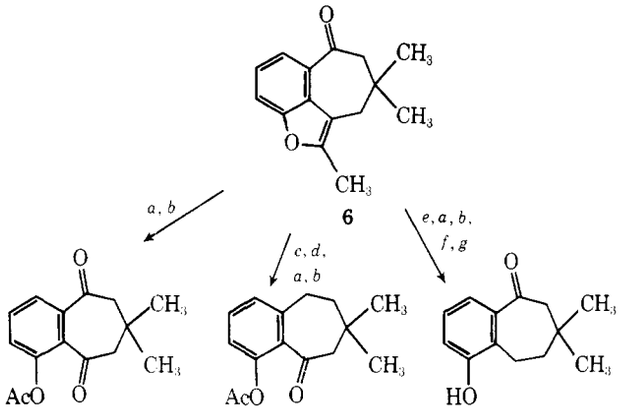
Scheme II



[a] O_3/CH_2Cl_2 (−78 °C). [b] CH_3SCH_3 (25 °C). [c] $TsNHNH_2$/EtOH. [d] $NaCNBH_4$.[7] [e] $LiAlH_4$/THF. [f] H_2NNH_2, KOH/H_2O. [g] H_2CrO_4/CH_3COCH_3.

Cathy Stein for preparation of lactone **9** and early studies of the behavior of **9** with Lewis acids.

References and Notes

(1) A. G. Schultz and R. D. Lucci, *J. Org. Chem.*, **40**, 1371 (1975).
(2) For a related conversion of an α-alkoxycyclohexanone to a seven-membered lactone, see Y. Kishi, M. Aratani, T. Fukuyama, F. Nakatsubo, T. Goto, S. Inoue, H. Tanino, S. Sugiura, and H. Kakoi, *J. Am. Chem. Soc.*, **94**, 9217 (1972).
(3) The Baeyer–Villiger reaction has been demonstrated to occur with retention of configuration; see J. A. Berson and S. Suzuki, *J. Am. Chem. Soc.*, **81**, 4088 (1959), and H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968).
(4) A. G. Schultz and W. Y. Fu, *J. Org. Chem.*, **41**, 1483 (1976).
(5) Construction of the ring system in **11** represents an interesting potential approach to the alkaloid colchicine.
(6) Compounds **2–4, 6, 11, 12–14** give correct elemental analyses.
(7) R. O. Hutchins, C. A. Milewski, and B. E. Maryanoff, *J. Am. Chem. Soc.*, **95**, 3662 (1973).
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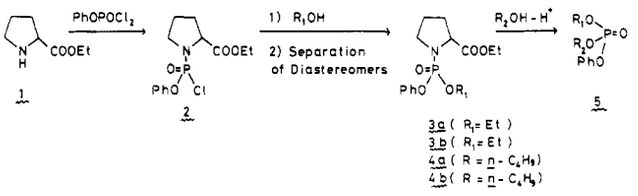
A Practical Method of Preparing Optically Active Dialkyl Phenyl Phosphates

Summary: A practical method for the preparation of optically active dialkyl phenyl phosphates using L-proline ethyl ester and requiring three overall steps is presented.

Scheme I



Sir: For the investigation of mechanistic aspects of chemical and enzymatic solvolysis of phosphotriesters, the use of chiral substrates offers an excellent approach.[1] However, to our knowledge, there have been only two methods for the preparation of optically active phosphotriesters. One[2] utilizes the enzymatic resolution of racemic phosphotriesters, and the other,[3] the first chemical method, employs the stereospecific alcoholysis of optically active tetrahydro-1,3,2-oxazaphosphorine or -oxazaphospholane derivatives. The latter method, however, requires more than five steps[4] to get trialkyl phosphates, and does not seem to be a practical method for obtaining chiral phosphotriesters in general.[5]

Herein we wish to report a new and simple method for the preparation of optically active dialkyl phenyl phosphates using easily available L-proline ethyl ester[6] as a chiral reagent. The reaction sequence of the present method, which is shown in Scheme I, consists of essentially three steps. A separation of diastereoisomeric phosphoramidates and their acid-catalyzed alcoholysis are the key steps.

