was lowered

into a dry ice/acetone bath and cooled to -78°C. A solution of sodium diphenylphosphide (100 mL of a 0.668 M solution in THF, 0.0668 mol) (**13**) was injected dropwise via syringe. After addition was complete, the dry ice bath was removed and the solution warmed to room temperature. The solution was left to react overnight. Analysis of the solution by ^{31}P NMR revealed the formation of compound **14**.

^{31}P (121 MHz, THF): P(δ-16.7) with an external H_3PO_4 standard.

3.4.11 Preparation of $Ph_2PCH_2CH_2CH_2Br$, (**15**)

A Schlenk flask was sealed with a rubber and septum and 1,3-Dibromopropane (3.89 mL, 38.2 mmol) was added via syringe. Dry, freshly distilled THF (~50 mL) was transferred into the flask via canula with stirring. The reaction flask was lowered into a dry ice/acetone bath and cooled to -78°C. A solution of sodium diphenylphosphide (10.0 mL of a 0.0764 M solution in THF, 7.64 mmol) (**13**) was injected dropwise via syringe. After addition was complete, the dry ice bath was removed and the solution warmed to room temperature. The solution was left to react overnight. Analysis of the solution by ^{31}P NMR revealed the formation of compound **15**.

^{31}P (121 MHz, THF): P(δ-17.5) with an external H_3PO_4 standard.

3.3.12 Preparation of $Ph_2PCH_2CH_2CH_3$, (**16**)

A Schlenk flask was dried in the oven and flushed with nitrogen. Bromopropane (6.94 mL, 76.4 mmol) was added to the flask along with a magnetic stirbar. The flask was sealed with a rubber septum and stirring was initiated. Dry, freshly distilled THF (~50 mL) was transferred into the flask via canula. The reaction flask was lowered into a dry ice/acetone bath and cooled to -78°C. A solution of sodium diphenylphosphide (100 mL of

a 0.0764 M solution in THF, 76.4 mmol) was injected dropwise via syringe. After addition was complete, the dry ice bath was removed and the solution warmed to room temperature. The solution was left to react overnight. Analysis of the solution by ^{31}P NMR revealed the formation of compound **16**.

^{31}P (121 MHz, THF): P(δ-18.0) with an external H_3PO_4 standard.

CHAPTER IV

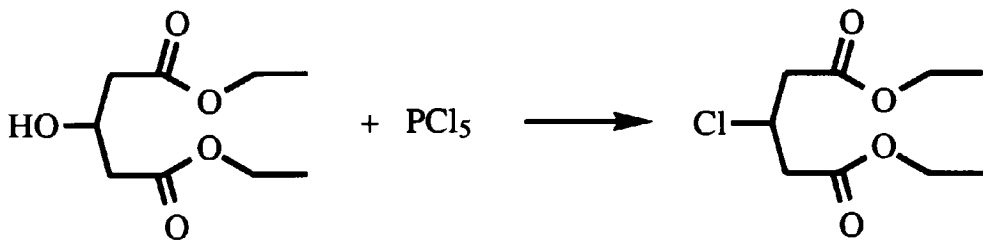
PROTOTYPE TWO:

1,1,1-TRIS(DIALKYLPHOSPHORYLETHYL)METHANE

4.1 Introduction

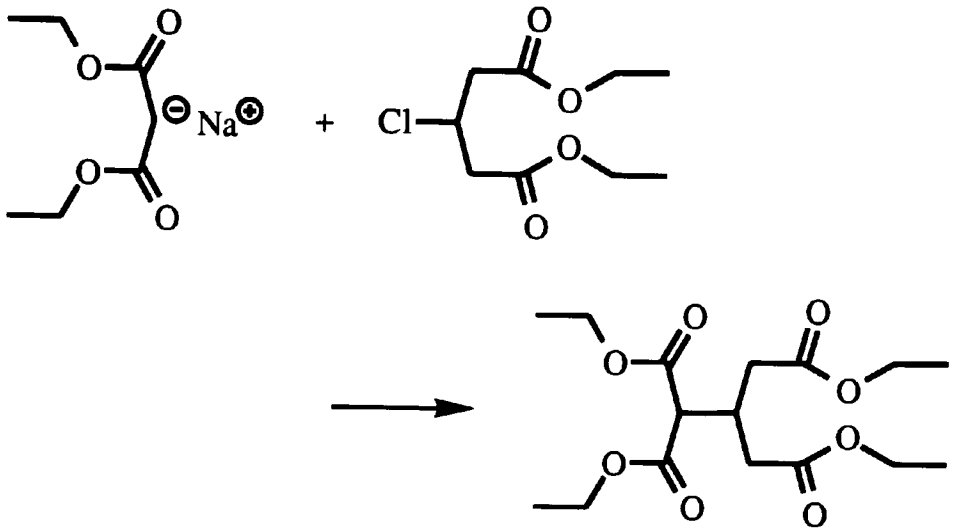
Synthesis of 1,1,1-tris(diphenylphosphorylethyl)methane, the second prototype in a series of ligands for the extraction of lanthanides and actinides from nuclear waste streams, was first thought to be achievable through the homologation of shorter legged tripodal triphosphines. When these homologation efforts failed, it was obvious that a total synthesis, from the ground up would be necessary.

In 1923, Dreifuss and Ingold detailed the synthesis of methane triacetic acid.[55] According to the article, diethyl-3-hydroxygluterate was reacted with phosphorus pentachloride to produce diethyl-3-chlorogluterate (see Scheme 4.1). Diethyl-3-chlorogluterate was coupled with the enolate of diethyl malonate through an S_N2

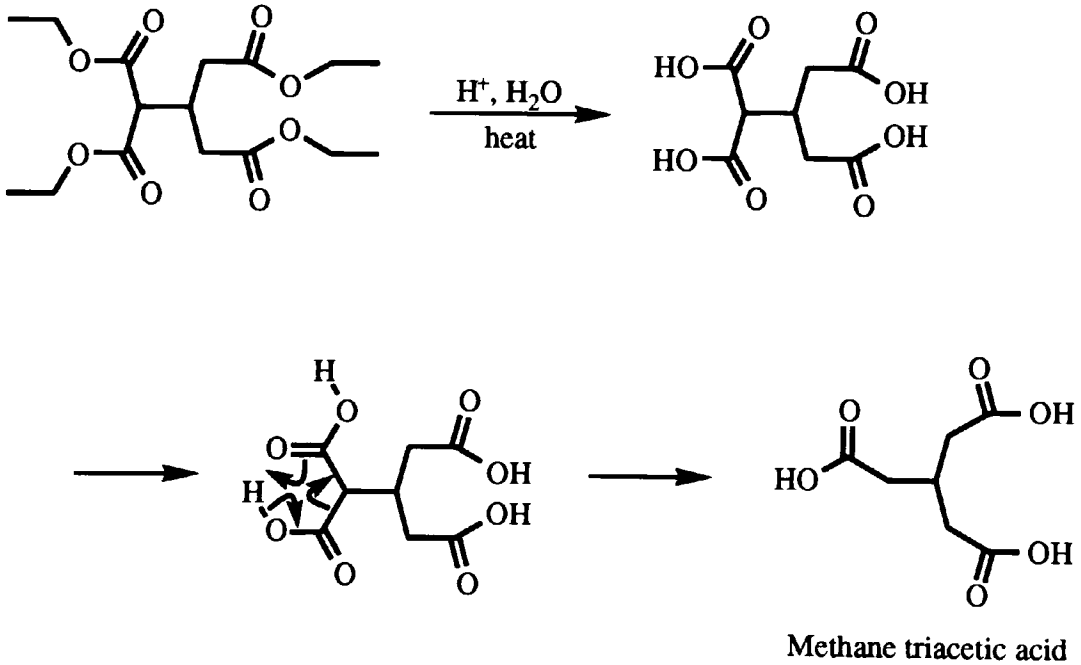


Scheme 4.1.

reaction (see Scheme 4.2). The tetraester was then hydrolyzed in dilute sulfuric acid with β-decarboxylation to form methane triacetic acid (Scheme 4.3).



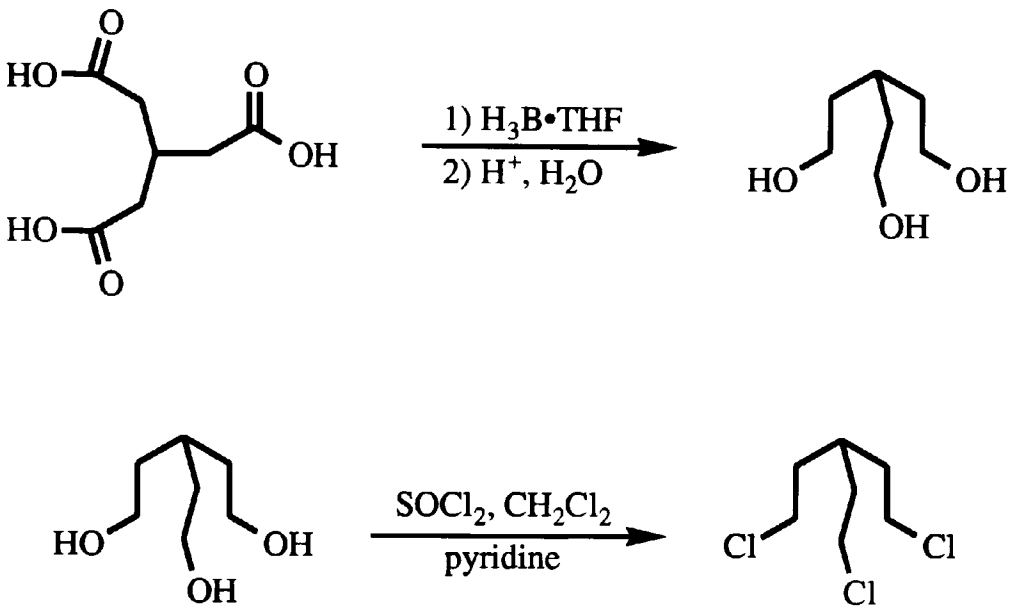
Scheme 4.2.



Scheme 4.3.

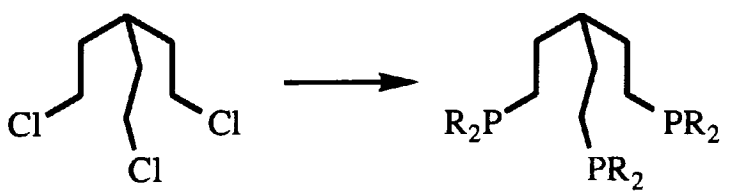
It was then postulated that methane triacetic acid could be reduced with borane[56] followed by hydrolysis to form the corresponding trisalcohol,

1,1,1-tris(hydroxyethyl)methane. Subsequent reaction with thionyl chloride in the presence of pyridine should produce 1,1,1-tris(chloroethyl)methane (see Scheme 4.4).



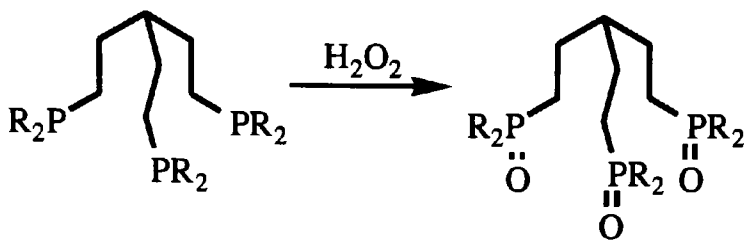
Scheme 4.4.

This compound, 1,1,1-tris(chloroethyl)methane, would then serve as an intermediate for further synthesis providing the backbone for a series of tripodal triphosphines. A sodium or potassium dialkylphosphide salt would then be used to substitute for the chloro groups to produce tripodal triphosphine compounds of interest (see



Scheme 4.5.

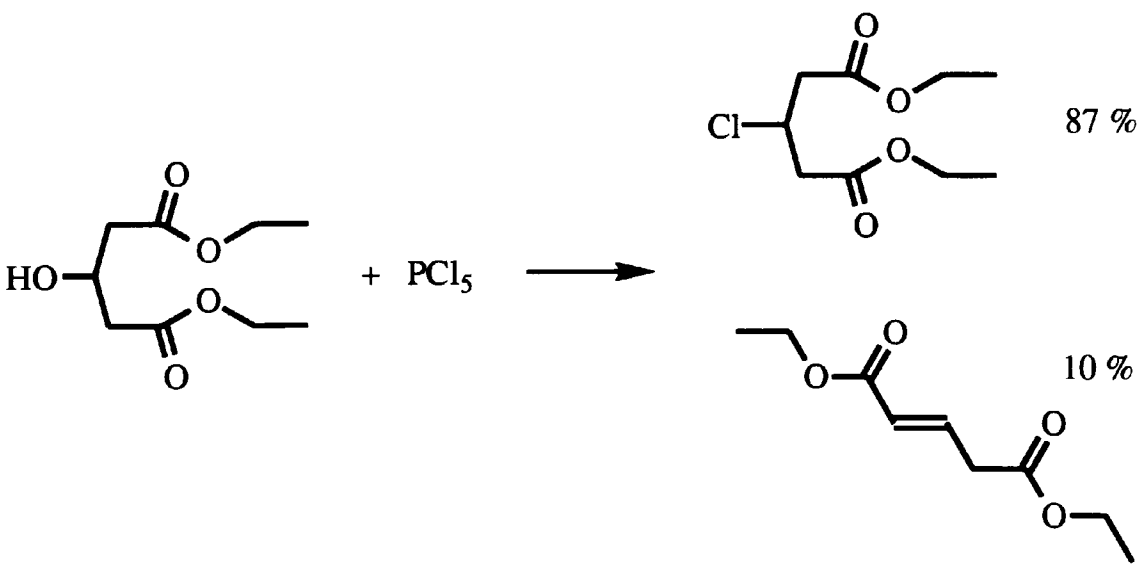
Scheme 4.5). Finally oxidation by hydrogen peroxide would produce the corresponding trioxide as depicted in Scheme 4.6.



Scheme 4.6.

4.2 Results And Discussion

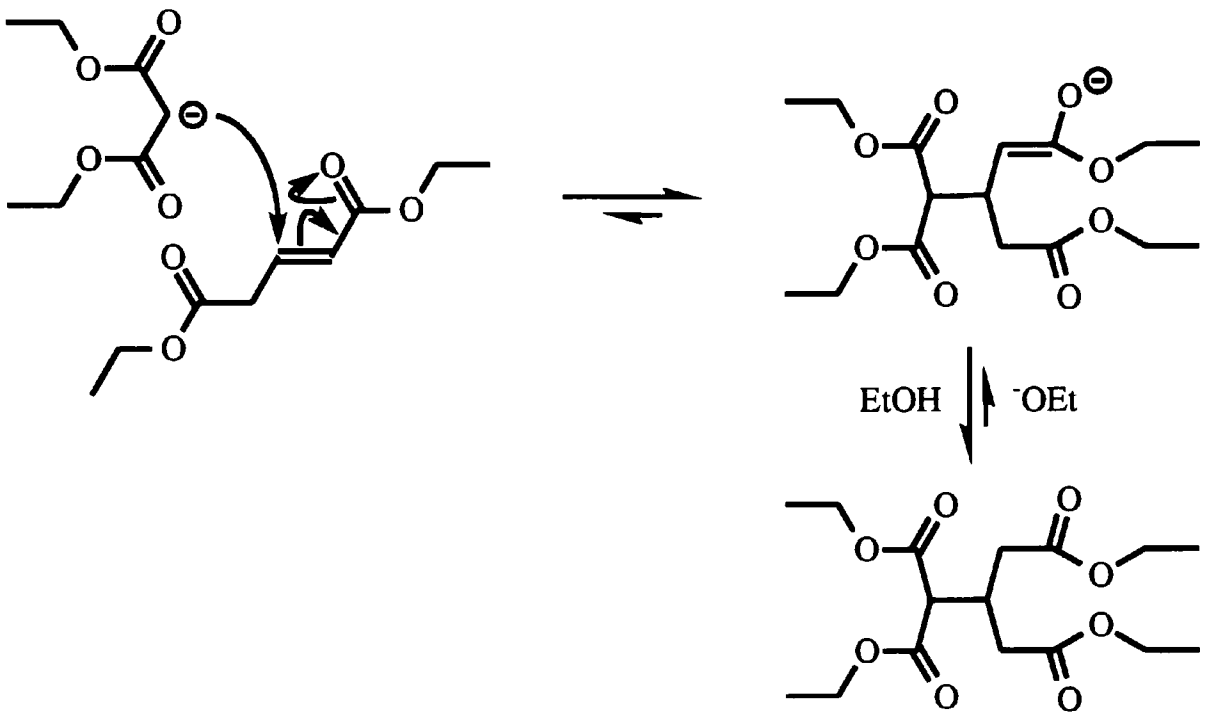
Closer examination of the reaction of PCl_5 with diethyl-3-hydroxyglutarate by ^1H NMR, a technique not available in 1923, revealed that the chloro substitution reaction was not as clean as first reported. Two products were actually formed. The major product was diethyl-3-chloroglutarate, but an elimination product was also formed (see Scheme 4.7).



Scheme 4.7.

