Dimetalation of Trivalent Organophosphines

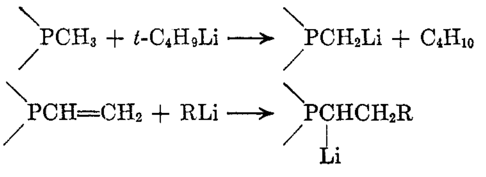
DONALD J. PETERSON AND JEROME H. COLLINS

The Procter and Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239

Received March 3, 1966

Mass spectral and ^{31}P nmr data have been obtained which demonstrate that dimethyl(alkyl and aryl)phosphines react with *t*-butyllithium to form, in addition to the expected monolithio compounds, varying amounts of dimetalated phosphines (up to 35%). In distinct contrast, di-*n*-hexylmethylphosphine has been found to undergo predominant monometalation under similar conditions.

In the previous papers of this series[1,2] two independent methods for the preparation of phosphinoalkyllithium compounds were reported. Firstly, it was found that dimethylphenylphosphine (I), dimethyldodecylphosphine (II), and diphenylmethylphosphine reacted with *t*-butyllithium to give the corresponding phosphinomethyllithium compounds in yields varying from 14–54%. Secondly, it was demonstrated that certain phosphinoalkyllithium compounds could be obtained by the nucleophilic additions of *n*- and *t*-butyllithium to vinylphosphines.



The phosphinomethyllithium compounds resulting from the metalation reactions were characterized by carbonation and by deuteration.[1] Although carbonation afforded the expected monocarboxylic acids from metalated I and metalated diphenylmethylphosphine as the only isolable products, derivatization of metalated II with deuterium oxide gave, in addition to the expected II-d_1 (56.2%), some (20.8%) II-d_2.[1] We now wish to report the results of a study that was conducted for the purpose of determining the mode of formation of II-d_2.

At the onset of this study, two reasonable possibilities appeared to exist for the formation of dideuterated phosphines from successive reactions of I and II with *t*-butyllithium and deuterium oxide, *i.e.*, from dimetalated dimethylphosphines (IV, reaction 1),[3] or from a relatively rapid transmetalation process (reaction 2) during the quenching reaction.

$$\mathrm{RP(CH_3)_2 + 2(CH_3)_3CLi \longrightarrow}$$
$$\underset{\mathrm{IV}}{\mathrm{RP(CH_2Li)_2}} \xrightarrow{\mathrm{D_2O}} \mathrm{RP(CH_2D)_2} \quad (1)$$

$$\mathrm{RP(CH_3)_2 + (CH_3)_3CLi \longrightarrow}$$
$$\underset{\mathrm{V}}{\mathrm{RP(CH_3)CH_2Li}} \xrightarrow{\mathrm{D_2O}} \mathrm{RP(CH_3)CH_2D} \xrightarrow[\mathrm{(CH_3)_3CLi}]{\text{V or}}$$
$$\mathrm{RP(CH_3)CHDLi}\text{ and/or }\mathrm{RP(CH_2Li)CH_2D} \xrightarrow{\mathrm{D_2O}} \mathrm{RPC_2H_4D_2} \quad (2)$$

Evidence for reaction scheme 1 has now been obtained by a detailed mass spectral analysis of a series of deuterium oxide quenched metalated tertiary phosphines, and by ^{31}P nmr spectral analysis of the lithium compounds.

The mass spectral data obtained from a series of metalations of I, II, and di-*n*-hexylmethylphosphine (III) by *t*-butyllithium in pentane, and subsequent characterization with deuterium oxide, are shown in Table I. The mass spectra were obtained on an Atlas CH-4 mass spectrometer using a high temperature inlet system maintained at 190°. The phosphines were analyzed as the corresponding phosphine sulfides since sulfides gave molecular ion peaks of appreciable intensity, even at low energies. Also, the phosphine sulfides were stable in the mass spectrometer inlet system, and unlike the phosphines, stable to air oxidation. All deuterium incorporation data were obtained by comparing the isotopic patterns of the molecular ions of the deuterated compounds with those of the corresponding undeuterated compounds using an ionizing energy of about 11 ev for the trialkylphosphine sulfides and generally 14 ev for dimethylphenylphosphine sulfide. This voltage was used instead of the more conventional 70 ev since the peaks at $M - 1$ and $M - 2$ were eliminated from the spectra at the lower energy, thus simplifying the analyses. Figures 1b and 1a show a comparison of the molecular ion patterns obtained for a sample containing 47.2% I-d_1 and 5.6% II-d_2 (Table I, expt 1) and the corresponding undeuterated dimethylphenylphosphine sulfide, respectively.[4]