The phosphoromonochloridate **2**, prepared in situ by the reaction[7] of L-proline ethyl ester (1.3 equiv mol) with phenyl phosphorodichloridate (1 equiv mol) in anhydrous pyridine, was reacted[8] with an excess of ethanol or with 1-butanol to afford a diastereoisomeric mixture of the corresponding alkyl phenyl phosphoramidate (**3** or **4**). The isomers were separated quite easily by column chromatography (silica gel, benzene–ethyl acetate) and isolated by distillation in fair yields: **3a**[9] (40%),[10] bp 173–180 °C (1.5 mm),[11] $[\alpha]^{17}_D$ −67° (*c* 1.7); **3b** (20%), bp 178–179 °C (1.7 mm), $[\alpha]^{16}_D$ −45° (*c* 3.0); **4a** (36%), bp 145 °C (0.015 mm), $[\alpha]^{23}_D$ −60° (*c* 2.6); **4b** (22%), bp 145 °C (0.015 mm), $[\alpha]^{24}_D$ −40° (*c* 3.0).

Acid-catalyzed alcoholysis[13] of each isomer at refluxing temperature gave the corresponding phosphotriester **5**[14] in a state of high optical purity.[15] The yields and physical data are listed in Table I.

Although the result is at present limited to the preparation of optically active dialkyl phenyl phosphates and the yields are not optimized,[16] the present method may well be applicable for the preparation of phosphotriesters in general, and also for other phosphoryl derivatives, such as phosphinates and phosphonates. Research along this line is now in progress in this laboratory and will be reported elsewhere.

Table I. Preparation of Optically Active Dialkyl Phenyl Phosphates by the Acid-Catalyzed Alcoholysis of Diastereomeric Phosphoramidates

Phosphoramidate	Dialkyl phenyl phosphate R_1	R_2	Yield, %	Bp, °C (mm)	$[\alpha]_D$, deg (*c*, °C)
3a	C_2H_5	CH_3	61	80 (0.02)	+3.4 (3.2, 25)
3b	C_2H_5	CH_3	63	76 (0.02)	−3.4 (3.6, 26)
4a	n-C_4H_9	CH_3	51	92 (0.03)	+5.5 (2.7, 21)
4b	n-C_4H_9	CH_3	54	90 (0.02)	−5.1 (2.9, 22)
4a	n-C_4H_9	C_2H_5	28[a]	85 (0.02)	+1.8 (1.5, 19)
4b	n-C_4H_9	C_2H_5	30[b]	85 (0.02)	−2.0 (1.7, 20)
4a	n-C_4H_9	n-C_3H_7	10	100 (0.01)	+0.9 (1.1, 24)
4b	n-C_4H_9	n-C_3H_7	11	100 (0.01)	−0.7 (1.5, 24)

[a] n-Butanolysis of **3b** gave the same compound [$[\alpha]_D$ +2.1° (1.4, 14)] in 19% yield. [b] n-Butanolysis of **3a** gave the same compound [$[\alpha]_D$ −2.0° (1.0, 19)] in 10% yield.

References and Notes

(1) It is established in the solvolysis of other phosphorus derivatives. (a) For general remarks, see: M. J. Gallagher and I. D. Jenkins, *Top. Stereochem.* **3,** Chapter 1 (1968). (b) For enzymatic solvolysis of cyclic phosphorothioates: W. Saenger, *Angew. Chem., Int. Ed. Engl.*, **12,** 591 (1973); D. A. Usher, D. I. Richardson, Jr., and F. Eckstein, *Nature (London)*, **228,** 663 (1970). (c) For nucleophilic substitution of chiral phosphorothioate: M. Mikolajczyk, J. Omelanczyk, and M. Para, *Tetrahedron*, **28,** 3855 (1972); J. Michalski and M. Mikolajczyk, *Chem. Ind. (London)*, 661 (1964). (d) For solvolysis of chiral phosphinamides: T. Koizumi, Y. Kobayashi, and E. Yoshii, *J. Chem. Soc., Chem. Commun.*, 678 (1974); *Chem. Pharm. Bull.*, **24,** 834 (1976).