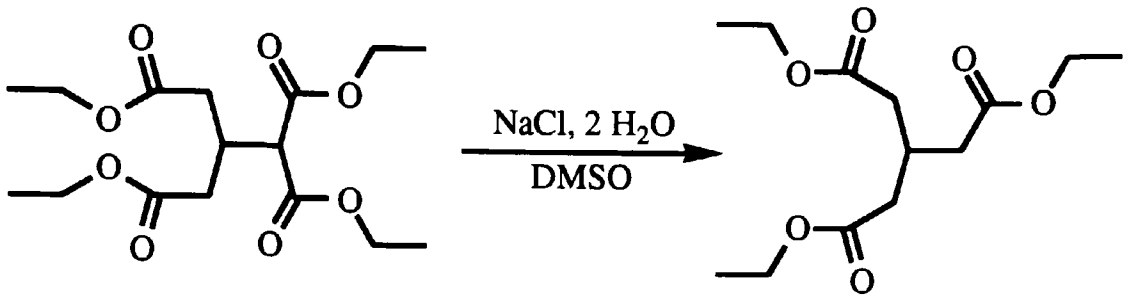
It was also found, however, that the coupling of the diethyl malonate anion to diethyl-3-chloroglutarate proceedes through the same elimination intermediate followed by a 1,4 or Michael addition (see Scheme 4.8). Dreifus and Ingold had reported a substitution

mechanism. In this case two wrongs really do make a right. Hydrolysis and β-decarboxylation of the tetraester take place as reported; however, the properties of the trisacetic acid, that is its polarity and hydrogen bonding characteristics, make its extraction from aqueous mixtures and subsequent purification difficult. An alternative preparation for the decarbonylation utilizing sodium chloride in DMSO was, therefore, adopted.[57]



Scheme 4.8.

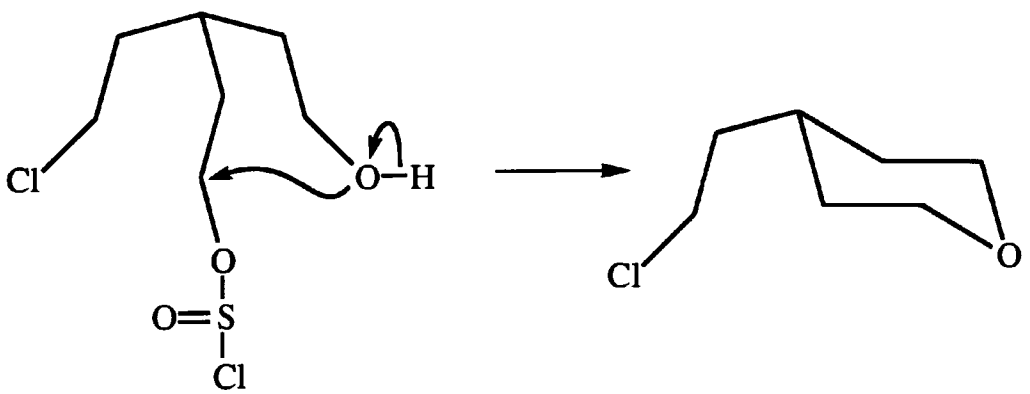
In the NaCl/DMSO reaction, a chloride ion readily displaces the carboalkyl group to yield the trisester (see Scheme 4.9). The trisester was further purified by vacuum distillation before reduction with borane to form 1,1,1-tris(hydroxyethyl)methane.



Scheme 4.9.

Attempts to reduce the trisacid or trisester with lithium aluminum hydride proceeded in poor yield. Presumably due to the chelation of the tris alcohol with aluminum, extraction of the product from the hydroxide matrix was not efficient. Substitution of borane for lithium aluminum hydride, however, afforded high yields of the trisalcohol.

Substitution of hydroxyl groups by chloro groups on 1,1,1-tris(hydroxyethyl)-methane (Scheme 4.4) proceeded in a 64% yield with the production of only minor impurities. Cyclization of the intermediate tripod via an intramolecular S_N2 reaction produced a monochlorocycloether by-product as depicted in Scheme 4.10.



Scheme 4.10.

Preparation of lithium diphenylphosphide was accomplished by the reduction of chlorodiphenylphosphine with sodium in THF. All other phosphides were produced from their corresponding tetraalkyldiphosphine disulfides, as in Scheme 4.11.[58,59]

$$ClPPh_2 + 2\,Na\,(metal) \longrightarrow NaPPh_2 + 2\,NaCl$$

$$R_2P(S)-(S)P_2R + Cu\,(powder) \longrightarrow Ph_2P\text{-}PPh_2 + CuS_2$$

$$R_2P-P_2R + Na\,(metal) \longrightarrow 2\,NaPR_2$$

Scheme 4.11.

The tetraalkyldiphosphine disulfide is reduced by copper to form the tetraalkyldiphosphine. The tetraalkyldiphosphine is then isolated and further reduced with sodium to produce the sodium dialkyldiphosphide. (Preparation of the ethyl and butyl phosphide salts were performed by Virginia DeMarquis, and are presented here for the sake of completeness.)[60]

Samples of 1,1,1-tris(diphenylphosphorylethyl)methane were shipped to Los Alamos National Laboratory where analytical tests on the extraction and separation characteristics of the ligand were performed. The competition of a ligand in an organic phase for a trivalent metal in an aqueous phase can be studied via extraction. Equation 4.1 indicates an organic phase containing a ligand , L, in equilibrium with an aqueous phase containing a trivalent cation, M^{3+}.

$$n\,L_{org} + M^{3+}_{aq} \rightleftharpoons L_nM^{3+}_{org} \qquad (4.1)$$

Assuming that the concentrations of free ligand in the aqueous phase and the uncomplexed metal in the organic phase are negligible, we can describe the equilibrium conditions by Equation 4.2.

$$K = \frac{[L_nM^{3+}]}{[L]^n_{org}\,[M^{3+}]_{aq}} \qquad (4.2)$$

The distribution coefficients can be defined as the ratio of the total metal concentration in the organic phase to the total metal concentration in the aqueous phase (see Equation 4.3).

$$D = \frac{[L_nM^{3+}]_{org} + [M^{3+}]_{org}}{[L_nM^{3+}]_{aq} + [M^{3+}]_{aq}} \qquad (4.3)$$

Because of the assumption previously discussed, Equation 4.3 reduces to:

$$D = \frac{[L_nM^{3+}]_{org}}{[M^{3+}]_{aq}} \qquad (4.4)$$

Substituting Equation 4.4 into Equation 4.2 gives:

$$K = \frac{D}{[L]^n_{org}} \qquad (4.5)$$

Taking the $\log_{10}$ of both sides of Equation 4.5 produces:

$$\log K = \log D - n \log L \qquad (4.6)$$

Algebraic rearrangement of Equation 4.6 produces:

$$\log D = n \log L + \log K \qquad (4.7)$$

Equation 4.7 is in the form of a linear equation, y=mx + b. Plotting log L versus log D and calculating a least squares linear fit will give a slope that is the value of n, where n is the number of ligands complexed per metal ion extracted.

The experimental procedure used by B.F. Smith, M.M. Jones, and G.D. Jarvenin for the extraction studies of 1,1,1-tris(diphenylphosphorylethyl)methane is described in section 2.4.

The pH dependence was empirically determined for Eu and Am. The maximum extraction for both metals occurred a $[H^+]$ of 5 M corresponds to a calculated pH of - 0.7, as observed in Figure 4.1. Extraction studies were performed at pH 5 by varying the ligand concentration while keeping all other factors constant. The distribution constant D was determined for each extraction. The results of the experiments are depicted in Figure 4.2 and it is observed that a linear least squares fit for both Eu (III) and Am (III) provides n=3.30. This value indicates that approximately three phosphine oxide units are coordinated to each metal ion.

Perhaps the most exciting result of this study was the ability of 1,1,1-tris(diphenyl-phosphorylethyl)methane to extract the metal ion from aqueous solution in very high efficiency. The y intercept of the plot above corresponds to log K=4.6. Therefore, K has a value of almost 40,000. A high value for K is indicative of good extraction. By increasing the ligand concentration from 0.02 M to 0.20 M, the distribution ratio, D, for $[Eu]_{org}$ to $[Eu]_{aq}$ increased 2300 fold from 0.11 to 253. Similar results for Am were observed, where the distribution ratio increased 2583 times from 0.12 to 310 over the same range of ligand concentration.

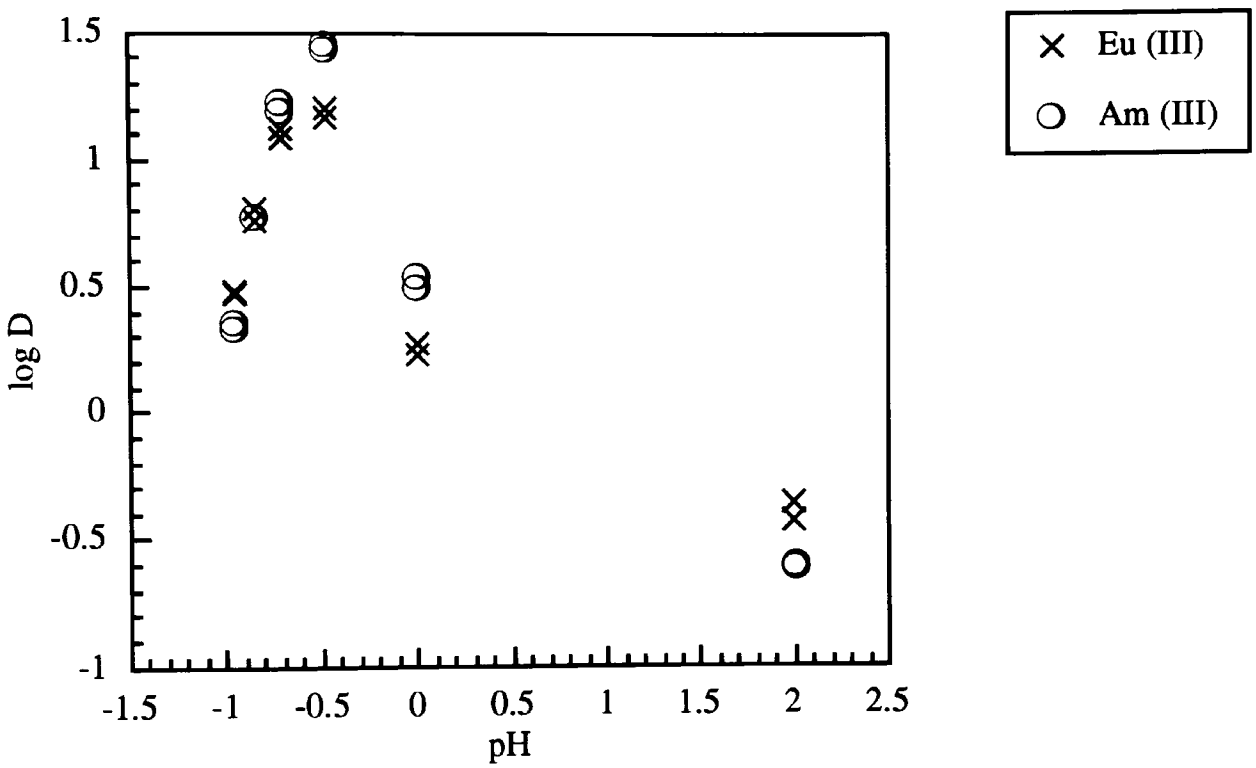


Figure 4.1.

The pH dependency of Eu (III) and Am (III) extraction by 1,1,1-tris(diphenylphosphoryl-ethyl)methane.

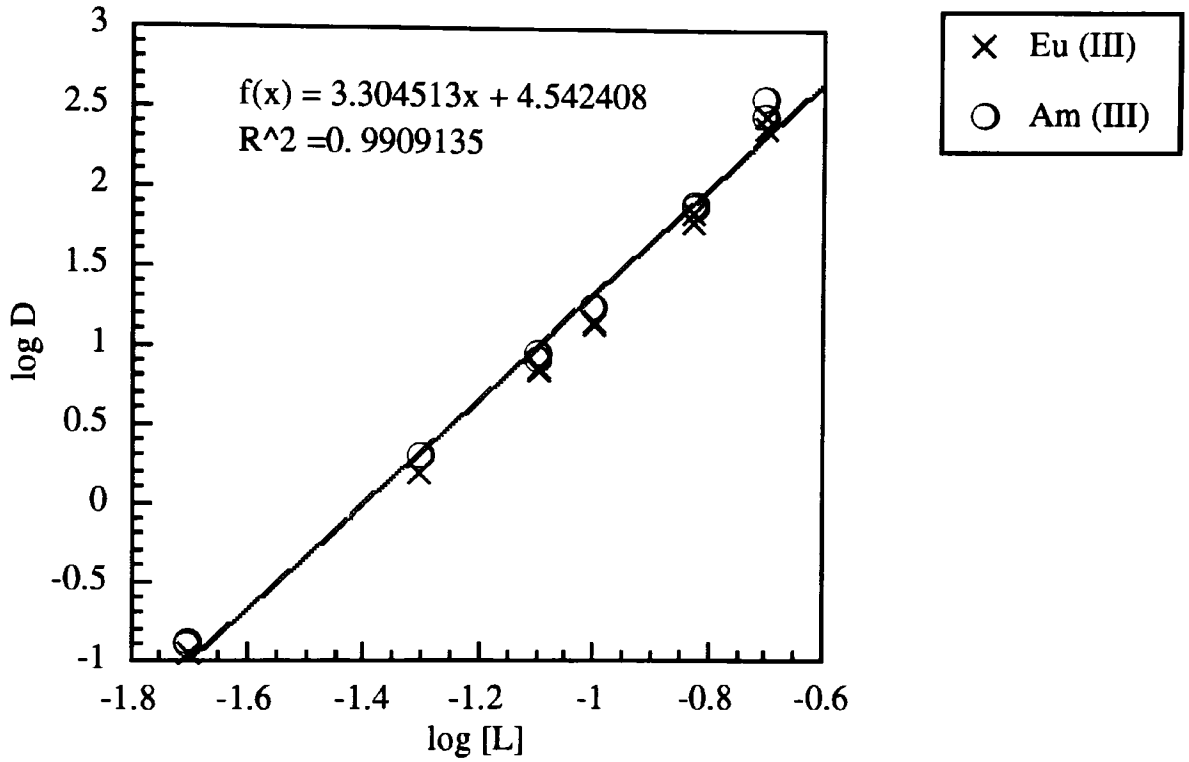


Figure 4.2.

Distribution ratio, D, of Eu (III) and Am (III) as a function of ligand concentration, [L], for compound 1,1,1-tris(diphenylphosphorylethyl)methane in a 5 M $HNO_3/CHCl_3$ system.

4.3 Experimental Procedure

4.3.1 Starting Materials

Diethyl-3-hydroxyglutarate, phosphorus pentachloride, potassium, diethyl malonate, 1M borane solution in THF, pyridine and, thionyl chloride were all purchased from Aldrich Chemical Company, and used without further purification. The tetramethyldiphosphine disulfide and tetraethyldiphosphine disulfide were obtained from Strem Chemical Company and sublimed under reduced pressure prior to use. Copper powder was obtained from the J.T. Baker Company and was flame dried under vacuum prior to use.

4.3.2 Preparation of $ClCH(CH_2C(O)OCH_2CH_3)_2$, (I), (**18**)

Diethyl-3-hydroxyglutarate (101.6 g; 0.4974 mol) was dissolved in 1L of anhydrous diethyl ether and chilled over an ice bath before slowly adding PCl_5 (113.9 g; 0.5471 mol), a 10% excess. The colorless reaction mixture was allowed to stir overnight where it turned clear yellow. Ice was added to quench the reaction resulting in an exothermic evolution of HCl. After the solution cooled to room temperature, it was extracted with diethyl ether. The ether layers were rinsed with cold 5% sodium bicarbonate solution and with deionized water. The ether extracts were dried over $MgSO_4$ and the diethyl ether was evaporated under reduced pressure leaving a clear, light-yellow liquid (106.62 g; 96.46% combined yield). The product was a mixture of $ClCH(CH_2C(O)OCH_2CH_3)_2$ and $CH_3CH_2OC(O)CHCHCH_2C(O)OCH_2CH_3$, (90:10).

$$ClC^{a}H(C^{b}H_2C^{c}(O)OC^{d}H_2C^{e}H_3)_2$$

$$C^{f}H_3C^{g}H_2OC^{h}(O)C^{i}H{=}C^{j}HC^{k}H_2C^{l}(O)OC^{m}H_2C^{n}H_3$$

^1H (300 MHz, $CDCl_3$): H^a(δ4.61, 1H, p); H^b(δ2.80, 4H, m); H^c(δ4.17, q); H^e(δ1.25, 6H, t); $H^{f,n}$(δ1.25, 6H, t); $H^{g,m}$(δ4.17, 4H, q); H^k(δ5.90, 1H, dot); H^j(δ7.01, 1H, dot); H^k(δ3.18, 2H, dod).

^{13}C (75 MHz, $CDCl_3$): C^a(δ52.1); C^b(δ42.6); C^c(δ169); C^d(δ61.1); C^e(δ14.1); $C^{f,n}$(δ14.1); $C^{g,m}$(δ61.1); C^h(δ169); C^i(δ124); C^j(δ139); C^k(δ37.4).

IR in cm^1: 3650w, 3545w, 3461w, 2983s, 2938s, 2909s, 2877m, 1878w, 1737s, 1660m, 1466m, 1447m, 1416s, 1396s, 1377s, 1344s, 1302s, 1262s, 1185s, 1095s, 1026s, 986m, 980m, 858m.