A consideration of the data in Table I allows the following arguments to be made against transmetalation and in favor of dimetalation. (1) Quenching of the metalation reaction mixture with deuterium oxide was established to be rapid enough (presumably diffusion controlled) to prevent any metalation of $R(CH_3)PCH_2D$ by *t*-butyllithium from occurring, since in two independent experiments it was demonstrated that II (Table I, expt 8) and I (Table I, expt 7) were metalated only to the extent of 13 and 15%, respectively, during 4 hr of contact with the organolithium compound. Intuitively, it is inviting to conclude that the phosphinocarbanions would not be sufficiently more reactive than *t*-butyllithium to effect substantial transmetalation (reaction 2) during the quenching process.[5] Also, the possibility of any exchange between $RP(CH_3)_2$

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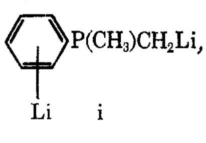
[1] D. J. Peterson and H. R. Hays, *J. Org. Chem.*, **30**, 1939 (1965).

[2] D. J. Peterson, *ibid.*, **31**, 950 (1966).

[3] For the sake of clarity, the other possible dimetalated isomers, $R'CHLiP(CH_3)CH_2Li$ and i, have been omitted from reaction scheme 1.



i

[4] Attempts were made to determine the positional distribution of deuterium within the molecule of deuterated dimethylphenylphosphine sulfide by measuring the isotopic ratios of the $(M - CH_3)^+$ ion at *m/e* 155 and the $C_6H_5^+$ ion (*m/e* 77). However, in both cases other ions (namely, *m/e* 154 and *m/e* 78) were present in the spectrum, even at low electron energies, and these peaks interfered with the analysis of the deuterium content of these ions.

[5] For a detailed discussion of possible complicating side reactions resulting from quenching of certain acid-base systems with deuterium oxide, see, for example, D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 44.

TABLE I

DERIVATIZATION OF METALATED METHYLPHOSPHINES[a] WITH DEUTERIUM OXIDE[b]

Expt	Phosphine	Time of metalation temp, °C	Molar ratio of t-C_4H_9Li/phosphine	% of Phosphine-containing 0-3 deuterium atoms/phosphine molecule: 0	1	2	3	Av deuterium atoms/molecule
1	I	3 da 20	1:1	47.2	47.2	5.6	0	0.58
2	I	3 da 20	2:1	36.7	55.6	7.3	0.4	0.71
3	I	3 da 20	4:1	36.2	54.7	8.8	0.4	0.73
4	I	7 da 20	4:1	16.5	67.8	15.0	0.7	1.0
5	I	3 da 20	2.4:1	26.7	62.3	10.8	0.2	0.85
6	I	3 da 60	2.4:1	13.2	57.3	27.9	1.6	1.18
7	I	4 hr 20	1:1	85.8	13.5	0.7	0	0.15
8	II	4 hr 20	1:1	87.4	12.1	0.5	0	0.13
9	II	4 da 20	2:1	22.2	56.2	20.8	0.7	0.99
10	III	3 da 20	2:1	17.4	82.0	0.6	0	0.83

[a] The metalations were carried out in metalation tubes as previously described.[1] [b] An excess of deuterium oxide was added dropwise (1–3 min) to the rapidly stirred, chilled metalation mixture. The organic layer was then removed by syringe and added dropwise to a suspension of excess sulfur in benzene.

