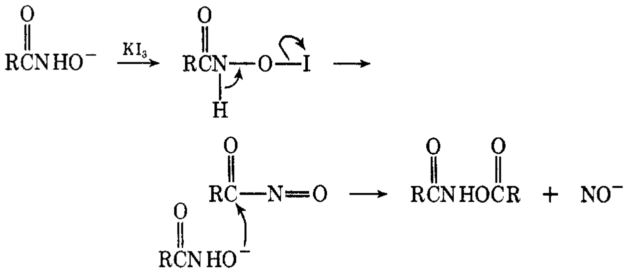

$$2NaNO + 2H^+ \longrightarrow 2HNO \longrightarrow N_2O + H_2O$$

Experimental Section[7]

Cinnamohydroxamic Acid (3).—This compound was prepared in 47% yield by the method of Jones and Mason.[8]

***N*,*O*-Dicinnamoylhydroxylamine (4).**—To a stirred suspension of cinnamohydroxamic acid (3) (3.00 g, 0.019 mol) in 100 ml of 0.5 *M* $NaHCO_3$ was added KI (20.0 g, 0.12 mol) and I_2 (10.2 g, 0.04 mol) in 100 ml of H_2O. The reaction mixture was stirred at 25° for 9 hr and extracted with $CHCl_3$ (three 50-ml portions). The combined $CHCl_3$ extracts were washed with 20% $Na_2S_2O_3$ (two 50-ml portions) and dried (Na_2SO_4), and the solvent was removed. The residue was recrystallized (MeOH) to yield 0.93 g (33%) of 4, mp 161–162°.

Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.78; H, 5.23; N, 4.78. Found: C, 74.18; H, 5.23; N, 4.78.

An authentic sample of *N*,*O*-dicinnamoylhydroxylamine was prepared by treating cinnamohydroxamic acid with cinnamoyl chloride[9]. Its spectra were identical with those of 4.

Dibenzoylhydroxylamine (6).—This compound was prepared by the same method as *N*,*O*-dicinnamoylhydroxylamine (4, 44%) and was found to be identical with an authentic sample prepared by the method of Renfrow and Hauser.[9]

***N*-Cyclohexylbenzamide (8).**—To a solution of benzohydroxamic acid (7) (2.75 g, 0.020 mol) in 25 ml of pyridine was added I_2 (2.53 g, 0.010 mol) and KI (4.98 g, 0.030 mol) in 10 ml of H_2O. To this reaction mixture was added 5 ml of cyclohexylamine followed by 200 ml of H_2O. After cooling, the insoluble material was removed by filtration and recrystallized (EtOH) to give 0.32 g (7.8%) of 8, mp 142–147° (lit.[10] 148°), whose spectra were identical with those of an authentic sample.

Registry No.—4, 30345-94-9; 8, 1759-68-8.

Acknowledgment.—The authors gratefully acknowledge the support of this project by the National Institutes of Health Grants GM-09254 and GM-01341.

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[7] Melting points were obtained on a calibrated Thomas-Hoover Unimelt and are corrected. Ir data were recorded on a Beckman IR-10 spectrophotometer and nmr data on Varian Associates A-60 and A-60A spectrometers (TMS). Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind., and on an F & M 185 C, H, N, analyzer, University of Kansas.

[8] L. W. Jones and J. P. Mason, *J. Amer. Chem. Soc.*, **49**, 2534 (1927).

[9] W. B. Renfrow, Jr., and C. R. Hauser, *ibid.*, **59**, 2308 (1937).

[10] I. Heilbron, "Dictionary of Organic Compounds," Vol. I, Oxford University Press, New York, N. Y., 1953, p 640.

The Preparation and Properties of a Seven-Membered Heterocyclic Phosphinic Acid[1]

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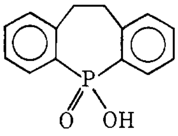
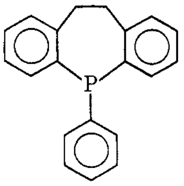
Although numerous heterocyclic derivatives of phosphorus have been prepared in recent years,[2] there are still relatively few phosphinic acids in which the phosphorus atom is a member of a ring system. Thus, a recent survey[1] indicates that only 38 such phosphinic acids have been described in the chemical literature; in these compounds the phosphorus atom was a member of a four-, five-, or six-membered ring. The present paper is concerned with the preparation and properties of the seven-membered heterocyclic phosphinic acid **1**.