4.3.3 Preparation of $(CH_3CH_2OC(O)CH_2)_2CHCH(C(O)OCH_2CH_3)_2$, (**19**)

The product mixture, (71.39 g) $ClCH(CH_2C(O)OCH_2CH_3)_2$ and $CH_3CH_2OC(O)CH{=}CHCH_2C(O)OCH_2CH_3$ was dissolved in 250 mL of 100% ethanol. A 1.1 M stock ethoxide solution was prepared by dissolving (12.69 g; 0.5520 mol) sodium metal in 500 mL of 100% ethanol. Diethyl malonate (51.44 g; 0.3212 mol) was added to 10% excess ethoxide reagent (320.0 mL, 0.3533 mol). The resulting diethyl malonate anion solution was added to the former solution. As the diethyl malonate anion was added, the solution turned milky-orange. The reaction pot was warmed over a steam bath (3 h, pH > 7) while stirring. The reaction was quenched by adding deionized water (300 mL). The ethanol was then evaporated under reduced pressure (40 °C). The residue was acidified with cold 50% HCl and extracted with diethyl ether. The ether layers were washed with cold, aqueous 5% sodium bicarbonate solution, then deionized water. The solution was dried over $MgSO_4$ and the ether was evaporated under reduced pressure. The clear orange residue was distilled under vacuum at 135 °C at 0.150 torr (64.31 g; 57.80%) of a clear, colorless liquid.

$$(C^aH_3C^bH_2OC^c(O)C^dH_2)_2C^eHC^fH(C^g(O)OC^hH_2C^iH_3)_2$$

^1H (300 MHz, $CDCl_3$): $H^{a,i}$(δ1.27, 12H, t); $H^{b,h}$(δ4.10, 8H, q); H^d(δ2.55, 4H, d); H^e(δ3.05, 1H, p); H^f(δ3.75, 1H, d) .

^{13}C (75 MHz, $CDCl_3$): $C^{a,i}$(δ14.1); C^b(60.4); C^c(δ168); C^d(δ35.3); C^e(δ28.6); C^f(δ50.8); C^g(δ171).

IR in cm^{-1}: 2982s, 2938m, 2907m, 2890w, 1734s, 1651m, 1575m, 1466m, 1446m, 1420m, 1371m, 1315m, 1158s, 1096m, 1027s, 938w, 862m, 762w, 694w.

4.3.4 Preparation of $HC(CH_2C(O)OCH_2CH_3)_3$, (**20**)[57]

Compound **19** (79.53 g; 0.2296 mol) was dissolved in DMSO (300 mL) with stirring. Sodium chloride (15.452 g; 0.2644 mol) was added to the solution along with distilled water (15 mL). The reaction flask was fitted with a reflux condenser and refluxed for 12 hours. The solution slowly changed from colorless to red-brown in color, but remained clear. After allowing the solution to cool, the contents of the reaction flask were washed into a separatory funnel with ethyl acetate and water. More water (500 mL) was added to the funnel, and then the aqueous phase was extracted three times with ethyl acetate. The ethyl acetate layers were then combined and rinsed twice with brine to remove most of the remaining DMSO. Finally, the organic solution was dried over $MgSO_4$ and the volatiles removed under reduced pressure (50°C). The product (62.01 g; 98.46%) was a clear, golden oil.

$$HC^a(C^bH_2C^c(O)OC^dH_2C^eH_3)_3$$

^1H (300 MHz, $CDCl_3$): H^a(δ2.65, 1H, s); H^b(δ2.41, 6H, d); H^d(δ4.07, 6H, q); H^e(δ1.20, 9H, t).

^{13}C (75 MHz, $CDCl_3$): C^a(δ28.7); C^b(δ37.7); C^c(δ171.8); C^d(δ60.3); C^e(δ14.1).

4.3.5 Preparation of $HC(CH_2CH_2OH)_3$, (**21**)[56,61]

Compound **20** (62.01 g; 0.2260 mol) was dissolved in dry THF under N_2. Borane (460 mL, 1 M in THF) was added dropwise by canula. The reaction flask was topped with a reflux condenser which was, in turn, connected to an oil bubbler. The solution was heated overnight at reflux. A large amount of a waxy white precipitate formed; however, the solution remained yellow and clear. The reaction flask was cooled in an ice bath and the reaction quenched by slowly adding deionized water. Water was added until the white solid dissolved and the solution ceased to effervesce. The solution was then acidified with HCl and stirred for 15 minutes. Anhydrous potassium carbonate was added until the reaction mixture separated into two phases. The organic phase was decanted and the THF removed under reduced pressure. Any remaining boric acid was removed by redisolving the residue in acetone (a small amount of methanol may be necessary to get the product to go into solution), followed by refrigeration and subsequent filtration. The solvent was removed under reduced pressure. Compound **21** (29.92 g; 89.32%) was clear and viscous.

$$HC^{a}(C^{b}H_2C^{c}H_2O^{d}H)_3$$

^1H (300 MHz, acetone-d_6): H^a(δ1.70, 1H, s); H^b(δ1.52, 6H, t); H^c(δ3.60, 6H, dot); H^d(δ2.92, 3H. b) .

^{13}C (300 MHz, acetone-d_6) C^a(δ30.1); C^b(δ37.9); C^c(δ62.2).

IR in cm^{-1}: 4213m, 3383s, 3018s, 2932s, 2399w, 1710m, 1483m, 1421s, 1336s, 1052m, 928w, 668s.

4.3.6 Preparation of $HC(CH_2CH_2Cl)_3$, (**22**)

Compound **21** (18.67 g; 0.1260 mol) was dissolved in dry dichloromethane (400 mL) under N_2. Pyridine (35.00 mL, 0.4328 mol) was added to the solution with stirring and the trialcohol gradually went into solution. The flask was cooled in an ice bath before slowly adding $SOCl_2$ (33.92 mL; 0.4671 mol) via syringe. A water-soluble white solid formed upon addition of the thionyl chloride. The ice bath was removed, and under flow of nitrogen, the flask was fitted with a reflux condenser which was topped with a $CaCl_2$ drying tube and N_2 flow was ceased. The reaction flask was fitted with a heating mantle and heating was started. Reflux was maintained overnight. As the reaction proceeded it slowly darkened in color to a rich red-brown color. The heating mantle was replaced with an ice bath and the solution allowed to cool before quenching with slivers of ice. There was an induction period for the quenching process, but the reaction was quite vigorous. The mixture was rinsed into a separatory funnel with dichloromethane and washed three times with brine. The organic phase was then dried over $MgSO_4$ and the solvent removed under reduced pressure. Compound **22** was vacuum distilled (73-75°C at 0.150 torr) to yield a clear, colorless oil (16.58 g, 64.65%).

$$HC^{a}(C^{b}H_2C^{c}H_2Cl)_3$$

^1H (300 MHz, $CDCl_3$): H^a(δ2.04, 1H, s); H^b(δ1.80, 6H, dot); H^c(δ3.55, 6H, t).

^{13}C (75 MHz, $CDCl_3$):C^a(δ31.1); C^b(δ36.1); C^c(δ42.1).

IR in cm^{-1}: 2954s, 2931s, 2848s, 1736m, 1443m, 1384w, 1366w, 1302m, 1184w, 1114m, 1090s, 1055m, 1014m, 990w, 831w, 726m, 655m.

4.3.7 Preparation of $HC(CH_2CH_2PPh_2)_3$, (**23**)

A 10% excess (244 mL; 0.0862 mol) of the 0.354 M $NaPPh_2$ solution (**13**) was transferred to a dry Schlenk flask equipped with a magnetic stirbar via canula. Compound **22** (5.32 g; 0.0261 mol) was added to the flask via canula and formed a white precipitate that disappeared upon stirring. The solution turned a rusty-orange color as more of compound **22** was added. Compound **23** was separated from all of the salt byproducts and was hydrolyzed by adding deoxygenated, deionized water into the solution. The THF layer was transferred to a fresh Schlenk flask and used directly in the next step. The identity of compound **23** was confirmed by ^1H and ^{31}P NMR spectroscopy.

$$HC^{a}(C^{b}H_2C^{c}H_2PPh^{d\text{-}g}{}_2)_3$$

^1H (300 MHz, C_6D_6): $H^{a,b}$(δ1.35, 7H, m); H^{c}(δ1.54, 6H, m); $H^{e\text{-}h}$(δ7.15-7.60, 30H, m).

^{31}P (121 MHz, THF): P^{d}(δ-14.90) with an external H_3PO_4 standard.

4.3.8 Preparation of $HC(CH_2CH_2P(O)Ph_2)_3$, (**24**)

Hydrogen peroxide (30%) was added to the solution of Compound **26** in THF from Section 4.3.7 with constant stirring until the rusty colored solution faded to clear and colorless. The solution was then extracted with CH_2Cl_2. The CH_2Cl_2 extracts were dried over $MgSO_4$ and the CH_2Cl_2 was removed under reduced pressure. The residue was a mixture of $HC(CH_2CH_2P(O)Ph_2)_3$, $HOP(O)Ph_2$, and $HP(O)Ph_2$, which was separated using column chromatography (silica gel, 4% CH_3OH: 96% CH_2Cl_2).

$HC^{a}(C^{b}H_2C^{c}H_2P(O)Ph^{d\text{-}g}{}_2)_3$

^1H (300 MHz, $CDCl_3$): $H^{a,b}$(δ1.52, 7H, m); H^{c}(δ2.07, 6H, m); H^{e}(δ7.64, 12H, m); $H^{f,g}$(δ7.24, 18H, m).

13C (75 MHz, CDCl3): C^{a}(δ39.7); C^{b}(δ23.7); C^{c}(δ26.2; $^1J_{PC}$=71.9); C^{d}(δ132.8; $^1J_{PC}$=98.2); C^{e}(δ128.6; $^2J_{PC}$=11.4); C^{f}(δ130.6; $^3J_{PC}$=9.1); C^{g}(δ131.7; $^4J_{PC}$=3.1).

^{13}C-^1H HeteroCOSY confirmed all expected cross-peaks.

^{31}P (121MHz, $CDCl_3$): P^{d}(δ32.56) with an external H_3PO_4 standard.

IR in cm^{-1}: 3423s, 3055s, 2925s, 2865s, 2840w, 2360w, 2348w, 1978w, 1907w, 1831w, 1772w, 1731w, 1638m, 1590m, 1484m, 1437s, 1384m, 1312w, 1173s, 1120s, 1103s, 1071m, 1026w, 997m, 927w, 849w, 790m, 750s, 719s, 696s, 545s, 512s.

Analysis: Calculated for $C_{43}H_{43}P_3O_3 \cdot 1/2H_2O$: C, 72.76; H, 6.24.

Found: C, 72.64; H, 6.22.

4.3.9 Preparation of $(CH_3)_2PP(CH_3)_2$, (**25**)[58,59,62]

Freshly sublimed tetramethyldiphosphine disulfide was transferred into a Schlenk flask along with copper powder under flow of nitrogen. The flask was then equipped as depicted in Figure 4.3 with a reflux condenser, a U-tube, a drip-tip, and a receiving flask. The stopcock on the reaction flask was closed so that N_2/vacuum was applied only through the receiving flask. A Dewar containing liquid nitrogen was placed around the receiving flask, and vigorous heating with a Bunsen burner was applied to the reaction vessel. At first the tetramethyldiphosphine disulfide sublimed up onto the walls of the reaction flask and into the reflux condenser, but as the apparatus heated up it quickly reacted with the copper to form a black solid (CuS_2) and a clear, colorless liquid.

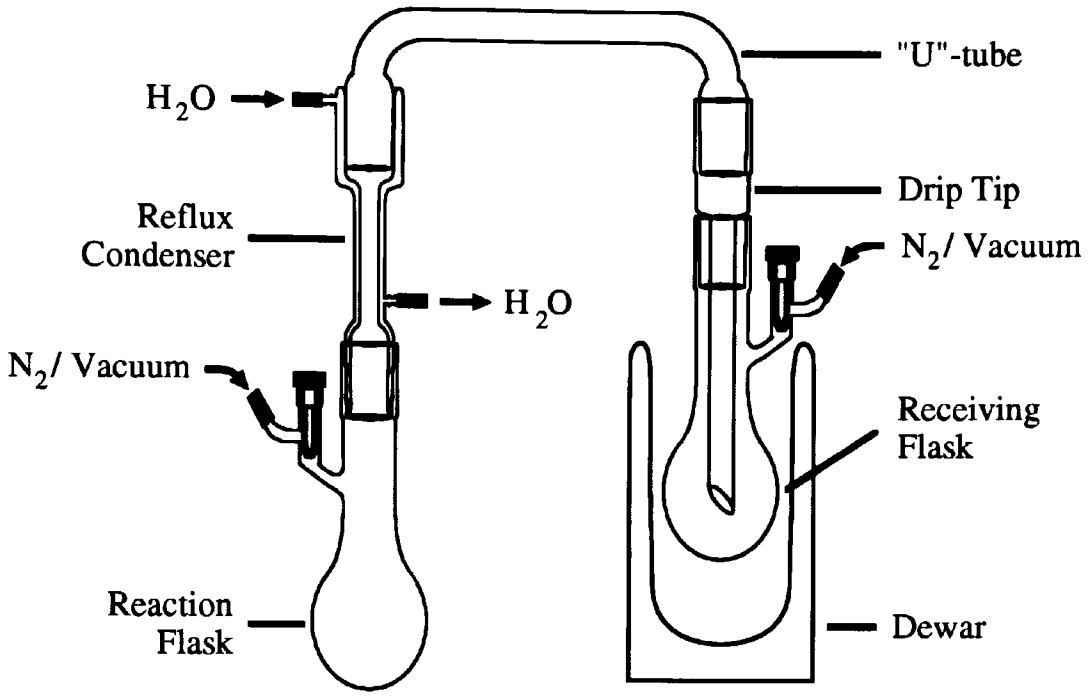


Figure 4.3.

Reaction apparatus for the preparation of tetramethyldiphosphine.

When all of the tetramethyldiphosphine disulfide had reacted, heating was stopped and the flask allowed to cool. Vacuum was then applied to the receiving flask and all volatile products distilled. The apparatus was returned to an N_2 environment and disassembled. The reaction flask was quickly capped with a 7/25 adapter with stopcock. Compound **25** was fractionally distilled on the high vacuum line through traps held at -23° C, -45° C, and -196° C.[58,59] Compound **25** was retained in the -45° C trap. Purity of the compound was verified by vapor pressure,[63,64] ^1H, ^{13}C,^{31}P NMR[64-66] and IR.[63]

^1H (300 MHz, C_6D_6): H(δ0.92, pseudo t).

^{13}C (75 MHz, C_6D_6): C(δ6.43, J_{PC}=11.07 Hz).

^{31}P (121 MHz, C_6D_6): P(δ-57.99) with an external H_3PO_4 standard.

IR(gas phase) 2980s, 2920s, 2820w, 2670w, 2195w, 1420m, 1290w, 945m, 890m, 710m, 705m, 680w.

4.3.10 Preparation of $KP(CH_3)_2$, (**26**)

Freshly distilled, dry THF was added to the Schlenk flask containing compound **25**. The flask was lowered into a dry ice/acetone bath (-78° C) and a magnetic stirbar was added. Stirring was initiated. Potassium rod was sliced into thin wafers under mineral oil, rinsed with dry ether and added to the solution. The solution gradually darkened until it became deep red in color. The formation of compound **26** was confirmed by ^{31}P NMR.

^{31}P (121 MHz, THF): P(δ–119.10) with an external H_3PO_4 standard.

4.3.11 Preparation of $HC(CH_2CH_2P(CH_3)_2)_3$, (**27**)

The solution from section 4.3.10 was transferred to a fresh Schlenk flask. Compound **22** (5.32 g; 0.0261 mol) was added to the flask via canula. A white precipitate was observed. The solution turned rusty-orange as more of compound **22** was added. The formation of **27** was confirmed by ^{31}P NMR.

^{31}P (121 MHz, THF): P(δ-51.34) with an external H_3PO_4 standard.

4.3.12 Preparation of $HC(CH_2CH_2P(O)(CH_3)_2)_3$, (**28**).

Hydrogen peroxide (30%) was added to the solution of Compound **27** in THF (from Section 4.3.11) with constant stirring until the rusty colored solution faded to clear and colorless. The solution was then extracted with dichloromethane. The extracts were dried over $MgSO_4$ and solvent removed on the rotary evaporator. The residue was a

mixture of $HC(CH_2CH_2P(O)(CH_3)_2)_3$, $HOP(O)(CH_3)_2$, and $HP(O)(CH_3)_2$, which was separated using column chromatography (silica gel, 4% CH_3OH: 96% CH_2Cl_2).

$$HC^{a}(C^{b}H_2C^{c}H_2P(O)(C^{d}H_3)_2)_3$$

^1H (300 MHz, $CDCl_3$): $H^{a,b}$(δ1.58, 7H, m); H^{c}(δ1.24, 6H, dot; $^1J_{PH}$=10.1); H^{d}(δ1.43, 12H, m; $^1J_{PH}$=12.5).

^{13}C (75 MHz, $CDCl_3$): C^{a}(δ35.91; $^3J_{PC}$=14.3); C^{b}(δ28.87; $^2J_{PC}$=35.5); C^{c}(δ28.43; $^1J_{PC}$=38.0); C^{d}(δ16.04; $^1J_{PC}$=68.2).