TABLE II

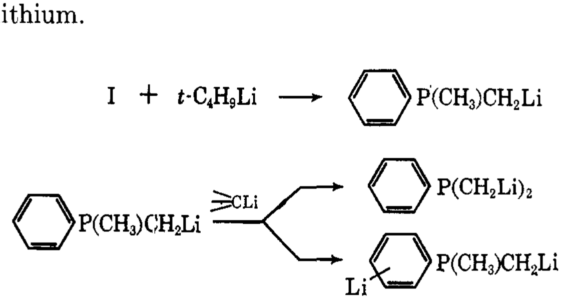
^{31}P NMR SPECTRAL DATA OF METALATED DIMETHYLPHENYLPHOSPHINE

			% compn of metalation mixture, signals, ppm					Deuterium content of quenched aliquots				
								Deuterium content				Av deuterium atoms/
Expt	t-C_4H_9Li/I	Time, days (temp, °C)	22.9	21	25	27.8	45.5	d_0	d_1	d_2	d_3	molecule
1	1/1	3 (20)	65	7	7		21					
2	1/1	3 (60)	54	8	8	8	22					
3	2.4/1	3 (45)	64	11	12	9	4	6.4	62.9	29.1	1.6	1.26
4	2.4/1	4 (60)	58	12	15	10	5	7.0	57.0	34.7	1.3	1.3

and $LiOD/D_2O$ and the remote possibility of any exchange between $RP(S)(CH_3)_2$ and $LiOD/D_2O$ under the reaction conditions employed was ruled out experimentally. (2) Furthermore, since it has been established (Table I, expt 7 and 8) that the reactions of I and II with t-butyllithium are slow enough to preclude the possiblity of any significant further metalation during the quenching process, the incorporation of more than 1 deuterium atom/molecule of phosphine on the average is consistent only with reaction 1. (3) The most convincing argument against transmetalation, but for dimetalation, was obtained from the results of the metalation of III (Table I, expt 10). Since it has been established previously[1] that α-methylene protons are not readily attacked by t-butyllithium, III would be expected to undergo predominantly monometalation and therefore afford no III-d_2 on deuteration if reaction 2 is of no consequence. Consistent with this concept is the finding that essentially only III-d_1 (82%) was realized from this reaction. This finding therefore excludes reaction 2 from consideration since an appreciable amount of III-d_2 (*ca.* 7–10%) should result if transmetalation, which should not be prohibited in this system, is operative.

Some additional information on the complexity of the metalation reactions was obtained by a combination of ^{31}P nmr spectral analysis of metalated I and II, and mass spectral analysis of deuterium oxide quenched aliquots of the organometallic compounds. As shown in Figure 2, the monometalated I (predominantly methylphenylphosphinomethyllithium) gives rise to a cleanly resolved signal at 22.9 ppm (relative to 85% H_3PO_4), while three poorly resolved signals are apparent at 21, 24.9, and 27.8 ppm. In mixtures containing a higher concentration of starting material a strong signal from nonmetalated I at 45.5 ppm[6] could be seen. Table II contains the results of a series of metalations (in pentane–heptane solvent mixtures) of I in which variations in ratios of t-butyllithium to I, temperature, and reaction times were investigated.[7] Aliquots of expt 3 and 4 were also quenched with deuterium oxide and analyzed for deuterium content. The ^{31}P nmr integration values of the signals, although crude, are in good agreement with the mass spectral data for the number of deuterium atoms incorporated per molecule, if the signals at 21, 24.9, and 27.8 ppm are regarded as dimetalated I.

The formation of three or more dimetalated isomers of I is of interest. Unlike the initial metalation, which has a high degree of selectivity for methyl metalation,[1] the second metalation is relatively nonselective; *i.e.*, ring metalation appears to be competitive with methyl metalation. The position of ring metalation is not known. However, the relatively complex nature of the spectrum suggests that the aromatic nucleus of methylphenylphosphinomethyllithium undergoes metalation in more than one position. Consequently, the following reaction sequence is advanced to account for the experimental findings on the metalation of I by t-butyllithium.