1



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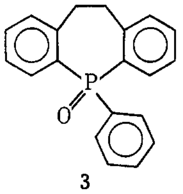

3

Since the tertiary phosphine **2** and the phosphine oxide **3** have been previously reported,[3] we used these compounds as precursors to the desired phosphinic acid **1**. The fusion of a tertiary phosphine oxide with sodium hydroxide leads to cleavage of a carbon–phosphorus bond and the formation of the sodium salt of a phosphinic acid (eq 1).[4] When phosphine oxides of the

$$R_3PO + NaOH \longrightarrow R_2PO_2Na + RH \qquad (1)$$

type $R_2R'PO$ are used, the group that is preferentially cleaved is the one that can form the more stable carbanion. This rule is usually followed when the phosphorus atom is a member of a ring system;[5] in two cases,[5a,c] however, a ring carbon–phosphorus bond was cleaved even though this meant formation of the less stable carbanion. We have now found that reaction of the phosphine oxide **3** with fused sodium hydroxide obeyed the general rule and led to a 92% yield of **1**; 7% of the starting material **3** was also isolated from the reaction mixture.

The reaction of tertiary phosphines with lithium (or other alkali metal) results in the formation of a phosphide ion and a carbanion (eq 2).[4b,6] Hydrolysis,

$$R_3P + 2Li \rightarrow R_2PLi + RLi \qquad (2)$$

oxidation, and acidification of the reaction mixture readily gives a phosphinic acid. The direction of cleavage for unsymmetrical phosphines has been shown to be thermodynamically controlled; *i.e.*, it is determined by the stability of the products.[6c,7] When a heterocyclic tertiary phosphine reacts with lithium, cleavage of the ring would result in the formation of a dianion. For a variety of phosphole derivatives, this pathway has proved to be of significantly higher energy than cleavage of the exocyclic carbon–phosphorus bond; in these cases, therefore, no cleavage of the heterocyclic ring was ob-

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[1] Abstracted from the M.S. Thesis of J. L. Suggs, North Carolina State University, Raleigh, N. C., 1971.

[2] F. G. Mann, "The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, and Bismuth," Wiley-Interscience, New York, N. Y., 1970, pp 3–354.

[3] F. G. Mann, I. T. Millar, and B. B. Smith, *J. Chem. Soc.*, 1130 (1953).

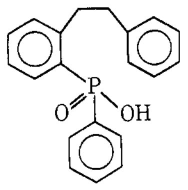
[4] (a) L. Horner, H. Hoffmann, and H. G. Wippel, *Chem. Ber.*, **91**, 64 (1958); (b) A. M. Aguiar, J. Beisler, and A. Mills, *J. Org. Chem.*, **27**, 1001 (1962); (c) E. Zbiral, *Tetrahedron Lett.*, 1649 (1964).

[5] (a) B. R. Ezzell and L. D. Freedman, *J. Org. Chem.*, **34**, 1777 (1969); (b) B. R. Ezzell and L. D. Freedman, *ibid.*, **35**, 241 (1970); (c) B. R. Ezzell, *ibid.*, **35**, 2426 (1970).

[6] (a) D. Wittenberg and H. Gilman, *ibid.*, **23**, 1063 (1958); (b) K. Issleib and H. O. Frohlich, *Z. Naturforsch., B*, **14**, 349 (1959); (c) K. Issleib, *Pure Appl. Chem.*, **9**, 205 (1964); (d) A. D. Britt and E. T. Kaiser, *J. Phys. Chem.*, **69**, 2775 (1965).

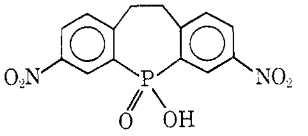
[7] B. R. Ezzell, Ph.D. Thesis, North Carolina State University, Raleigh, N. C., 1969.

served.[7,8] When the tertiary phosphine **2** was allowed to react with lithium, we obtained from the reaction mixture a 52% yield of the heterocyclic phosphinic acid **1**. A second phosphinic acid, however, was also isolated. Although it was not obtained analytically pure, its mass spectrum strongly suggested that it was compound **4**, formed *via* cleavage of a ring carbon–phosphorus bond. This is the first case yet reported in which the reaction of a tertiary phosphine with an alkali metal has led to a mixture of phosphinic acids.