^{31}P (121 MHz, $CDCl_3$): P^{d}(δ42.92) with an external H_3PO_4 standard.

4.3.13 Preparation of $(CH_3CH_2)_2PP(CH_2CH_3)_2$, (**29**)[58-60,62]

Tetraethyldiphosphine disulfide (4.570 g, 18.86 mmol) was transferred into a Schlenk flask along with activated copper powder (14.36g, 225.9 mmol) under flow of nitrogen. The flask was then equipped as depicted in figure 4.4 with a reflux condenser, a U-tube, a drip-tip, and a receiving flask. The stopcock on the reaction flask was closed so that N_2/vacuum was applied only through the stopcock of the receiving flask. A Dewar containing liquid nitrogen was placed around the receiving flask, and vigorous heating with a Bunsen burner was applied to the reaction vessel. After approximately three minutes, the tetraethyldiphosphine disulfide melted and began to reflux. The tetraethyldiphosphine disulfide gradually reacted with the copper powder to form a black solid (CuS_2) and a clear, colorless liquid. Periodically, the flask was allowed to cool and a vacuum was

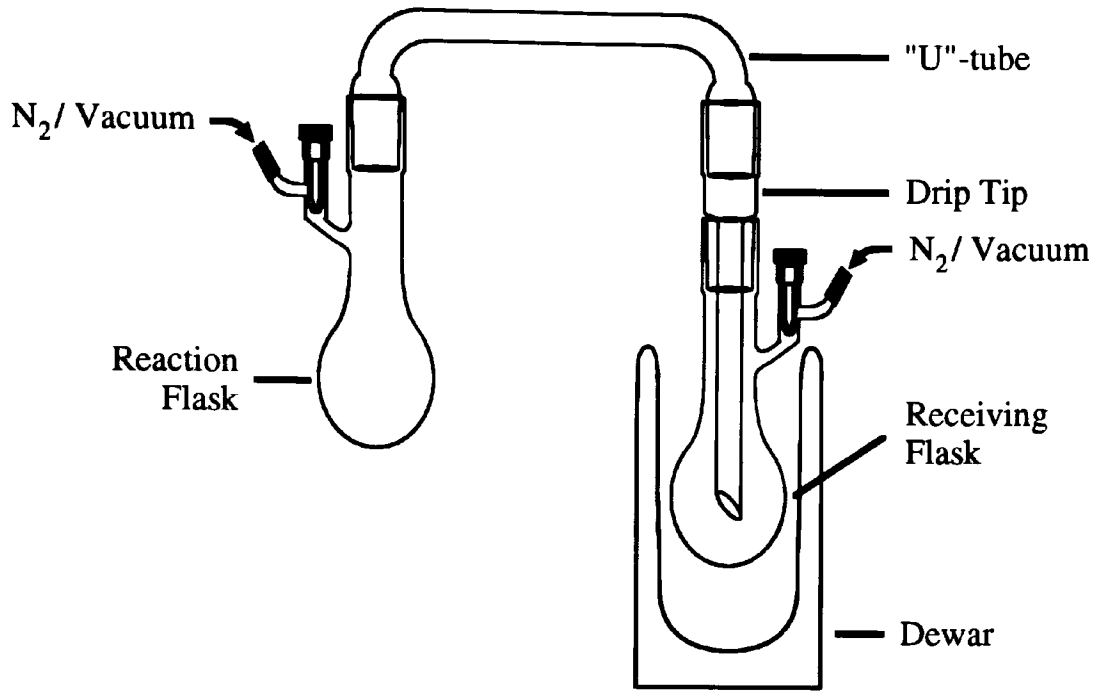


Figure 4.4.

Reaction apparatus for the preparation of tetraethyldiphosphine (**29**).

applied to the apparatus to distill the tetraethyldiphosphine (**29**) into the recieving flask. The reaction flask was then heated again under vacuum to get the last traces of tetraethyldiphosphine (**29**) to distill.

$$(C^aH_3C^bH_2)_2PP(CH_2CH_3)_2$$

^1H (300 MHz, $CDCl_3$): H^a(δ0.20–1.14, m); H^b(δ1.37–1.52, m).

^{13}C (75 MHz, $CDCl_3$): C^a(δ11.74, $^1J_{PC}$=10.51 Hz); C^b(δ16.47, $^2J_{PC}$=4.14 Hz).

^{31}P (121 MHz, THF): P(δ-32.44) with an external H_3PO_4 standard.

4.3.14 Preparation of $KP(CH_2CH_3)_2$, (**30**)[60]

Freshly distilled, dry THF was added to the Schlenck flask containing compound **29**. The flask was lowered into a dry ice/acetone bath (-78° C) and a magnetic stirbar was

added. Stirring was initiated. Potassium rod was sliced into thin wafers under mineral oil, rinsed with dry ether and added to the solution. The solution gradually darkened until it became deep red in color. The formation of compound **30** was confirmed by ^{31}P NMR.

^{31}P (121 MHz, THF): P(δ-35.1) with an external H_3PO_4 standard.

4.3.15 Preparation of $HC(CH_2CH_2P(CH_2CH_3)_2)_3$, (**31**).[60]

A 10% excess (100.0 mL; 0.0342 mol) of the 0.342 M $NaP(CH_2CH_3)_2$ solution (**30**) was transferred to a dry Schlenk flask equipped with a magnetic stirbar via canula. Compound **22** (3.823 g; 0.01878 mol) was added to the flask via canula and formed a white precipitate that disappeared upon stirring. The solution turned a rusty-orange color as more of compound **22** was added. Compound **31** was separated from all of the salt byproducts and was hydrolyzed by adding deoxygenated, deionized water into the solution. The THF layer was transferred to a fresh Schlenk flask.

^{31}P (121 MHz, THF): P(δ-21.6) with an external H_3PO_4 standard.

4.3.16 Preparation of $HC(CH_2CH_2P(O)(CH_2CH_3)_2)_3$, (**32**)[60]

Hydrogen peroxide (30%) was added to the solution of Compound **31** in THF under N_2 while stirring constantly until the rusty colored solution faded to clear and colorless. The solution was then extracted with CH_2Cl_2. The CH_2Cl_2 extracts were dried over $MgSO_4$ and the CH_2Cl_2 was removed on the rotary evaporator at 30°C. The residue was a mixture of $HC(CH_2CH_2P(O)(CH_2CH_3)_2)_3$, $HOP(O)(CH_2CCH_2H_3)_2$, and $HP(O)(CH_2CH_3)_2$, which was separated using column chromatography (silica gel, 15% CH_3OH: 85% CH_2Cl_2).

$HC^a(C^bH_2C^cH_2P(O)(C^dH_2C^eH_3)_2)_3$

^1H (300 MHz, $CDCl_3$): $H^{a-c,e}$(δ1.61-1.78, 25H, m); H^d(δ1.01-1.21, 18H, dot).

^{13}C (75 MHz, $CDCl_3$): C^a(δ40.89; $^3J_{PC}$=12.8); C^b(δ24.04; $^2J_{PC}$=3.9); C^c(δ23.79; $^1J_{PC}$=64.6); C^d(δ20.31; $^1J_{PC}$=66.3); C^e(δ5.89; $^2J_{PC}$=4.6).

^{31}P (121 MHz, $CDCl_3$): P^d(δ51.46) with an external H_3PO_4 standard.

IR in cm^{-1}: 2973s, 2942w, 2883s, 2355w, 2155w, 1651s, 1485s, 1412s, 1384m, 1270m, 1239m, 1131s, 1041s, 984m, 802m, 770m.

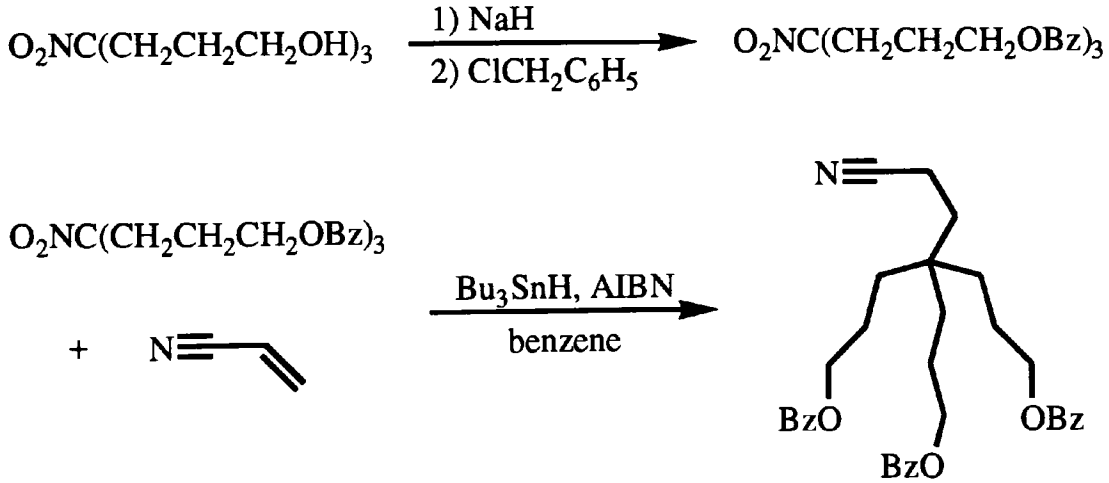
CHAPTER V

PROTOTYPE THREE:

1,1,1-TRIS(DIALKYLPHOSPHORYLPROPYL)METHANE

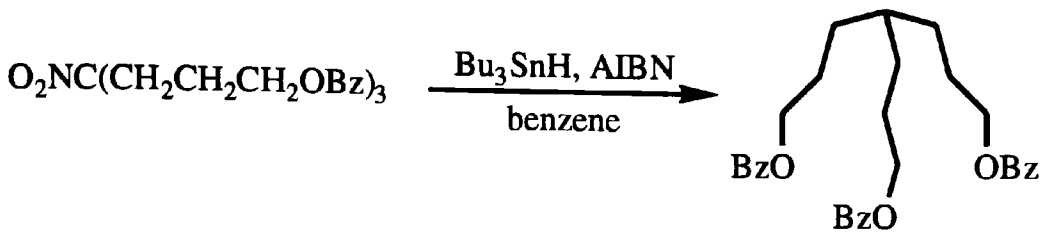
5.1 Introduction

The commercially available compound, nitromethanetrispropanol, was indicated as a possible starting material for the synthesis of 1,1,1-tris(diphenylphosphorylpropyl)-methane in an article by George Newkome.[67] In the article Newkome and his co-workers produced a series of cascade polymers by iterative synthesis using nitromethane-trispropanol as a starting point. They were able to replace the nitro group with a cyanoethyl group through a free radical reduction using tributyltin hydride. Protection of the hydroxyl groups was necessary prior to the reaction (see Scheme 5.1).



Scheme 5.1.

The introduction of the cyanoethyl group serves as a readily available point for the attachment of a solid support.

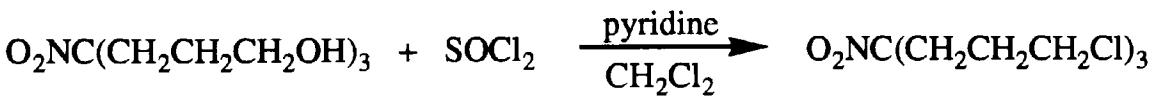


Scheme 5.2.

In the absence of an electron poor olefin, denitrohydrogenation occurs (see Scheme 5.2). Tributyltin hydride is reported to cleanly reduce nitro groups, leaving other reducible groups in polyfunctional compounds untouched.

5.2 Results and Discussion

Nitromethanetrisopropanol was readily reacted with thionyl chloride to produce 1,1,1-tris(chloropropyl)methane in high yields (84 %, see Scheme 5.3). The trichloro



Scheme 5.3.

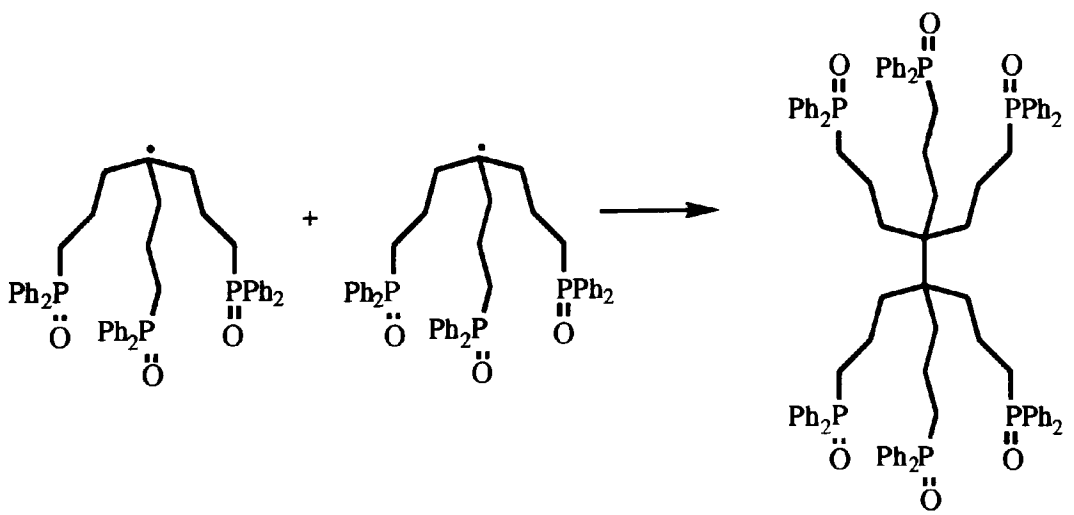
tripod was then reacted with sodium diphenylphosphide to produce 1,1,1-tris(diphenyl-phosphinopropyl)methane. However, the reaction did not go as cleanly as predicted. Multiple products were indicated by ^{31}P NMR. The phosphine mixture was oxidized with hydrogen peroxide and purified, by passing the mixture through a series of silica gel columns. Infrared spectroscopy confirmed the presence of P=O, but did not show an absorbance for NO_2. ^{1}H and ^{13}C NMR also revealed that all of the chloro groups were replaced by diphenylphosphino groups; however, no peaks corresponding to the apical carbon were found. The absence of signals in the IR and ^{1}H NMR spectra ruled out the

possibility of a simple reduction of the nitro group to an amine. Thus the lithium diphenylphosphide had effectively removed the nitrogroup from the tripod.

It is not uncommon for phosphides to participate in single electron transfer reactions to produce free radicals (see Scheme 5.4).[68]

Scheme 5.4.

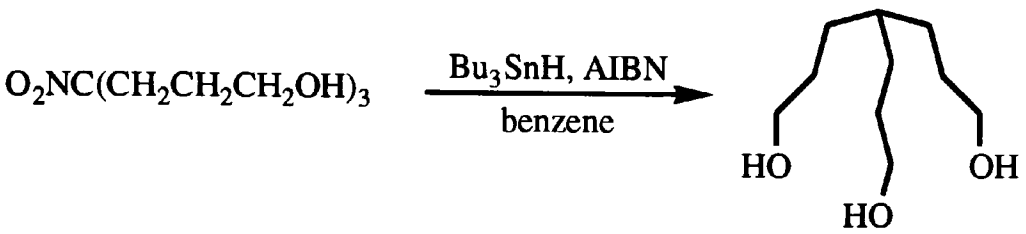
The alkyl radical can then go on to either abstract a proton from the surrounding solvent or couple with another free radical in solution. Abstraction of a proton from the solvent did not occur as confirmed by the absence signals in the ^{1}H and ^{13}C-DEPT experiments. No peaks were found for the apical carbon or its corresponding proton. The coupling of the alkyl radical with a diphenylphosphide radical was also ruled out. No species was found in the ^{13}C NMR with appropriate splitting pattern. The most likely possibility, using this mechanism, would be the coupling of two alkyl radicals to form a hexapodal ligand (see Scheme 5.5).



Scheme 5.5.

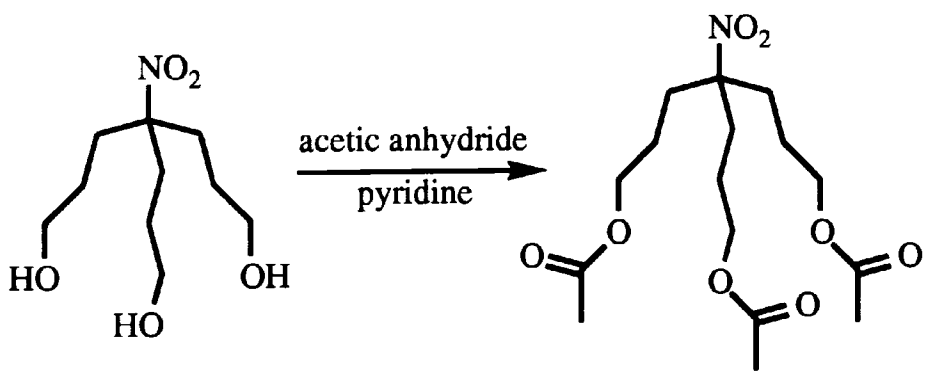
The presence of a hexapodal species was neither confirmed or denied by the spectroscopic evidence. No definite assignment for the apical C-C linkage could be made.