(3)

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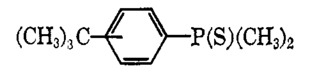
[6] W. A. Henderson and S. A. Buckler, *J. Am. Chem. Soc.*, **82**, 5794 (1960), reported +46 ppm.

[7] Due to the insolubility of metalated I in hydrocarbon solvents, it was necessary to remove the metalation solvents *in vacuo* and dissolve the residue in freshly distilled tetrahydrofuran. The ^{31}P nmr spectral determinations were then made immediately using a Varian HR-60 spectrometer operating at 24.3 Mc. A spinning 9-mm tube was employed.

Under the more drastic conditions (Table II, expt 3 and 4), a small amount of an additional compound was formed. Based on the mass spectral fragmentation pattern, *i.e.*, mol wt 226 (M) and strong peaks at 211 ($M - CH_3$), 194 ($M - S$), and 179 ($M - CH_3 - S$), it has been tentatively concluded that the compound is one of the isomeric *t*-butylphenyldimethylphosphine sulfides.



The formation of a small amount of this compound is not entirely unexpected since it is known that benzene and other aromatic compounds are alkylated by *t*-butyllithium at relatively high temperatures.[8]

Several attempts to similarly analyze II–*t*-butyllithium reaction mixtures by the ^{31}P nmr spectroscopic method failed due to extremely poor resolution. However, based on the finding that di-*n*-hexylmethylphosphine undergoes dimetalation to only a very slight extent (Table I, expt 10), *i.e.*, little α-methylene metalation occurs[9] to give $C_5H_{11}CHLiP(C_6H_{13})CH_2Li$, it is expected that II would form predominantly the symmetrically dimetalated species, $C_{12}H_{25}P(CH_2Li)_2$.

A rationale for the formation of dimetalated phosphines from the reactions of dimethyl(alkyl or phenyl)phosphines with *t*-butyllithium is not readily apparent. Thus, this phenomenon requires that at some concentration monometalated phosphines undergo metalation by *t*-butyllithium at a rate comparable to that of the parent compounds, and/or that the monometalated phosphines are capable of disproportionating.

$$2R(CH_3)PCH_2Li \rightleftharpoons RP(CH_2Li)_2 + RP(CH_3)_2$$

We are unaware of any direct analogies to this type of dimetalation in the literature. However, there have been some examples of related polylithiated species reported recently. For example, Seyferth and Rochow[10] have prepared bis(lithiomethyl)diphenylsilane from the reaction of the corresponding bis(chloromethyl) compound with lithium in ether. Alkynes have been shown to undergo mono-, di-, tri-, and tetrametalation when treated with *n*-butyllithium.[11] Also, Benkeser and Bach demonstrated that ferrocenes undergo dimetalation with *n*-butyllithium and that the dilithio compounds exist in the presence of the parent compounds.[12]

Further chemical characterization of metalated I (from 1.4:1 ratio of *t*-butyllithium–I, 3 days at 20°) by derivatization with chlorotrimethylsilane and subsequent treatment with sulfur was found to be quite complex, and complete resolution of the reaction products was not achieved. In addition to the expected methylphenyl(trimethylsilylmethyl)phosphine sulfide (VI) and bis(trimethylsilylmethyl)phenylphosphine sulfide (VII), some $[(CH_3)_3Si]_2CH\overset{\overset{S}{\uparrow}}{P}(C_6H_5)CH_2Si(CH_3)_3$ (VIII), and a tetrasilyl derivative of I were obtained.