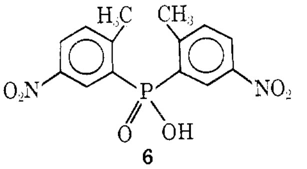


4

Nitration of the phosphinic acid **1** with 90% nitric acid at room temperature gave an 87% yield of a dinitro derivative. Although the structure of this substance was not proven, it is probably the 3,7-dinitro compound **5**, since the nitration of di-*o*-tolylphosphinic acid under similar conditions was found to give bis(5-nitro-2-tolyl)phosphinic acid (**6**). The structure of **6** was established by comparison with an authentic sample.[9]



5



6

Ultraviolet Spectra.—Table I gives uv absorption data for the heterocyclic phosphinic acids **1** and **5** and for several related organophosphorus compounds. It will be noted that the spectra of **1** and di-*o*-tolylphosphinic acid are very similar. This result suggests that the limited resonance interaction between a phosphinico (PO_2H) group and the aromatic systems attached to it is not appreciably altered by incorporating the phosphorus atom in a heterocyclic ring.[10] The spectrum of the tertiary phosphine oxide **3** also resembles the spectrum of **1**; the intensity of absorption of **3** is somewhat greater, since it contains a third aromatic ring. The spectra of the dinitro derivative **5** and bis(5-nitro-2-tolyl)phosphinic acid (**6**) are virtually identical and help to establish the structure assigned to the former compound.

TABLE I

ULTRAVIOLET ABSORPTION MAXIMA[a]

Compd	λ_{max}, nm	ϵ_{max}
10,11-Dihydro-5-hydroxy-5*H*-dibenzo[*b*,*f*]phosphepin 5-oxide (1)	230	10,040
	270	1,616
	277	1,393
Di-*o*-tolylphosphinic acid	223	15,620
	270	2,046
	277	2,012
10,11-Dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepin 5-oxide (**3**)	232	21,320
	270	2,152
10,11-Dihydro-3,7-dinitro-5-hydroxy-5*H*-dibenzo[*b*,*f*]phosphepin 5-oxide (**5**)	219	27,240
	278	16,190
Bis(5-nitro-2-tolyl)phosphinic acid (6)	219	29,360
	277.5	17,500

[a] The spectra were determined in 95% ethanol with a Cary 14 Model 50 recording spectrophotometer.

Experimental Section[11]

10,11-Dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepin 5-Oxide (3).—*o*-Bromobenzyl bromide was prepared by the bromination of *o*-bromotoluene and was converted to 2,2′-dibromobibenzyl by the procedure of Letsinger and Skoog.[12] The reaction of this dibromide with *n*-butyllithium and phenylphosphonous dichloride was carried out essentially as described by Mann and coworkers.[3] When the reaction mixture was hydrolyzed and the organic layer was dried and distilled, a pale amber syrup, bp 170–230° at 0.025 Torr, was obtained. This syrup, which presumably consisted mainly of the tertiary phosphine **2**, could not be crystallized. Mann and coworkers[3] had a similar difficulty at this point, but they succeeded in inducing crystallization by seeding the oil with the analogous arsine. We dissolved the oil in acetone and oxidized it with an excess of 3% hydrogen peroxide. When the acetone was allowed to evaporate, a gummy material was obtained which was readily recrystallized from absolute ethanol: yield of **3**, based on 2,2′-dibromobibenzyl, 23%; mp 172–174° (lit.[3] mp 173–174°); nmr ($CDCl_3$) τ 7.02 (m, 4, CH_2CH_2), 2.72 (m, 11, aromatic H), 1.7 (m, 2, aromatic H); mass spectrum *m/e* (rel intensity) 306 (2), 305 (21), 304 (100), 303 (41), 225 (7), 214 (9), 213 (65), 183 (9), 179 (11), 178 (25), 165 (13), 152 (7), 91 (6), 77 (8).

10,11-Dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepin (2).—The tertiary phosphine oxide **3** (3.00 g, 9.89 mmol) was dissolved in 75 ml of dry benzene and reduced with trichlorosilane (2.86 g, 19.8 mmol) by the method of Fritzsche and coworkers.[13] After the mixture was refluxed for 2 hr, it was cooled and treated with 50 ml of 40% aqueous sodium hydroxide. The organic layer was then separated, washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to yield a thick orange oil, which crystallized after being washed with a little absolute ethanol. Recrystallization from absolute ethanol gave 1.5 g (53%) of pure **2**: mp 91–93° (lit.[3] mp 94.5–95°); nmr ($CDCl_3$) τ 6.96 (s, 4, CH_2CH_2), 2.83 (m, 13, aromatic H); mass spectrum *m/e* (rel intensity) 290 (3), 289 (18), 288 (85), 287 (9), 274 (15), 273 (77), 210 (23), 209 (29), 208 (10), 207 (30), 197 (30), 196 (35), 183 (55), 179 (35), 178 (100), 177 (12), 176 (15), 170 (12), 166 (14), 165 (67), 157 (10), 152 (33), 151 (10), 139 (10), 133 (33), 115 (23), 109 (23), 108 (23), 107 (41), 91 (33), 89 (23), 78 (53), 77 (53).