(2) N. P. B. Dudman and B. Zerner, *J. Am. Chem. Soc.*, **95,** 3019 (1973).

(3) (a) C. R. Hall, T. D. Inch, G. J. Lewis, and R. A. Chittenden, *J. Chem. Soc., Chem. Commun.*, 720 (1975); (b) D. B. Cooper, C. R. Hall, and T. D. Inch, *ibid.*, 721 (1975); (c) D. B. Cooper, J. M. Harrison, and T. D. Inch, *Tetrahedron Lett.*, 2697 (1974); (d) J. M. Harrison, T. D. Inch, and G. J. Lewis, *J. Chem. Soc., Perkin Trans. 1*, 1892 (1975).

(4) In the case of ref 3a, several steps were required to secure the sugar moiety.

(5) It seems rather difficult to prepare dialkyl aryl phosphates by this method because the P–OAr bond is very labile to alkaline conditions.

(6) The use of L-proline derivatives for the asymmetric synthesis of chiral carbon compounds has been extensively studied by S.-I. Yamada and his collaborators: S.-I. Yamada, K. Hiroi, and K. Achiwa, *Tetrahedron Lett.*, 4233 (1969); S.-I. Yamada, and G. Otani, *ibid.*, 4237 (1969); 1133 (1971); K. Hiroi, K. Achiwa, and S.-I. Yamada, *Chem. Pharm. Bull.*, **20,** 246 (1972); K. Hiroi and S.-I. Yamada, *ibid.*, **23,** 1103 (1975); T. Sone, S. Terashima, and S.-I. Yamada, *ibid.*, **24,** 1273, 1288 (1976).

(7) The reaction was carried out at room temperature for 3–4 h.

(8) The reaction was carried out at room temperature for 8–12 h.

(9) All new compounds gave satisfactory elemental analyses and spectral data.

(10) Yields are based on phenyl phosphorodichloridate in the case of **3a, 3b, 4a,** and **4b.**

(11) All distillations were performed with a short-path distillation apparatus and bath temperatures are described.

(12) All $[\alpha]_D$ measurements were taken in carbon tetrachloride solution.

(13) The alcoholysis was performed with 0.4–1.0 mmol of the phosphoramidate in 4–10 mL of 1 M H_2SO_4–alcohol for 4 h.

(14) The reaction mixture was diluted with H_2O and extracted with Et_2O. After washings with dilute HCl, H_2O, dilute $NaHCO_3$, and H_2O there was obtained almost pure oily dialkyl phenyl phosphate, which was subjected to microdistillation.

(15) The enantiomeric purities of methyl ethyl phenyl phosphate and methyl *n*-butyl phenyl phosphate were determined as >97% according to Hall's method (ref 3a and 3b). When a twofold excess of $Eu(hfc)_3$ was added to a carbon tetrachloride solution of each enantiomer, only one P–OMe doublet was observed, whereas a pair of doublets was detected with a mixture (3:97) of enantiomers. Since the acid-catalyzed alcoholysis of phosphoramidate (**3** and **4**) should proceed through A-2 mechanism, other dialkyl phenyl phosphates are considered to possess a comparable degree of optical purity. The observed differences in $[\alpha]_D$ could be attributable to some experimental errors.

(16) Reaction conditions (temperature, acids, and acid concentration) and workup procedure for obtaining maximum yields are being investigated.

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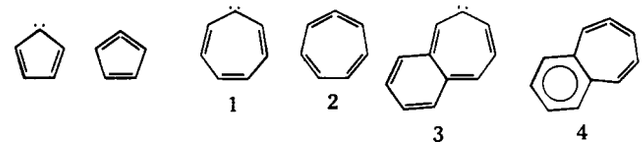
4,5-Benzo-1,2,4,6-cycloheptatetraene

Summary: 4,5-Benzo-1,2,4,6-cycloheptatetraene and one of its methyl derivatives have been generated by the dehydrohalogenation of benzohalocycloheptatrienes.