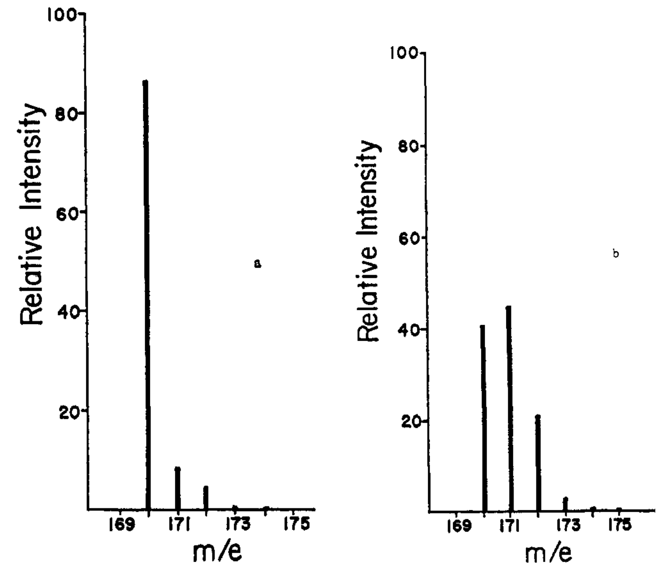


Figure 1.—Mass spectra of dimethylphenylphosphine sulfide (a) and deuterated dimethylphenylphosphine sulfide (b).

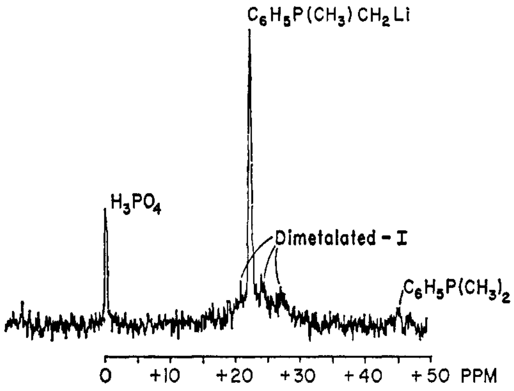


Figure 2.—^{31}P nmr spectrum of metalated dimethylphenylphosphine in tetrahydrofuran.

Since these results differ significantly from derivatization with deuterium oxide, *i.e.*, substantial amounts of tri- and tetraderivatized compounds are obtained, it is apparent that a complicating side reaction is occurring in the former process. We suggest that in the chlorosilane derivatization, unlike the relatively rapid quenching reaction with deuterium oxide, transmetalation is occurring to a significant extent. Consequently, the chlorosilane derivatization method could not be used to establish the kind and ratio of metalated phosphines resulting from the reaction of *t*-butyllithium with I.

Experimental Section

All reactions involving organophosphines and organometallic compounds were conducted under an atmosphere of oxygen-free argon. The air-sensitive compounds were transferred by syringe techniques.

The phosphines were prepared as previously described.[1] The *t*-butylithium was obtained from the Lithium Corp. of America.

Proton nmr spectra were recorded on a Varian HA-100 spectrometer operating at 100 Mc. A H_2SO_4 capillary was used as a field/frequency locking signal. The sweep offset was calibrated with tetramethylsilane as the internal reference to give τ values directly. All samples were dissolved in $CDCl_3$.

Metalation of I. Derivatization with Chlorotrimethylsilane.—To an argon-flushed 180-ml metalation tube[1] there was added by

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[8] J. A. Dixon and D. Fishman, *J. Am. Chem. Soc.*, **85**, 1356 (1963).

[9] This is also consistent with the earlier finding[1] that tri-*n*-butylphosphine is relatively inert to metalation by *t*-butyllithium under these conditions.

[10] D. Seyferth and E. G. Rochow, *J. Am. Chem. Soc.*, **77**, 907 (1955).

[11] (a) K. C. Eberly and H. E. Adams, *J. Organometal. Chem.*, **3**, 165 (1965); (b) R. West, P. A. Carney, and I. C. Mineo, *J. Am. Chem. Soc.*, **87**, 3788 (1965).

[12] R. A. Benkeser and J. L. Bach, *ibid.*, **86**, 890 (1964).

syringe 6.9 g (0.05 mole) of I, 38 ml of 1.8 *M* *t*-butyllithium (0.07 mole), and 40 ml of pentane. A yellow precipitate was observed within 0.5 hr. Subsequent to stirring for 3 days at room temperature, 7.8 g (0.08 mole) of chlorotrimethylsilane was slowly added to the chilled metalation mixture resulting in the formation of a white precipitate. After warming to room temperature and an additional 3 hr of stirring, the reaction mixture was slowly added to a dispersion of 1.75 g (0.055 g-atom) of sulfur in 25 ml of benzene (exothermic reaction) and stirred overnight.