10,11-Dihydro-5-hydroxy-5*H*-dibenzo[*b*,*f*]phosphepin 5-Oxide (1). A. From the Fusion of 3 with Sodium Hydroxide.—The phosphine oxide **3** (1.50 g, 4.90 mmol) was thoroughly mixed with finely powdered NaOH (0.40 g, 9.8 mmol) in a 25-ml pear-shaped flask equipped with a condenser. The flask was slowly heated to 250° and maintained between 250 and 260° for 2 hr. During this time 0.35 ml of benzene (identified by ir) distilled. After being cooled, the contents of the flask were dissolved in 100 ml of water, filtered to remove 0.10 g (7%) of phosphine oxide **3**, treated with charcoal, cooled, and acidified to yield 1.1 g (92%) of the phosphinic acid **1**: mp[14] 246–251° after recrystallization

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[8] (a) A. D. Britt and E. T. Kaiser, *J. Org. Chem.*, **31**, 112 (1966); (b) E. H. Braye, U. S. Patent 3,338,941 (1967).

[9] L. D. Freedman and G. O. Doak, *J. Org. Chem.*, **26**, 2082 (1961).

[10] The ultraviolet spectra of tetracoordinate organophosphorus compounds have been recently reviewed by B. G. Ramsey, "Electronic Transitions in Organometalloids," Academic Press, New York, N. Y., 1969, pp 173–181.

[11] Melting points were taken with a Mel-Temp capillary melting point apparatus and are uncorrected. Nmr spectra were taken with a Varian HA-100 spectrometer, and tetramethylsilane was used as an internal standard. All solvents used for Grignard or organolithium reagents were distilled over sodium. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

[12] R. L. Letsinger and I. H. Skoog, *J. Amer. Chem. Soc.*, **77**, 5176 (1955).

[13] H. Fritzsche, U. Hasserodt, and F. Korte, *Chem. Ber.*, **97**, 1988 (1964).

[14] The broad melting point ranges observed with many arylphosphonic and diarylphosphinic acids are probably due to their rapid decomposition at temperatures above 240°; *cf.* ref 9.

from 95% ethanol; nmr (CF_3CO_2H) τ 6.73 (s, 4, CH_2CH_2), 2.63 (m, 6, aromatic H), 2.0 (m, 2, aromatic H); mass spectrum *m/e* (rel intensity) 488 (<0.1), 246 (2), 245 (15), 244 (100), 243 (37), 229 (10), 226 (21), 225 (22), 209 (3), 208 (3), 183 (3), 179 (20), 178 (45), 165 (15), 152 (11), 91 (9), 89 (17), 77 (14).

Anal. Calcd for $C_{14}H_{13}O_2P$: C, 68.85; H, 5.37. Found: C, 69.04; H, 5.54.

B. From the Cleavage of 2 with Lithium.—The tertiary phosphine **2** (0.80 g, 2.78 mmol) was dissolved in 25 ml of dry tetrahydrofuran (THF) and treated with lithium wire (0.06 g, 9 mg-atom) by the procedure of Aguiar and coworkers.[4b] After the mixture was stirred and refluxed for 3 hr, it was cooled, hydrolyzed, and then oxidized with an excess of 3% hydrogen peroxide. The resulting solution was extracted with ether to remove any phosphine oxide formed from unreacted **2**, and the aqueous layer was acidified with hydrochloric acid and cooled. The gummy solid which separated was purified by reprecipitation from aqueous base and then dried, yield 0.70 g. Washing this substance with 10 ml of ether extracted an acidic substance discussed in the paragraph below and left as a residue 0.35 g (52%) of the desired heterocyclic phosphinic acid **1**, mp[14] 249–254° after recrystallization from 95% ethanol. This acid was identical (mixture melting point and mass spectrum) with the sample prepared *via* the fusion of **3** with sodium hydroxide.

The 10-ml ether extract mentioned in the above paragraph was evaporated to dryness, and the oily residue was converted to a solid by reprecipitation from alkaline solution: yield 0.30 g; mp 38–65°; nmr ($CDCl_3$) τ 6.43 (m, 4, CH_2CH_2), 2.55 (m, 14, aromatic H); mass spectrum displayed a base peak at *m/e* 322, which corresponds to the molecular weight of the nonheterocyclic compound **4**.