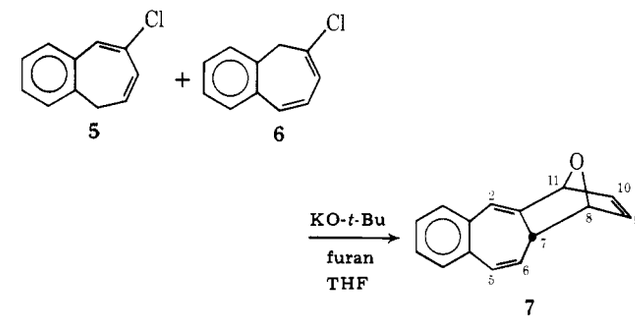
Sir: Cyclic, fully conjugated carbenes have been the subject of considerable research interest.[1] In principle, valence isomeric allene structures can be postulated for each of the carbenes. While there has been no need to invoke an allenic isomer of cyclopentadienylidene, the situation has not been as clear with cycloheptatrienylidene.[2] The chemistry of the C_7H_6



1 2 3 4

intermediate generated from the photolysis or thermolysis of the sodium salt of tropone tosylhydrazone has been logically interpreted in terms of **1**.[3] The intermediate shows low reactivity with electron-rich alkenes[3a] and a positive ρ value in its addition to substituted styrenes.[3b] These properties are consistent with extended Hückel calculations which predict **1** to be a relatively nucleophilic carbene in its lowest energy singlet state.[4] Untch's report of the dehydrochlorination of 1-chloro-1,3,5-cycloheptatriene[5] generated interest in the cycloheptatetraene **2,** since the product, heptafulvalene, had previously been isolated from reactions where the intermediacy of **1** had been implicated.[3] The possibility that **2** might be involved in the reactions of **1** was increased when Jones, Sabin, and co-workers reported the results of INDO calculations which concluded that **2** (nonplanar) was more stable than **1** (planar) by 14 kcal/mol.[6,7] These calculations also indicated that the appropriate benzo annelation of the seven-membered ring would further stabilize the allene form (**4**) relative to its carbene analogue (**3**). In this paper, we wish to report the generation of **4** and one of its methyl derivatives.

When a mixture of **5** and **6**[8,9] was treated with potassium *tert*-butoxide (KO-*t*-Bu) in tetrahydrofuran (THF), a rapid, slightly exothermic reaction produced a golden polymer (81%).[10] When the reaction was carried out in the presence of excess furan, the adduct **7** was isolated (21%) along with some



5 6 7

polymer. The use of $Eu(dpm)_3$ as a chemical shift reagent aided in the structure assignment of **7.**[11]

When the reaction was conducted in the presence of excess styrene, **8** was formed in 35% yield. The structure proof for **8** rests on its normal and decoupled NMR spectra and the analogous spectra for **9,** which was prepared by using β,β'-

Table I. NMR Data for 8 and 9 (CCl_4, Me_4Si, δ)

	H_2 and H_5	H_6	H_7	H_8	H_9, $H_{9'}$	H_{arom}
8	6.1–6.5 (m, 2 H)	5.62 (d of d, 11.8 and 2.0 Hz)	3.95 (br m, 1H)	3.2–3.8 (m, 1 H)	2.8–3.2 (m, 2 H)	7.2 and 7.4 (br s, 9 H)
9[a]	6.2–6.5 (m, 2 H)	5.62 (d of d, 11.8 and 2.0 Hz)	3.95 (d of m, 8.8 Hz)	3.49 (br d, 8.8 Hz)		7.2 and 7.4 (br s, 9 H total)

[a] When H_7 of **9** is irradiated in a decoupling experiment, H_5 collapses to a doublet (δ 6.32, $J_{5,6}$ = 11.8 Hz) and H_2 becomes a singlet (δ 6.26).