Because the nitro group was found to be a problem during phosphination a new synthetic strategy was developed. In the new strategy the nitro group was removed prior to chlorination and subsequent phosphination by using tributyltin hydride in a free radical reduction (see Scheme 5.6).[69] The reaction, however, was not without complications, and



Scheme 5.6.

it was found necessary to protect the hydroxyl groups with acetyl groups prior to free radical reduction (see Scheme 5.7). The trisester was then reacted with tributyltin hydride

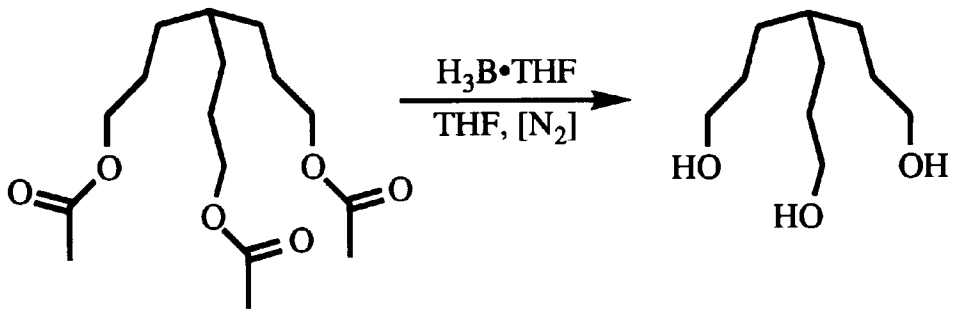


Scheme 5.7.

in benzene to yield the denitrogenated product. Large amounts of tributyltin residues were present in the product which were not readily removed by column chromatography. It was, however, possible to remove most of the residue by dissolving the crude compound

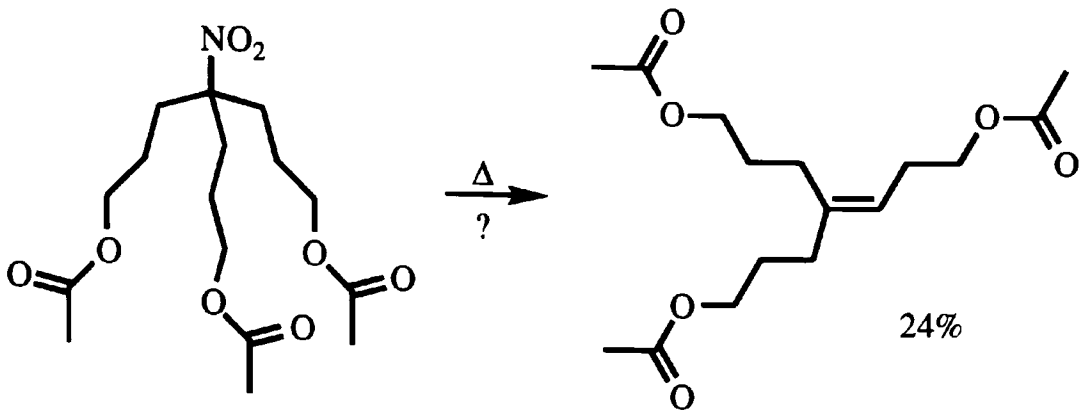
in acetonitrile and washing the resulting solution six to eight times with separate aliquots of hexane.[70] After extraction the tributyltin residue was no longer evident in the ^{1}H NMR spectra. Reduction of the apical nitrogroup to a proton was indicated in both the ^{1}H and ^{13}C NMR spectra and was confimed by a ^{1}H - ^{13}C heteroCOSY experiment.

Further manipulation of the denitrogenated ester was attempted using borane to reduce the acetyl protecting groups to produce the desired product, 1,1,1-tris(hydroxy-propyl)methane (see Scheme 5.8). The reaction did not go smoothly. The presence of minute tributyltin residuals, as confirmed by ^{119}Sn NMR, caused complete degradation of the product.



Scheme 5.8.

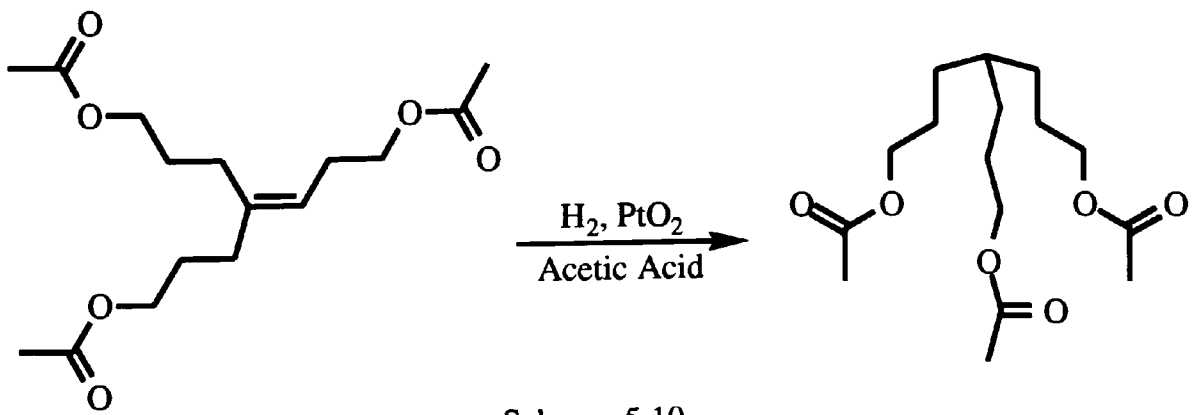
A second batch of the nitrotrisester was synthesized as in Scheme 5.7, but instead of removing the pyridine by extraction, the reaction solution was vacuum distilled. A brown gas (NO_2) was evolved and the ^{1}H NMR spectra revealed a by-product. Analysis of the spectra including ^{13}C NMR and IR, revealed that an elimination reaction had taken place. Of the original nitrotrisester 24 % had reacted to form an alkene derivative while the other 76 % remained unreacted (see Scheme 5.9). The first fraction of product from the



Scheme 5.9.

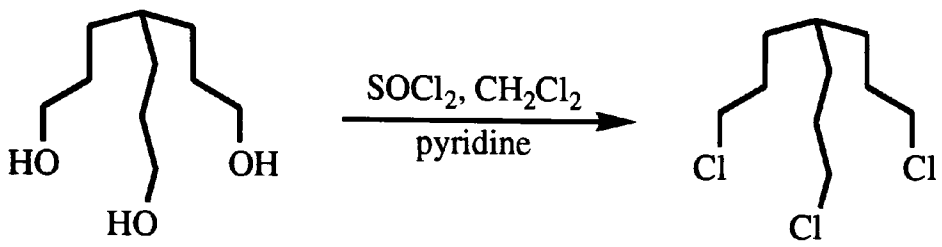
distillation also contained a small amount of pyridine. One of the later fractions, which was pure, was heated and maintained at reflux in vacuo for three hours, but no further elimination was observed. It was determined that the reaction was base catalyzed. The same fraction was submitted to reflux in pyridine for three hours followed by vacuum distillation. Only a small amount of the nitrotrisester was observed to undergo elimination. Finally, a sample of the nitrotrisester was refluxed in dry quinoline, a much higher boiling solvent (bp 237°C) than pyridine (bp 115°C). Heating the sample overnight succeded in pushing the reaction to completion.

Hydrogenation of the alkene to the alkane was easily accomplished utilizing Adam's catalyst (PtO_2/acetic acid) under pressure of hydrogen (see Scheme 5.10).



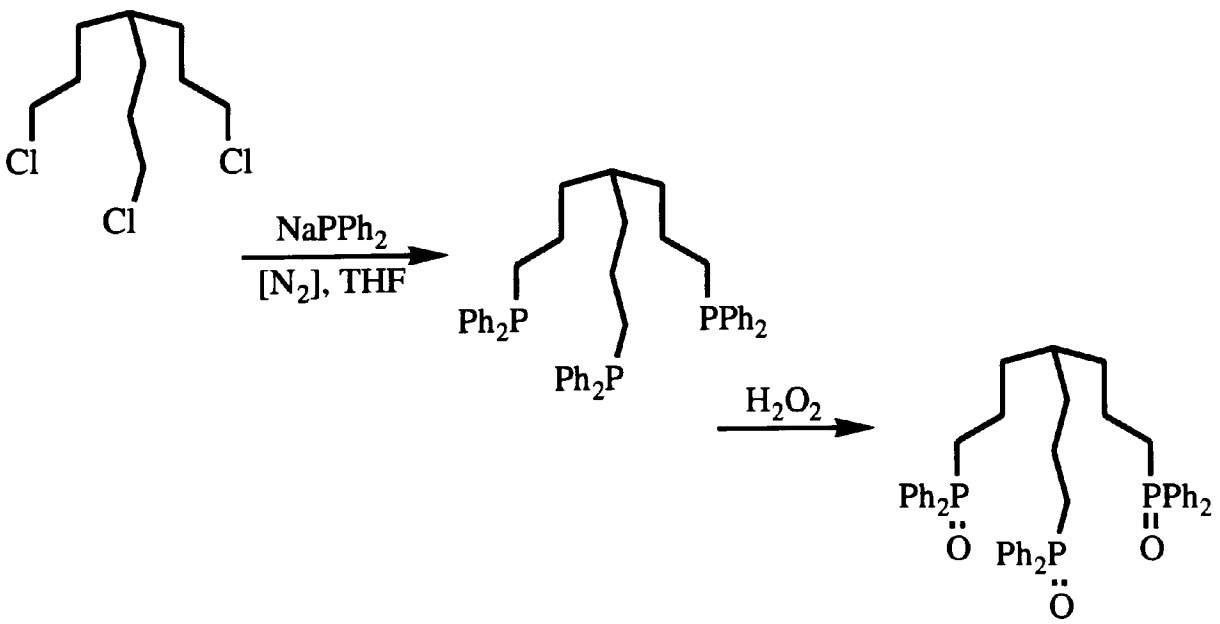
Scheme 5.10.

Subsequent conversion of the trisacetate to 1,1,1-tris(hydroxypropyl)methane, as previously depicted in Scheme 5.8, also proceeded in high yields. Substitution of the hydroxyl groups by chloro groups proceeded with only minor complications (see Scheme



Scheme 5.11.

5.11). Finally the trichloro tripod was phosphinated (as previously described in Chapter 4) followed by oxidation with hydrogen peroxide to give the final product, 1,1,1-tris-(diphenylphosphorylpropyl)methane (see Scheme 5.12).



Scheme 5.12.

5.3 Experimental Procedure

5.3.1 Starting Materials

Dichloromethane was distilled under nitrogen from calcium hydride immediately before use. Pyridine and quinoline were distilled and stored under nitrogen prior to use. The compound 2,2'-azobis(2-methylpropionitrile), AIBN, was recrystallized from methanol. All other materials were purchased from Aldrich Chemical Company and used without further purification.

5.3.2 Preparation of $O_2NC(CH_2CH_2CH_2Cl)_3$, (**37**)

Nitromethanetrispropanol (4.722 g; 20.17 mmol) was dissolved in dry dichloromethane (400 mL) under N_2. Pyridine (1.6 mL, 21 mmol) was added to the solution along with a magnetic stirbar. Stirring was initiated and the trialcohol gradually went into solution. The flask was cooled in an ice bath before slowly adding $SOCl_2$ (15.0 mL; 208 mmol) via syringe. The ice bath was removed. The flask was warmed to room temperature and left to react overnight. As the solution reacted it slowly darkened in color to a dark amber color. The flask cooled in an ice bath before quenching with slivers of ice. The mixture was rinsed into a separatory funnel with dichloromethane and then washed with brine. The acidic solution was washed with 5% aqueous sodium bicarbonate until basic. The organic phase was then washed three times with brine. The organic phase was then dried over $MgSO_4$ and the solvent removed on the rotary evaporator. The trichloro compound was a clear, amber oil (4.89 g, 84%).

$$O_2NC^a(C^bH_2C^cH_2C^dH_2Cl)_3$$

^1H (300 MHz, $CDCl_3$): H^b(δ2.09, 6H, m); H^c(δ1.71, 6H, m); H^d(δ3.54, 6H, t).

^{13}C (75 MHz, $CDCl_3$): C^a(δ93.0); C^b(δ33.0); C^c(δ44.3); C^d(δ26.7).

5.3.3 Attempted preparation of $O_2NC(CH_2CH_2CH_2PPh_2)_3$, (**38**)

A Schlenk flask was dried in the oven and flushed with nitrogen. Compound **37**, 1,1,1-tris(chloropropyl)methane (4.89 g, 16.9 mmol) was added to the flask, along with a magnetic stirbar. Stirring was initiated. The flask was sealed with a rubber septum, and lithium diphenylphosphide solution (150.0 mL of a 0.3162 M solution in THF, 55.34 mmol) was added dropwise via canula. ^{31}P NMR revealed a bevy of peaks from 91.09 to-39.97 ppm. The reaction definitely did not go cleanly.

5.3.4 Attempted preparation of $O_2NC(CH_2CH_2CH_2P(O)Ph_2)_3$, (**39**)

Water was added to the reaction flask in section 5.4.3. The flask was opened to air and a five-fold excess of hydrogen peroxide (30%) was added slowly to the solution. The mixture was extracted twice with diethyl ether. The ether phases were then combined and dried over $MgSO_4$. Solvent was removed on the rotory evaporator. Two silica gel columns, used in series, were required to purify the product (silica gel, 3% CH_3OH: 97% CH_2Cl_2; followed by a second column silica gel, 5% CH_3OH: 95% CH_2Cl_2). IR spectroscopy revealed that the nitro group had been reduced off; however, a corresponding peak for the proton on the apical carbon of the expected by-product, $HC(CH_2CH_2CH_2P(O)Ph_2)_3$, was never found. Signals corresponding to H^{b-h}, and C^{b-h} were all identified and confirmed by ^1H-^{13}C HeteroCOSY NMR. One other possible product, through a radical reaction mechanism, is the hexapod, $(Ph_2P(O)CH_2CH_2CH_2)_3CC(CH_2CH_2CH_2P(O)Ph_2)_3$; however, the identity of this product was never confirmed, because the ^1H and ^{13}C NMR spectra were still not clean enough for verification.

$$O_2NC^a(C^bH_2C^cH_2C^dH_2P(O)Ph^{e-h}{}_2)_3$$

^{1}H (300 MHz, $CDCl_3$): H^b(δ1.63, 6H, m); H^c(δ2.24, 6H, m); H^d(δ3.57, 6H, t); H^{e-h}(δ7.44, 30H, m).

^{13}C (75 MHz, $CDCl_3$): C^b(δ17.9, $^4J_{PH}$=3.7 Hz); C^c(δ33.4, $^3J_{PH}$=12.7 Hz); C^d(δ29.1, $^2J_{PH}$=71.8 Hz); C^e(δ128, $^1J_{PC}$=12.8 Hz); C^f(δ129, $^2J_{PC}$=11.6 Hz); C^g(δ131, $^3J_{PC}$=9.1 Hz); C^h(δ132).

^{31}P (121 MHz, $CDCl_3$): P(δ28.26) with an external H_3PO_4 standard.

IR in cm^1: 3378s(br), 3060m, 2943m, 2872m, 1660w(br), 1590w, 1484w, 1437s, 1314w, 1179s(br), 1120s, 1067s, 1026m, 997m, 950m, 785w, 753m, 726s, 697s, 550s, 526m.

5.3.5 Preparation of $O_2NC(CH_2CH_2CH_2OC(O)CH_3)_3$, (**40**)

Nitromethanetrispropanol (26.078 g; 0.11084 mol) was dissolved in 500 mL of pyridine. Acetic anhydride (50.0 mL, 0.529 mol) was added to the solution with constant stirring. The solution was capped with a $CaCl_2$-drying-tube and left to react overnight. The clear golden solution was quenched with water and then extracted twice with dichloromethane. The organic layers were rinsed twice with brine. The organic extracts were dried over $MgSO_4$ and the dichloromethane was evaporated under reduced pressure leaving a clear, amber oil. Compound **40** was vacuum distilled (200°C at 0.150 torr) to yield a clear, colorless oil (29.32 g, 73%).

$$O_2NC^a(C^bH_2C^cH_2C^dH_2OC^e(O)C^fH_3)_3$$

^{1}H (300 MHz, $CDCl_3$): H^b(δ1.53 6H, m); H^c(δ1.93 6H, m); H^d(δ4.03, 6H, t); H^f(δ2.03, 9H, s).

^{13}C (75 MHz, $CDCl_3$): C^a(δ93.2); C^b(δ20.8); C^c(δ23.0); C^d(δ63.5); C^e(δ171); C^f(δ31.9).

IR in cm^{-1}: 2955s, 2896m, 1737s, 1537s, 1454m, 1384s, 1367s, 1243s, 1038s, 632w, 609m.