The reacion mixture was then washed thoroughly with aqueous ammonium chloride and concentrated. A ^{31}P nmr spectrum of the concentrate revealed the presence of at least four compounds, as evidenced by distinct signals at −32.4, −36.8, −40.4, and −44.7 ppm, corresponding to *ca.* 26, 49, 19, and 6% of the total phosphorus, respectively. Also, a minimum of four compounds was shown to be present by glpc on a 5-ft 10% Apiezon Fluropak column at 240°. These compounds had the following retention times: 3 min, dimethylphenylphosphine sulfide; 6 min, VI; 9 min, VII; and 13 min, VIII.

The complex reaction mixture was partially resolved by alumina column chromatography. Elution with several solvents afforded the following fractions: (1) hexane–sulfur; (2) 3:2 hexane–carbon tetrachloride, 2.87 g of a mixture of VII and VIII in the ratio of *ca.* 3:1 [The VIII was separated by glpc. A ^1H nmr spectrum consisted of signals centered at τ 2.34 (aromatic), 8.13 and 8.28 (two ABX quartets, J_{AP} = 16.7 cps, J_{BP} = 12.8 cps, and J_{AB} = 13.9 cps, methylene), 8.7 (doublet, J = 16.1 cps, methine), 9.52 (singlet, methyl), 10.02 (singlet, methyl), and 10.08 (singlet, methyl) in the area ratios of *ca.* 5:2:1:9:9:9, respectively. Consistent with the structure assignment, the mass spectrum of VIII exhibited a strong parent peak of 386. In addition, a mass peak of 458 was observed, which suggests the presence of a small amount of the tetrasilyl derivative of I. The VII was shown to be identical with an authentic sample.]; (3) carbon tetrachloride, 0.7 g of VI; (4) benzene, 3.44 g of VI, mp 55–56°.

Anal. Calcd for $C_{11}H_{19}PSSi$: mol wt, 242; C, 54.6; H, 7.85. Found: mol wt (mass spectral), 242; C, 55.1; H, 8.3.

The compound exhibited a ^{31}P nmr signal at −36.6 ppm and ^1H signals centered at τ 2.35 (aromatic), 8.01 (doublet, J = 12.6 cps, methyl), 8.3 (doublet, J = 16.4 cps, methylene), and 9.91 (singlet, methyl) in the correct ratios.

Continued elution with benzene produced fraction 5, a mixture of VI and dimethylphenylphosphine sulfide. No attempt was made to resolve this mixture.

Preparation of Bis(trimethylsilylmethyl)phenylphosphine Sulfide (VII).—To a solution of trimethylsilylmethylmagnesium chloride, prepared[13] from 24.5 g (0.2 mole) of chloromethyltrimethylsilane and an excess (7.2 g, 0.3 g-atom) of magnesium turnings in 200 ml of tetrahydrofuran, there was added dropwise 15.7 g (0.09 mole) of phenyldichlorophosphine dissolved in 65 ml of tetrahydrofuran. Subsequent to the complete addition, the reaction mixture was refluxed for 2.5 hr, cooled, and hydrolyzed with chilled aqueous ammonium chloride. Approximately one-third of the organic layer was removed and added slowly to an excess of sulfur dispersed in benzene and stirred for 0.5 hr. The excess sulfur was removed by filtration and the filtrate was concentrated to give a solid that was dissolved in boiling hexane. On cooling, 6.5 g (65%) of VII, mp 89–91°, crystallized. A second crystallization from the same solvent narrowed the melting point to 90–91.5°.

Anal. Calcd for $C_{14}H_{27}PSSi_2$: C, 53.5; H, 8.6. Found: C, 53.9; H, 9.4.