5.3.6 First preparation of $HC(CH_2CH_2CH_2OC(O)CH_3)_3$, (**41**)

Compound **40** (25.032 g, 0.10639 mol), benzene (9.00 mL), AIBN (2,2'-azobis[2-methyl-propionitrile]), 8.311 g,0.0506 mol), and tributyltin hydride (31.5 mL, 0.117 mol) were added to a Schlenk flask under flow of nitrogen. A magnetic stirbar was added to the reaction flask and stirring was initiated. The flask was topped with a reflux condenser which was in turn capped with a T-tube adapter. One arm of the adapter was connected to the nitrogen line and the other was connected to an oil bubbler see Figure 5.1). N_2 flow was redirected to flow through the T-tube and the stopcock on the flask was

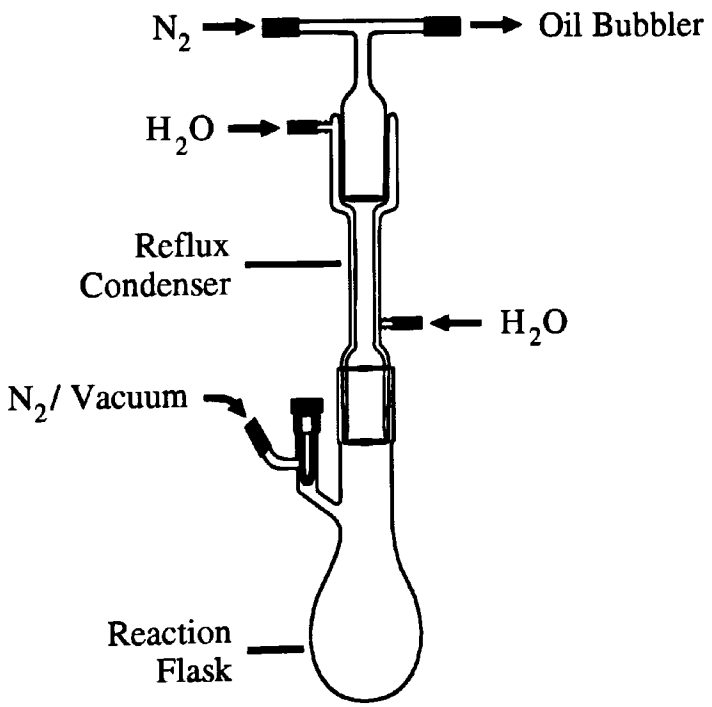


Figure 5.1.

Reaction apparatus for the preparation of $HC(CH_2CH_2CH_2OC(O)CH_3)_3$, (**41**).

closed. A steambath was used to heat the reaction mixture to 100°C for 3 hours. The benzene was then evaporated under reduced pressure. The resulting mixture was washed into a separatory funnel with acetonitrile and the solution washed 6 times with hexane to remove most of the tributyl tin derivatives. The acetonitrile phase was then evaporated under reduced pressure to yield a clear, yellow oil. The oil was vacuum distilled (200°C at 0.150 torr) to yield a clear, golden oil (19.56 g, 58.1% - mixture: 72% **41**, 28% **42**).

$$HC^{a}(C^{b}H_2C^{c}H_2C^{d}H_2OC^{e}(O)C^{f}H_3)_3$$

^{1}H (300 MHz, $CDCl_3$): H^{a}(δ1.93 6H, m); H^{b}(δ1.53 6H, m); H^{c}(δ1.93 6H, m); H^{d}(δ4.03, 6H, t); H^{f}(δ2.03, 9H, s).

^{13}C (75 MHz, $CDCl_3$): C^{a}(δ93.2); C^{b}(δ20.8); C^{c}(δ23.0); C^{d}(δ63.5); C^{e}(δ171); C^{f}(δ31.9).

IR in cm^{1}: 2955s, 2896m, 1737s, 1537s, 1454m, 1384s, 1367s, 1243s, 1038s, 632w, 609m.

5.3.7 Preparation of $CH_3C(O)OCH_2CH_2CH=C(CH_2CH_2CH_2OC(O)CH_3)_2$, (**42**)

Compound **40** (9.710 g, 26.86 mmol) was dissolved in freshly distilled, dry quinoline (~300 mL). The reaction flask was fitted with a reflux condenser, a magnetic stirbar and a heating mantle. The reflux condenser was capped with a T-tube adapter. One arm of the adapter was connected to the nitrogen line and the other was connected to an oil bubbler (see Figure 5.1). N_2 flow was redirected to flow through the T-tube and the stopcock on the flask was closed. The solution was refluxed with constant stirring overnight. The solution gradually changed color from yellow to black-brown. A brown gas was evolved. The reaction mixture was rinsed into a separatory funnel with water and ethyl acetate. Aqueous HCl was added to the mixture until the aqueous phase tested acidic.

The aqueous phase was extracted twice with ethyl acetate. The organic layer was decanted off of the aqueous phase, being careful to leave behind as much of the emulsion as possible. The organic solution was filtered through a paper filter to remove the last of the emulsion, washed once with water and dried over $MgSO_4$. The solvent was evaporated under reduced pressure leaving a clear, amber liquid. The oil was then vacuum distilled (205°C at 0.150 torr) to yield a clear, golden oil (7.73 g, 91.6%).

$$C^{a}H_3C^{b}(O)OC^{c}H_2C^{d}H_2C^{e}HC^{f}(C^{g}H_2C^{h}H_2C^{i}H_2OC^{j}(O)C^{k}H_3)_2$$

^1H (300 MHz, $CDCl_3$): $H^{a,g,k}$(δ2.03 13H, m); $H^{c,i}$(δ4.00 6H, t); H^{d}(δ2.30 2H, q); H^{e}(δ5.13, 1H, t); H^{h}(δ1.69 4H, m).

^{13}C (75 MHz, $CDCl_3$): $C^{a,k}$(δ20.9); $C^{b,j}$(δ171); $C^{c,i}$(δ63.9); C^{d}(δ27.2); C^{e}(δ121); C^{f}(δ140); C^{g}(δ32.7); $C^{g'}$(δ26.1); C^{h}(δ27.1); $C^{h'}$(δ26.8).

IR in cm^{1}: 3118w, 3111w, 3111w, 2954s, 2895m, 1736s, 1666w, 1537w, 1454m(br), 1384s, 1367s, 1243s, 1038s, 979m, 950m, 891m, 773w, 756w, 632w, 609m, 474w.

5.3.8 Second preparation of $HC(CH_2CH_2CH_2OC(O)CH_3)_3$, (**43**)

Compound **42** (18.67 g; 0.1260 mol) was dissolved in glacial acetic acid (50 mL). Platinum dioxide (~1.5 mg) was added to the solution and the mixture was placed on a Parr hydrogenator (60 psi H_2, 24 hours). After hydrogenation, the solution was filtered through Celite and a fine glass fritt. The filtrate was washed into a separatory funnel with water and ethyl acetate. The organic layer was then washed with aqueous sodium bicarbonate until it tested basic to pH paper. The organic solution was washed twice with brine to remove the excess base, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure leaving a clear, amber liquid.

$HC^{a}(C^{b}H_2C^{c}H_2C^{d}H_2OC^{e}(O)C^{f}H_3)_3$

^1H (300 MHz, $CDCl_3$): $H^{a,b}$(δ1.30 7H, m); H^{c}(δ1.57 6H, m); H^{d}(δ4.02 6H, t); H^{f}(δ2.03, 9H, s).

^{13}C (75 MHz, $CDCl_3$): C^{a}(δ36.4); C^{b}(δ25.6); C^{c}(δ29.4); C^{d}(δ64.8); C^{e}(δ171); C^{f}(δ20.9).

IR in cm^1: 3625w, 3555w,3461w, 2944s, 2861m, 1737s, 1455m, 1435m, 1387m, 1365s, 1238s, 1034s, 635w, 605w.

5.3.9 Preparation of $HC(CH_2CH_2CH_2OH)_3$, (**44**)

Compound **43** (4.90 g; 15.5 mmol) was dissolved in dry THF under N_2. Borane (51.5 mL, 1 M in THF) was added dropwise by canula. The reaction flask was fitted with a reflux condenser, which was toped with a T-tube adapter. One arm of the adapter was connected to the nitrogen line and the other was attached to an oil-bubbler as depicted in Figure 5.1. The solution was heated overnight at reflux. A large amount of a waxy white precipitate formed; however, the solution remained yellow and clear. The reaction flask was cooled in an ice bath and the reaction quenched by slowly adding deionized water. Water was added until the white solid dissolved and the solution ceased to effervesce. The solution was then acidified with HCl and stirred for 15 minutes. Anhydrous potassium carbonate was added until the reaction mixture separated into two phases. The organic phase was decanted and the THF removed under reduced pressure. Any remaining boric acid was removed by redisolving the residue in acetone (a small amount of methanol may be necessary to get the product to go into solution), followed by refrigeration and subsequent filtration. The solvent was removed under reduced pressure. Compound **44** (2.69 g, 91.3%) was clear and viscous.

$HC^{a}(C^{b}H_2C^{c}H_2C^{d}H_2O^{e}H)_3$

^1H (200 MHz, $CDCl_3$): $H^{a,b}$(δ1.26 7H, m); H^{c}(δ1.54 6H, t); H^{d}(δ3.60, 6H, s).

^{13}C (75 MHz, $CDCl_3$): C^{a}(δ19.7); C^{b}(δ30.3); C^{c}(δ36.7); C^{d}(δ63.4).

IR in cm^1: 3342s(br), 2931s, 2861s, 1725w, 1602w, 1455s, 1378m, 1337m, 1260m, 1055s, 1032s, 908w, 803w, 738w, 697w, 650w, 579w.

5.3.10 Preparation of $HC(CH_2CH_2CH_2Cl)_3$, (**45**)

Time did not permit the completion of this project. Please refer to section 4.3.6 for a parallel procedure.

5.3.11 Preparation of $HC(CH_2CH_2CH_2PPh_2)_3$, (**46**).

Time did not permit the completion of this project. Please refer to section 4.3.7 for a parallel procedure.

5.3.12 Preparation of $HC(CH_2CH_2CH_2P(O)Ph_2)_3$, (**47**).

Time did not permit the completion of this project. Please refer to section 4.3.8 for a parallel procedure.

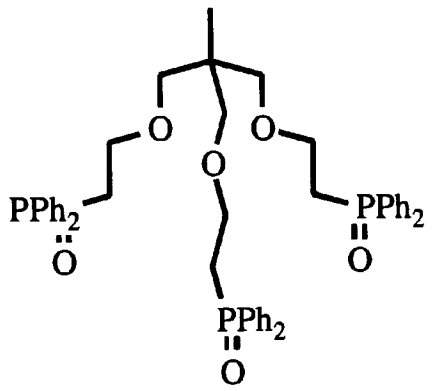
CHAPTER VI

PROTOTYPE FOUR:

1,1,1-TRIS(DIPHENYLPHOSPHORYLETHOXYMETHYL)ETHANE

6.1 Introduction

Attempts to increase the length of 1,1,1-tris(hydroxymethyl)ethane were repeatedly unsuccessful. As an alternative approach, 1,1,1-tris(diphenylphosphorylethoxymethyl)-ethane (**55**) was synthesized. Compound **55** differs from the generic tripodal triphosphine oxide in that it contains ether linkages within each leg (see Scheme 6.1).



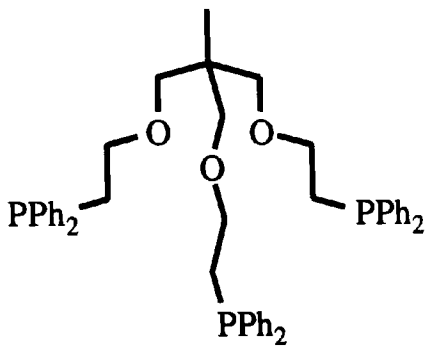
55

Scheme 6.1.

The oxygen linkages should increase the flexibility of the tripod and lessen steric strain during chelation. The oxygen atoms may also act as electron donors to aid in the coordination of metal ions as observed in crown ethers.

The intermediate phosphine 1,1,1-tris(diphenylphosphinoethoxymethyl)ethane (**54**) should also be of particular interest to transition metal and organometallic chemists. Its six heteroatomic binding sites should allow the potential for octahedral coordination. The compound 1,1,1-tris-(diphenylphosphoryletoxymethyl)ethane bears a striking resemblance

to cryptands which have been studied extensively by Engelhardt, Geue, and Osvath (see Scheme 6.2).[71-73] Both heteroatom placement and function are analogous to **54**.



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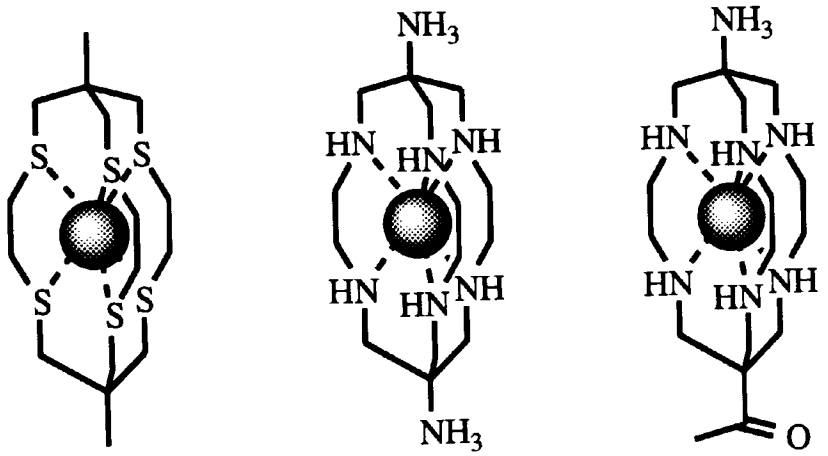


Scheme 6.2.

The ether linkages employed in this synthesis afforded a method to easily extend the legs of the starting material and may contribute to the complexation ability of the ligand.

6.2 Results and Discussion

The compound 1,1,1-tris(diphenylphosphorylethoxymethyl)ethane was not the original target compound for this synthesis; rather, 1,1,1-tris(diphenylphosphoryl-methoxymethyl)ethane was initially pursued.

The synthesis of a similar compound, 1,3-dibromodimethyl ether, was reported by Don Kyle, a former member of the Marx research group, in his Ph.D. dissertation of 1987.[74] In the synthesis, Kyle reacted bromine with a mixture of red phosphorus and paraformaldehyde in water to yield 1,3-dibromodimethyl ether (see Scheme 6.3).

$$Br_2 + P\,(red) + H_2C{=}O + H_2O \longrightarrow BrCH_2OCH_2Br$$

Scheme 6.3.

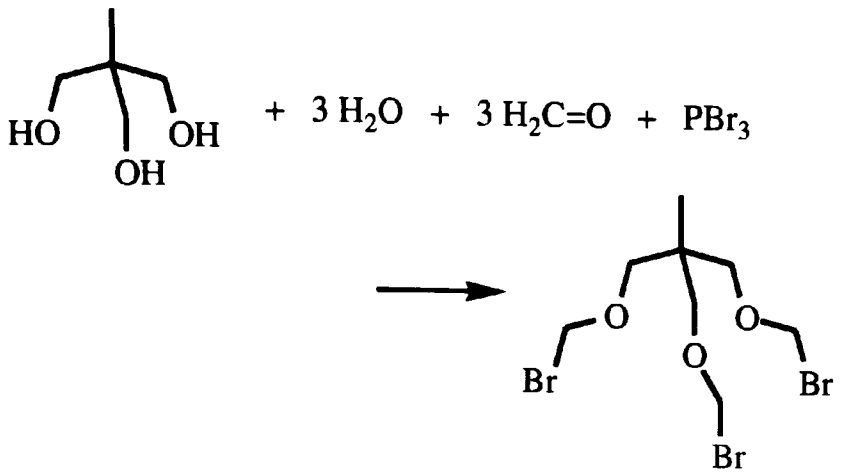
Two years later, Shipov et al. reported a more general preparation for the synthesis of alkyl chloromethyl ethers (see Scheme 6.4).[75]

$$ROH + H_2C{=}O + Me_3SiCl \longrightarrow ROCH_2Cl + HCl + Me_3SiOSiMe_3$$

Scheme 6.4.

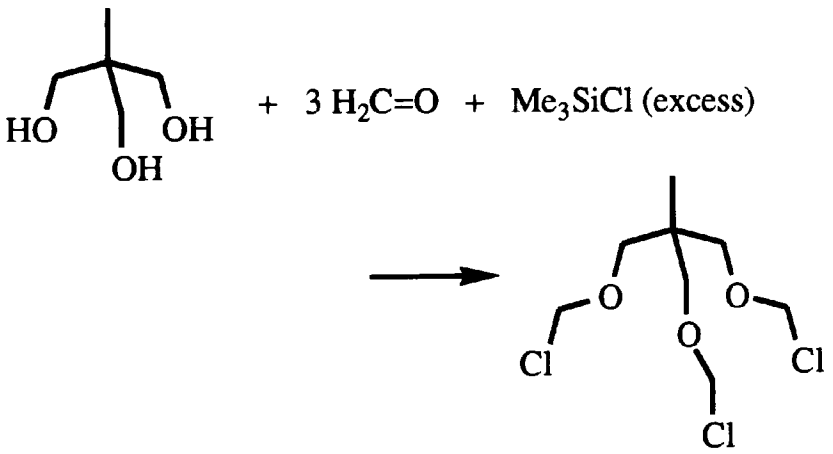
Both approaches toward the synthesis of a trishalomethyl ether were employed.

The compound 1,1,1-tris(hydroxymethyl)ethane was reacted first with phosphorus tribromide and paraformaldehyde in water. The expected product was 1,1,1-tris(chloromethyl)ethane (see Scheme 6.5). Some supporting evidence for the formation of



Scheme 6.5.

the product was found, but the ^{1}H and ^{13}C NMR were very complex. A by-product with a second-order ^{1}H NMR spectrum was observed. Shipov's synthesis, Scheme 6.6, was then attempted, but it resulted in the same



Scheme 6.6.

by-product. The second-order spectrum implied a cyclic product with a high degree of symmetry (see Figure 5.1). The identity of the compound was confirmed by ^{13}C NMR along with massspectrometry and IR. The proposed mechanism for its formation is shown in Scheme 6.7.

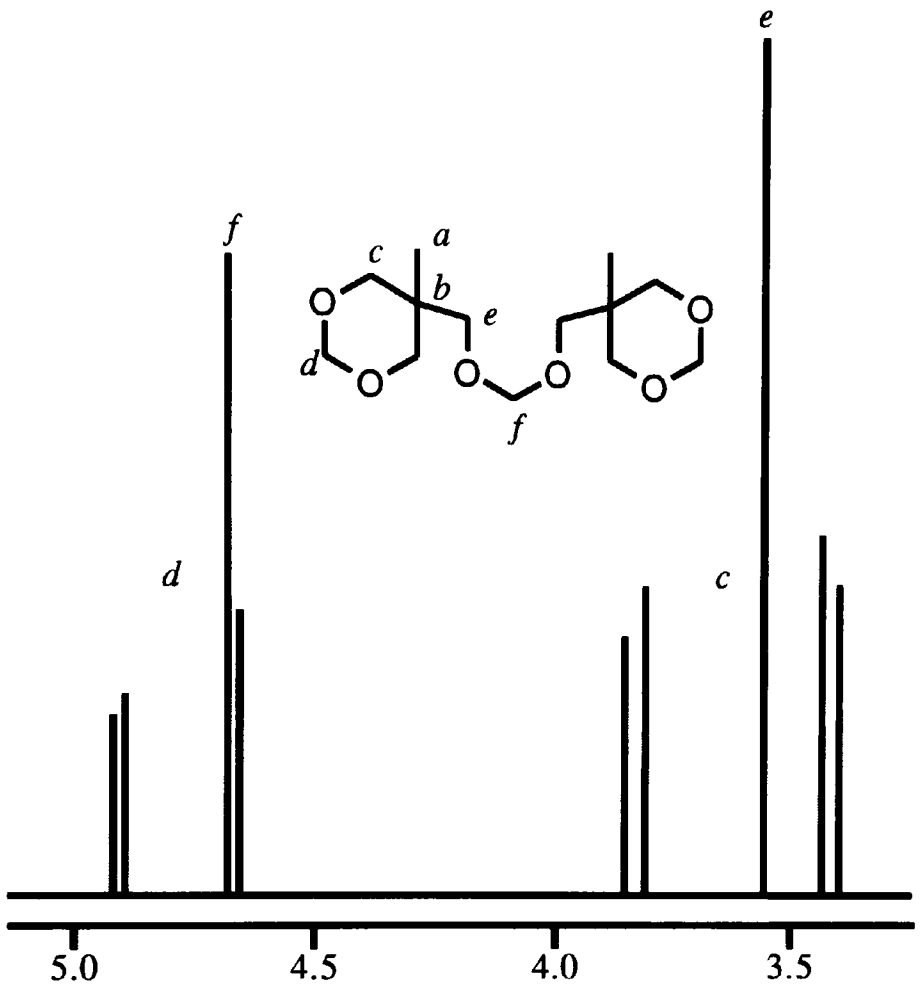
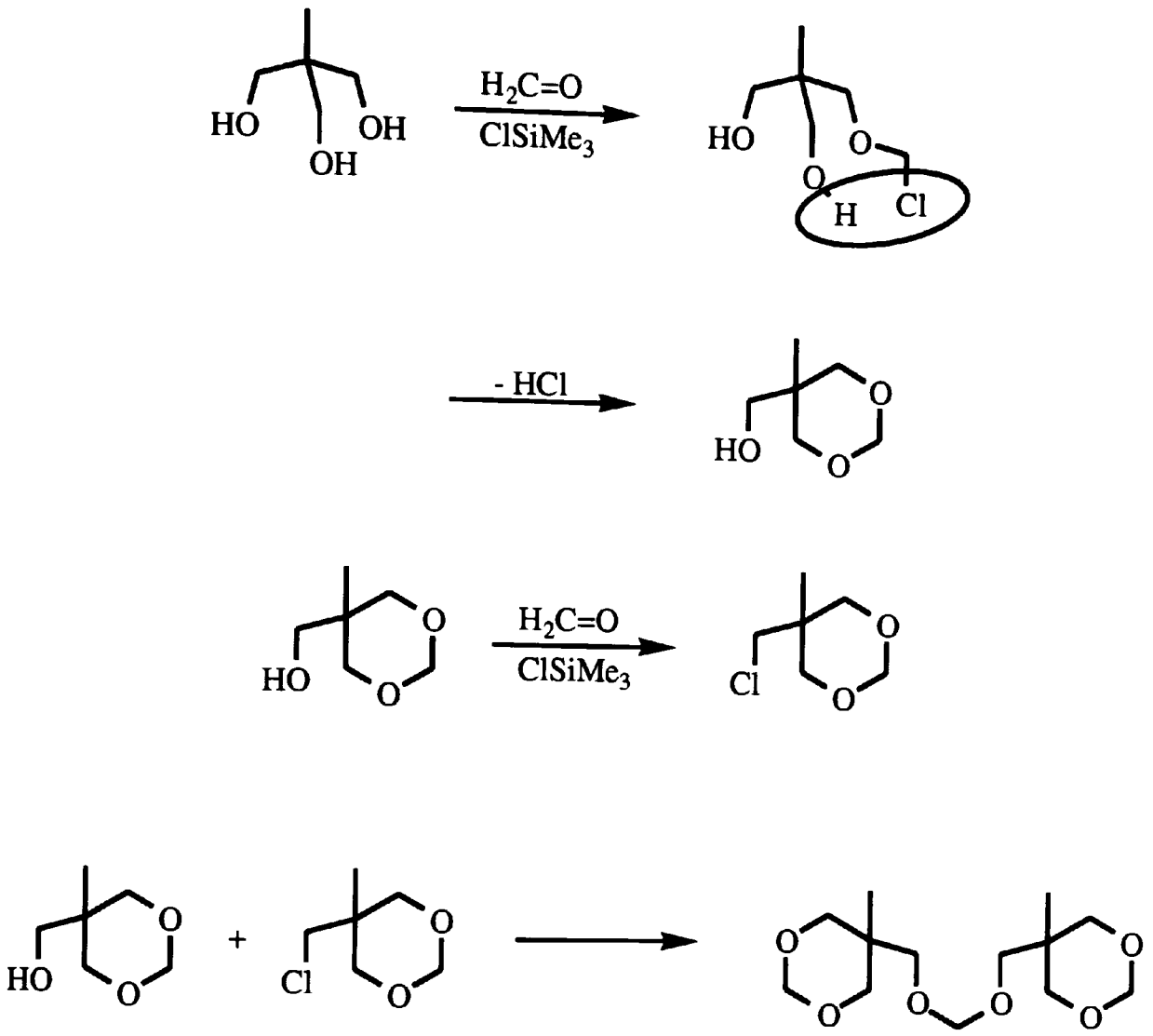


Figure 6.1.

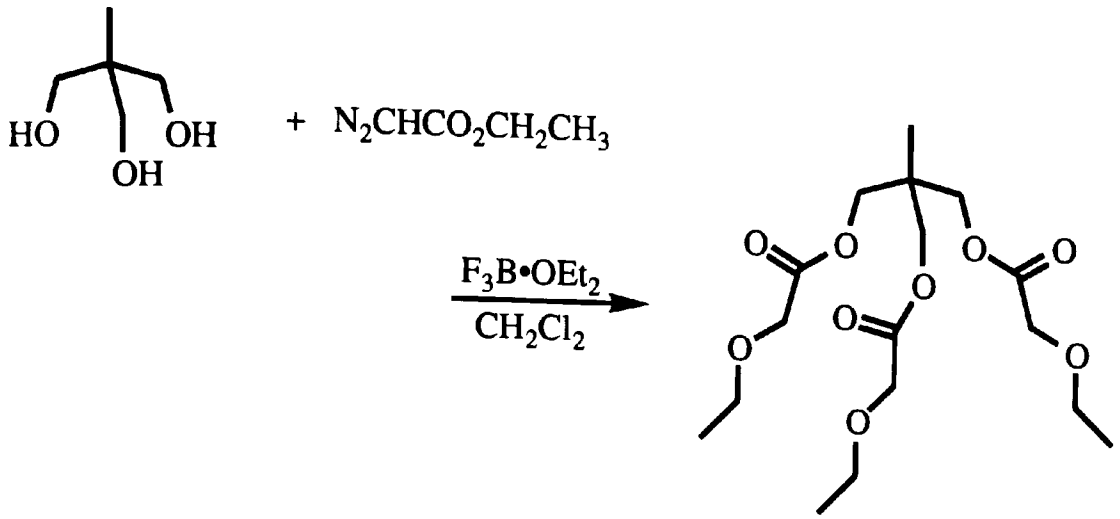
Trace of 300 MHz ^1H NMR of bicyclo dimer in $CDCl_3$.

With the failure of this key first step, the synthesis of 1,1,1-tris(chloromethoxy-methyl)ethane was abandoned in favor of the synthesis of 1,1,1-tris(chloroethoxymethyl)-ethane (**53**). The addition of a methylene unit to each leg in the tripod should decrease the chances of intramolecular cyclization. Eight membered rings are not thermodynamically favored and therefore cyclization should not occur.



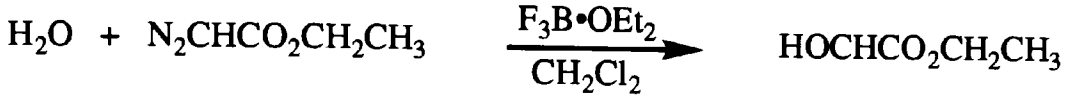
Scheme 6.7.

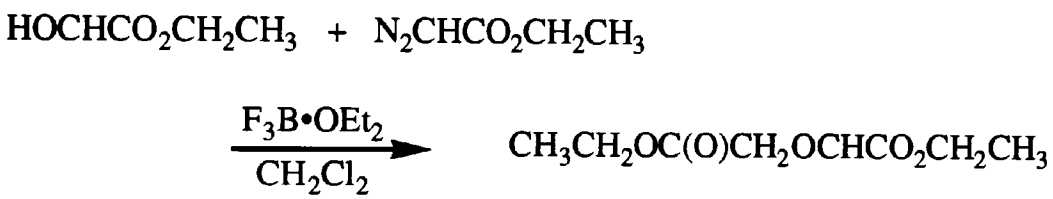
In a 1976 article by Güggi et al.[76], the preparation of 1,1,1-tris(3'-ethoxycarbonyl-2'-oxapropyl)propane from 1,1,1-tris(hydroxymethyl)propane and diazoethyl acetate in dichloromethane is reported. By substituting the commercially available compound 1,1,1-tris(hydroxymethyl)ethane for 1,1,1-tris(hydroxymethyl)propane under the same conditions, it is possible to produce 1,1,1-tris(3'-ethoxycarbonyl-2'-oxapropyl)ethane (**51**) (see Scheme 6.8). It is imperative that the trisalcohol be completely dry prior to reaction with diazoethyl acetate to prevent unwanted side reactions (see Scheme 6.9).



51

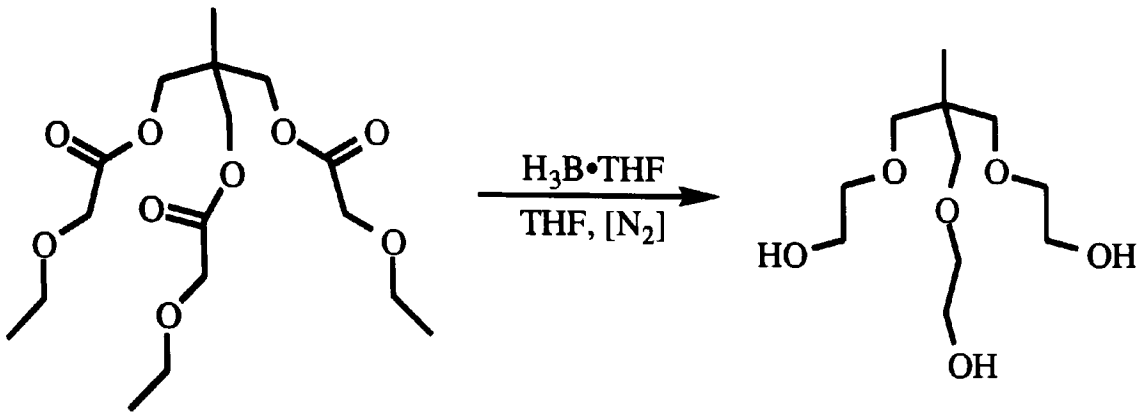
Scheme 6.8.



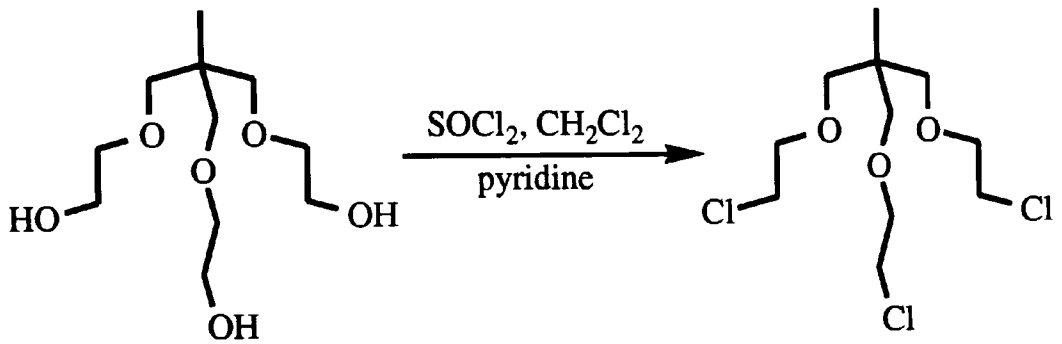


Scheme 6.9.

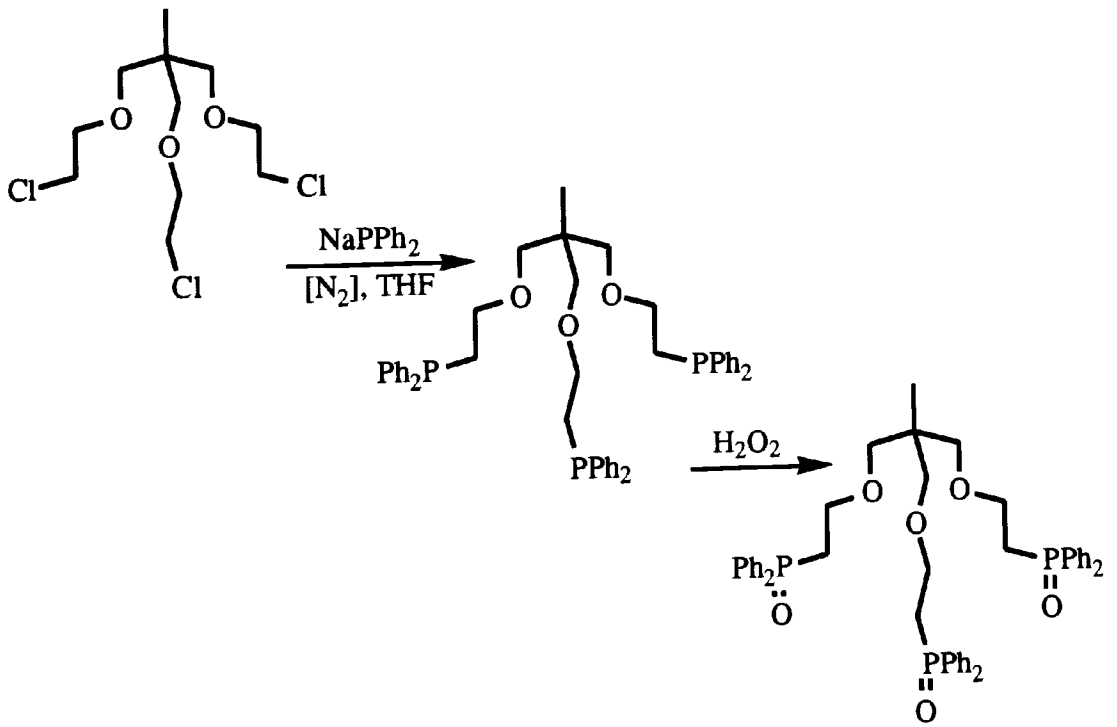
Subsequent conversion of the trisacetate ester to the trisalcohol ether 1,1,1-tris(hydroxy-ethoxymethyl)ethane (**52**) was accomplished through a borane reduction as depicted in Scheme 6.10. Substitution of the hydroxyl groups by chloro groups proceeded cleanly to produce the trichloro ether 1,1,1-tris(chloroxyethoxymethyl)ethane (**53**) (see Scheme 6.11). Finally, the trichloro tripod was phosphinated (as previously described in Chapter 4) followed by oxidation with hydrogen peroxide to yield the final product, 1,1,1-tris(diphenylphosphorylethoxymethyl)ethane (**55**) (see Scheme 6.12).



Scheme 6.10.



Scheme 6.11.



Scheme 6.12.

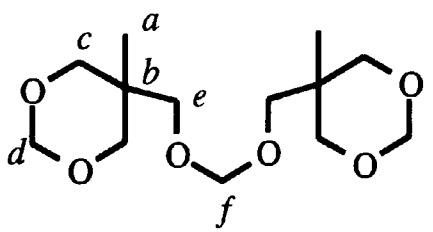
6.3 Experimental Procedure

6.3.1 Starting Materials

Dichloromethane was distilled under nitrogen from calcium hydride immediately before use. The compound 1,1,1-tris-(hydroxymethyl)ethane was purchased from Strem Chemical Company and was dried prior to use in vacuo. All other chemicals were purchased from Aldrich Chemical Company and were used without further purification.