The phosphine sulfide exhibited a ^{31}P nmr signal at −38.8 ppm and ^1H nmr signals centered at τ 2.35 (aromatic), 8.37 (doublet, J = 15.2 cps, methylene), and 9.98 (methyl).

Attempted Base-Catalyzed Hydrogen Exchange of Dimethylphenylphosphine Sulfide.—To a suspension of lithium deuteroxide and deuterium oxide in hexane, obtained from the addition of 1.5 ml (0.1 mole) of deuterium oxide to 14.4 ml (0.02 mole) of 1.4 *M* *n*-butyllithium in hexane, there was added 1.7 g (0.01 mole) of dimethylphenylphosphine sulfide. Subsequent to stirring for 1 hr, the reaction mixture was poured into chilled aqueous ammonium chloride. The organic phase was rapidly extracted with ether, dried over sodium sulfate, and concentrated to give 1.34 g of dimethylphenylphosphine sulfide, mp 40–42°. A mass spectral analysis of the phosphine sulfide revealed the sample to contain 99.4% $\geqslant$P(S)-d_0 and 0.6% $\geqslant$P(S)-d_1.

Acknowledgments.—The authors are grateful to Dr. T. J. Logan for many helpful discussions during the course of this study and to Dr. J. J. McLeskey for the interpretation of one of the nmr spectra.

[13] F. C. Whitmore and H. H. Sommer, *J. Am. Chem. Soc.*, **68**, 481 (1946).

Intramolecular Diels–Alder Reactions. III. Cyclizations of *trans*-Cinnamyl and Phenylpropargyl Phenylpropiolates[1a]

L. H. KLEMM, D. HSU LEE,[1b] K. W. GOPINATH,[1c] AND C. E. KLOPFENSTEIN[1d]

Department of Chemistry, University of Oregon, Eugene, Oregon

Received December 20, 1965

Intramolecular Diels–Alder reactions on crude *trans*-cinnamyl phenylpropiolate and phenylpropargyl phenylpropiolate produced 1-phenyl-3-hydroxymethyl-3,4-dihydro-2-naphthoic acid lactone (II) and 1-phenyl-3-hydroxymethyl-2-naphthoic acid lactone (V), respectively. Structures were assigned on the basis of conversion of II to V, oxidative degradation of II, and analysis of the nmr spectra of II and its di- and trideuterated compounds.

In an earlier communication[2] we reported the syntheses of γ-apopicropodophyllin and one of its analogs by means of intramolecular Diels–Alder condensation of substituted *trans*-cinnamyl phenylpropiolates. The method represents a simple synthetic approach to lignans of the arylhydronaphthalene type. More generally, one may visualize as starting materials in such cyclizations a series of nine types of unsaturated open-chain esters of the formula $Ar(C_2)CO_2CH_2(C_2)Ar'$, where each C_2 unit may take the form of a *cis*-CH=CH, a *trans*-CH=CH, or a C≡C grouping. We have embarked on a program to synthesize all of these types,[3] including the parent (unsubstituted) esters where Ar = Ar′ = phenyl, in order to study the stereochemical requirements of the cyclization process and to elucidate the structures of such products as may result. The present paper is concerned with the syntheses and successful cyclizations of two parent esters, *viz.*, *trans*-cinnamyl phenylpropiolate (I) (Scheme I) itself, and phenylpropargyl phenylpropiolate (IV). Meanwhile, two other parent esters, *trans*-cinnamyl *trans*-cinnamate

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[1] (a) This investigation was supported by Research Grants No. CY-3097 from the National Cancer Institute and No. GM 12730 from the National Institute of General Medical Sciences, U. S. Public Health Service. (b) Research Assistant, 1962–1964. (c) Research Associate, 1962–1964. (d) Research Assistant, 1963–1966.

[2] Paper I: L. H. Klemm and K. W. Gopinath, *Tetrahedron Letters*, 1243 1963).

[3] Paper IV: L. H. Klemm, K. W. Gopinath, D. H. Lee, F. W. Kelly, E. Trod, and T. M. McGuire, *Tetrahedron*, in press.