6.3.2 Attempted preparation of $H_3C(CH_2OCH_2Br)_3$, (**48**)

Paraformaldehyde (1.138 g, 37.99 mmol) and 1,1,1-tris(hydroxymethyl)ethane (1.134g, 9.439 mmol) were added to a Schlenk tube. The tube was sealed with a rubber septum, so that it was open only to the nitrogen line and a Hg bubbler. Water (0.676 g, 37.6 mmol) was added via syringe. The reaction tube was cooled in an ice bath and stirring initiated. PBr_3 (1.192 mL, 12.53 mmol) was slowly added, dropwise, via syringe. After waiting 15 minutes, the ice bath was removed. The mixture was left to react for overnight. All of the solids eventually went into solution. The next day there were two layers, an upper clear, colorless layer, and a lower clear, yellow layer. Both layers were washed into a separatory funnel with water and extracted with benzene. The resulting benzene phase was washed three times with water, dried over $MgSO_4$, and filtered. Solvent was removed on the rotary evaporator at 40°C. ^1H and ^{13}C NMR revealed that none of the desired product was produced, only the by-product below was formed:



^1H (300 MHz, $CDCl_3$): H^a(δ0.85 6H, s); H^c(δ3.56 8H, s); H^d(δ4.78 4H, m); H^e(δ3.61, 4H, m); H^f(δ4.68 2H, s).

^{13}C (75 MHz, $CDCl_3$): C^a(δ18.1); C^b(δ34.9); C^c(δ73.1); C^d(δ94.1); C^e(δ70.3); C^f(δ95.8).

^{13}C-^1H HeteroCOSY confirmed all expected cross-peaks.

6.3.3 Attempted preparation of $H_3C(CH_2OCH_2Cl)_3$, (**49**)[75]

Trimethylchloro-silane (~50 mL) was added to a Schlenk flask along with a magnetic stirbar. Stirring was initiated and paraformaldehyde (3.603 g, 120.0 mmol) was added slowly. Most of the paraformaldehyde was allowed to dissolve before 1,1,1-tris(hydroxymethyl)ethane (3.993 g, 33.23 mmol) was added. The flask was fitted with a bubbler filled with aqueous sodium hydroxide. Slow nitrogen flow was maintained to prevent water from diffusing back into the reaction flask. Some of the NaOH pellets were observed to dissolve as the reaction progressed. After reacting for 72 hours, the reaction was quenched with slivers of ice. The solution was washed into a separatory funnel with water and extracted with benzene. The resulting benzene phase was washed three times with brine, dried over $MgSO_4$, and filtered. Solvent was removed on the rotary evaporator. ^1H and ^{13}C NMR revealed that none of the desired product was produced, only the by-product reported in section 6.3.2 was observed.

6.3.4 Attempted preparation of $H_3C(CH_2OCH_2CO_2K)_3$, (**50**)[67]

Tert-butyl alcohol (excess, ~150 mL) was added to a three-neck, round bottom flask. Potassium metal (5.742 g, 146.9 mmol) was added to the alcohol with stirring. The potassium reacted quickly at first, but slowed as the solution became saturated. The solution was refluxed until all of the potassium had reacted. Bromoacetic acid (10.211, 73.490 mmol) was then added to the reaction pot. After a one hour period, 1,1,1-

tris(hydroxymethyl)ethane (2.910 g, 24.22 mmol) was added. Reflux was maintained for two hours. The solution was left to react at room temperature overnight. The reaction mixture was washed into a separatory funnel with water and extracted twice with ethyl acetate. The ethyl acetate solutions were combined, washed twice with water, and dried over $MgSO_4$. Solvent was removed on the rotary evaporator to yield 3.01 g of a clear, yellow oil. ^1H and ^{13}C NMR revealed that none of the desired product was produced.

6.3.5 Preparation of $H_3C(CH_2OCH_2CH_2OC(O)CH_3)_3$, (**51**)

The compound 1,1,1-tris(hydroxymethyl)ethane (10.108 g, 84.124 mmol) along with a magnetic stirbar was added to a Schlenk flask. The flask was then sealed with a rubber septum. Dry, freshly distilled dichloromethane (~250 mL) was added to the flask via canula. The flask was lowered into an ice bath and stirring of the reaction mixture was initiated. The tris-alcohol was not soluble in dichloromethane. Borontrifluoro etherate (2 mL) was added to the solution via syringe. Once the flask had cooled, very slow addition of ethyl diazoacetate (29.194 mL, 277.6 mmol) was begun via syringe. The solution effervesced quite violently upon addition of the ethyl diazoacetate. Once addition was complete, the reaction flask was fitted with a reflux condenser, which was topped with a T-tube adapter. One arm of the adapter was connected to the nitrogen line and the other was attached to an oil-bubbler as depicted in Figure 5.1. The stopcock on the reaction flask was closed so that nitrogen flow was redirected over the top of the condenser. The solution was heated and reflux was maintained for 12 hours. The solution remained clear, but gradually became darker eventually changing from yellow to dark purple. Heating was ceased and the solution allowed to cool. Any excess ethyl diazoacetate was quenched by adding methanol. The solution was then washed into a separatory funnel with diethyl ether and washed three times with brine. The organic extracts were dried over $MgSO_4$ and the solvent was removed on the rotary evaporator leaving a clear, amber liquid. The crude oil

was then vacuum distilled (180°C at 0.150 torr) using a vacuum-jacketed, one-piece, vigerux distillation apparatus to yield a clear, yellow oil (24.49 g, 76.94%). Close analysis of the ^1H NMR integration revealed the presence of a small amount of $O(CH_2CO_2CH_2CH_3)_2$.

$$H_3C^a(C^bH_2OC^cH_2C^dH_2OC^e(O)C^fH_3)_3$$

^1H (200 MHz, $CDCl_3$): H^a(δ1.00 3H, s); H^c(δ3.44 6H, s); H^d(δ4.03 6H, s); H^f(δ4.18 6H, q); H^g(δ1.24 9H, t).

^{13}C (50 MHz, $CDCl_3$): C^a(δ17.0); C^b(δ41.0); C^c(δ68.9); C^d(δ74.3); C^e(δ171); C^f(δ60.59); C^g(δ14.1).

6.3.6 Preparation of $H_3C(CH_2OCH_2CH_2OH)_3$, (**52**)[56,61]

Compound **51** (62.01 g; 0.2260 mol) was dissolved in dry THF under N_2. Borane (460 mL, 1M in THF) was added dropwise by canula. Under flow of nitrogen, the reaction flask was topped with a reflux condenser. The condenser was then fitted with a tube adapter which was, in turn, connected to an oil bubbler as in Figure 5.1. The solution was refluxed overnight. The solution remained yellow and clear. The reaction flask was cooled in an ice bath and the reaction quenched by slowly adding deionized water. Water was added until the solution ceased to effervesce. The solution was then acidified with HCl and allowed to stir for 15 minutes. Anhydrous potassium carbonate was added until the reaction mixture separated into an aqueous and an organic phase. The organic phase was decanted and the THF removed on the rotary evaporator. Any remaining boric acid was removed by redisolving the residue in acetone, followed by refrigeration and subsequent filtration. The acetone was removed on the rotary evaporator at 40°C.

Compound **52** (49.3 g; 86.5%) was clear and viscous. Close analysis of the ^1H NMR integration reveals that there is a small amount of $O(CH_2CH_2OH)_2$.

$$H_3C^a(C^bH_2OC^cH_2C^dH_2O^eH)_3$$

^1H (200 MHz, $CDCl_3$): H^a(δ0.83 3H, s); H^c(δ3.28 6H, s); H^d(δ3.45 6H, m); H^e(δ3.59 7H, m).

^{13}C (50 MHz, $CDCl_3$): C^a(δ17.6); C^b(δ40.7); C^c(δ61.2); C^d(δ72.2); C^e(δ73.6).

6.3.7 Preparation of $H_3CC(CH_2OCH_2CH_2Cl)_3$, (**53**)

Methylene chloride (~250 mL of HPLC grade) was added to a three-neck, round bottom flask. Pyridine (10.0 mL, 124 mmol) and compound **52** (8.42 g, 33.4 mmol) were added to the solution with stirring. The flask was cooled in an ice bath.Thionyl chloride (7.97 mL, 110 mmol) was slowly added. The solution change from colorless to deep yellow as the thionyl chloride was added. The flask was fitted with a reflux condenser which was topped with a $CaCl_2$ drying tube. The solution was refluxed overnight. The solution remained clear, but its color changed to red. The flask was cooled in an ice bath and the excess thionyl chloride was quenched by adding slivers of ice. The solution was washed into a separatory funnel with more methylene chloride. The methylene chloride solution was then washed three times with brine, dried over $MgSO_4$, and filtered. The solvent was removed on the rotary evaporator. The product, compound **53** (7.43g, 72%) was a viscous brown oil. Close analysis of the ^1H NMR integration reveals that there is a small amount of $O(CH_2CH_2Cl)_2$.

$$H_3C^aC^b(C^cH_2OC^dH_2C^eH_2Cl)_3$$

^1H (200 MHz, $CDCl_3$): H^a(δ0.92 3H, s); H^c(δ3.33 6H, s); $H^{d,e}$(δ3.60 12H, m).

^{13}C (50 MHz, $CDCl_3$): C^a(δ17.2); C^b(δ41.1); C^c(δ73.3); C^d(δ71.4); C^e(δ42.8).

IR revealed no OH peak.

6.3.8 Preparation of $H_3CC(CH_2OCH_2CH_2PPh_2)_3$, (**54**)

Compound **53** (7.43 g, 24.2 mmol) was added to a three neck, round bottom flask along with a magnetic stirbar. The flask was sealed with rubber septum. Dry, freshly distilled THF (~100 mL) was added to the flask via canula. A solution of sodium diphenylphosphide in THF (300 mL of a 0.333 M solution, 100 mmol) was added dropwise to the reaction pot via canula with stirring. The formation of compound **54** was confirmed by ^{31}P NMR.

^{31}P (121 MHz, THF): P(δ–19.8) with an external H_3PO_4 standard.

6.3.9 Preparation of $H_3CC(CH_2OCH_2CH_2P(O)Ph_2)_3$, (**55**)

The solution containing compound **54** from section 6.3.8 was opened to air. Distilled water (100 mL) was added to the solution. The flask was lowered into an ice bath and stirring initiated. Hydrogen peroxide (~30 mL of a 30% aqueous solution) was added dropwise to the solution. The reaction was very vigorous. The dichloromethane layer changed from brown to yellow. The ice bath was removed and the solution warmed to room temperature. The mixture was left to react for eight hours. The solution was washed into a separatory funnel with dichloromethane. The organic phase was washed twice with brine, dried over $MgSO_4$, and filtered. Solvent was removed on the rotary evaporator at 45°C. The residue was a mixture of $HC(CH_2OCH_2CH_2P(O)Ph_2)_3$, $HOP(O)Ph_2$, and $HP(O)Ph_2$, which was separated using column chromatography (silica gel, 5% CH_3OH: 95% CH_2Cl_2).

$H_3C^aC^b(C^cH_2OC^dH_2{}^eCH_2P(O)Ph^{f\text{-}i}{}_2)_3$

^1H (300 MHz, $CDCl_3$): H^a(δ0.44 3H, s); H^c(δ2.77 6H, s); H^d(δ3.55 6H, d of t; $^3J_{PH}$=11.1 Hz); H^e(δ2.52 6H, d of t; $^2J_{PH}$=11.4 Hz); $H^{g,h}$(δ7.43 24H, m); H^i(δ7.68 6H, m).

^{13}C (75 MHz, $CDCl_3$): C^a(δ16.9); C^b(δ40.1); C^c(δ73.2); C^d(δ64.6); C^e(δ30.5, $^1J_{PC}$=71.2 Hz); C^f(δ133, $^1J_{PC}$=99.8 Hz); C^g(δ129, $^3J_{PC}$=11.7 Hz); C^h(δ132, $^2J_{PC}$=2.0 Hz); C^i(δ131, $^4J_{PC}$=9.6 Hz).

^{31}P (121 MHz, $CDCl_3$): (δ30.3) with an external H_3PO_4 standard.

^{13}C-^1H HeteroCOSY confirmed all expected cross-peaks.

CHAPTER VII

SUMMARY AND CONCLUSIONS

A series of tripodal triphosphines and their oxides have been synthesized for the chelation of lanthanides and actinides in nuclear waste streams. These ligands have either undergone or are scheduled to undergo testing via extraction studies at Los Alamos National Laboratory. All ligands were characterized by multinuclear and two-dimensional NMR spectroscopy.

The first prototype submitted for testing at Los Alamos, compound **2**, was found to be ineffective for the extraction of Am (III) or Eu (III) ions from aqueous solutions, even at high ligand concentrations. It was determined through molecular modeling studies, that the methylene linkages or "legs" of the tripod were too short; therefore, the bite-size of the ligand was too small to effectively coordinate the metal ions (see Figure 2.1). In light of this, several synthetic strategies were employed to lengthen the legs of the tripod.

Repeated attempts at the homologation of the compound **2** failed due to the neopentyl nature of the starting material. Reaction of 1,1,1-tris(chloromethyl)ethane with potassium cyanide under various conditions resulted in only mono- and di-substituted products. In attempted preparations with lithium acetylide, lithiomethyldiphenylphosphine oxide, and sodium diethylmalonate enolate, little or no reaction was observed. Therefore, a complete synthetic strategy for the ethyl-legged tripod 1,1,1-tris(dialkylphosphorylethyl)-methane was developed.

In the synthesis, the commercially available compound diethyl-3-hydroxy gluterate was converted in several steps to 1,1,1-tris(hydroxyethyl)methane. Subsequent reaction with thionyl chloride in the presence of pyridine yielded the trichloro tripod 1,1,1-tris(chloroethyl)methane (**22**). Substitution of dialkylphosphino groups for the chloro groups of compound **22** followed by oxidation with hydrogen peroxide produced the

tripodal triphosphine oxides of interest. Compounds containing dimethyl-, diethyl- and diphenylphophoryl groups were all synthesized and characterized.

Compound **24**, 1,1,1-tris(diphenylphosphorylethyl)-methane, was found to extract in very high efficiency both Am (III) and Eu (III) ions from aqueous solution. Compounds **28** and **32**, 1,1,1-tris(dimethylphosphorylethyl)methane and 1,1,1-tris(diethylphosphoryl-ethyl)methane, respectively, await analytical testing.

Prototype three 1,1,1-tris(diphenylphosphorylpropyl)methane (**47**) was synthesized from the commercially available compound nitomethane trispropanol. Removal of the nitro group through a free radical elimination reaction followed by hydrogenation using Adam's catalyst resulted in the formation of 1,1,1-tris(hydroxypropyl)methane. As in the previous synthetic series, subsequent reaction with thionyl chloride in the presence of pyridine yielded the analogous trichloro tripod 1,1,1-tris(chloropropyl)methane (**44**). Phosphination of **44** with sodium diphenylphosphide followed by oxidation with hydrogen peroxide produced the product, compound **47**.

Prototype four 1,1,1-tris(diphenylphosphorylethoxymethyl)ethane (**55**) differs from prototypes one, two, and three in that its legs contain ether linkages. These linkages should increase the flexibility of the tripod and lessen steric strain during chelation. The oxygen atoms may also act as electron donors to aid in the coordination of metal ions as observed in crown ethers. Compound **55** was synthesized from the commercially available compound 1,1,1-tris(hydroxymethyl)ethane. Reaction of the trialcohol with ethyl diazoacetate followed by borane reduction resulted in the compound 1,1,1-tris(hydroxy-ethoxymethyl)ethane (**52**). Substitution of the hydroxyl groups by chloro groups produced 1,1,1-tris(chloroethoxymethyl)ethane (**53**), which was then phosphinated with sodium diphenylphosphide to yield 1,1,1-tris(diphenylphosphinoethoxymethyl)ethane (**54**). Oxidation of **54** with hydrogen peroxide produced 1,1,1-tris(diphenylphosphoryl-ethoxymethyl)ethane **55** in high yield.

Prototypes three and four still await analytical testing to determine their extraction and separation abilities with respect to lanthanide and actinide ions.

Future synthetic targets should include the methyl, ethyl, and butyl derivatives of both 1,1,1-tris(diphenylphosphorylpropyl)methane and 1,1,1-tris(alkylphosphoryl-ethoxymethyl)ethane. Further coordination studies involving all of the aforementioned ligands to determine both their affinity towards hard/soft ions and their true coordination state should be performed. X-ray crystal structures of the coordinated ligands should determine whether chelation plays a major part in extraction efficiency as postulated. Although coordination compounds with rings involving ten or more atoms are not common, some have been isolated and characterized in the work of both Kapoor[77,78] and Bennett and Clark.[79]

Future work should also include chelation studies involving the parent tripodal triphosphine ligands towards softer acids. Tetraphos (**1**) has been extensively studied as a ligand for the coordination of transition metals and shoul serve as a model for studies including 1,1,1-tris(diphenylphosphinoethyl)methane(**23**), 1,1,1-tris(diphenylphosphino-propyl)methane(**46**), and 1,1,1-tris(diphenylphosphinoethoxymethyl)ethane(**54**).

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