Anal. Calcd for $C_{20}H_{19}O_2P$: C, 74.52; H, 5.94. Found: C, 72.29; H, 5.79.

10,11-Dihydro-3,7-dinitro-5-hydroxy-5*H*-dibenzo[*b,f*]phosphepin 5-Oxide (**5**).—The heterocyclic phosphinic acid **1** (0.50 g) was nitrated at about 30° with 30 ml of 90% nitric acid (*d* 1.5). The reaction mixture was poured onto 250 g of crushed ice, whereupon 0.60 g (87%) of dinitro compound crystallized from solution: mp[14] 320–330° dec after recrystallization from 95% ethanol.

Anal. Calcd for $C_{14}H_{11}N_2O_6P$: C, 50.31; H, 3.32; N, 8.38. Found: C, 50.12; H, 3.42; N, 8.57.

Di-*o*-tolylphosphinic Acid.[15]—A solution of freshly distilled *o*-chlorotoluene (126.6 g, 1.00 mol) in 250 ml of dry THF was converted to *o*-tolylmagnesium chloride in the usual manner[16] and then treated with di-*n*-butyl phosphonate as in the procedure used by Crofts and coworkers[17] for the preparation of diarylphosphine oxides. After the reaction mixture was hydrolyzed with dilute hydrochloric acid and the THF was removed under reduced pressure, an aqueous solution and a supernatant yellow oil were obtained. On cooling, the oil solidified to give 72.4 g of crude di-*o*-tolylphosphine oxide: mp 94–95° after recrystallization from toluene and drying at 90° *in vacuo;* nmr ($CDCl_3$) τ 7.61 (s, 6, CH_3), 2.75 (m, 6, aromatic H), 2.35 (m, 2, aromatic H).

Anal. Calcd for $C_{14}H_{15}OP$: C, 73.03; H, 6.57. Found: C, 72.73; H, 6.71.

The crude di-*o*-tolylphosphine oxide (from 1.00 mol of *o*-chlorotoluene) was suspended in dilute sodium hydroxide and oxidized with 50 ml of 30% hydrogen peroxide. The resulting alkaline solution was filtered to remove a trace of insoluble material and then acidified with hydrochloric acid to precipitate the phosphinic acid. It was purified by recrystallization from 95% ethanol: yield 47.5 g (58% based on *o*-chlorotoluene); mp 175–177°; nmr ($CDCl_3$) τ 7.77 (s, 6, CH_3), 2.85 (m, 6, aromatic H), 2.20 (m, 2, aromatic H).

Anal. Calcd for $C_{14}H_{15}O_2P$: C, 68.29; H, 6.14; mol wt, 246. Found: C, 68.56; H, 6.35; mol wt, 244 (in 95% ethanol with a Thomas isothermal molecular weight apparatus).

Di-*o*-tolylphosphinic acid was also prepared from *o*-bromotoluene. The Grignard reagent was prepared in ether in the conventional manner and converted to di-*o*-tolylphosphine oxide by the procedure described above. Oxidation of the phosphine oxide with hydrogen peroxide gave a 74% yield of phosphinic acid.

Bis(5-nitro-2-tolyl)phosphinic Acid (**6**).—Di-*o*-tolylphosphinic acid (10.0 g) was nitrated with 100 ml of 90% nitric acid by the procedure described above for the nitration of the heterocyclic phosphinic acid **1**. The yield was 13.0 g (95%), mp[14] 231–241° after recrystallization from 95% ethanol (lit.[9] mp 243–245°). This compound was shown (mixture melting point and ir) to be identical with an authentic sample of **6**.[9]

Anal. Calcd for $C_{14}H_{13}N_2O_6P$: C, 50.01; H, 3.90. Found: C, 49.81; H, 4.08.

Registry No.—**1**, 30309-73-0; **2**, 30309-74-1; **3**, 30309-75-2; **4**, 30309-76-3; **5**, 30309-77-4; **6**, 30309-78-5; di-*o*-tolylphosphinic acid, 18593-19-6; di-*o*-tolylphosphine oxide, 30309-80-9.

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[15] This acid was first prepared by A. Michaelis and F. Wegner, *Ber.*, **48**, 316 (1915), but they gave no information about its properties. V. M. Plets, Dissertation, Kazan, 1938 (quoted by G. M. Kosolapoff, "Organophosphorus Compounds," Wiley, New York, N. Y., 1950, p 170) reported that the compound melts at 101° and can be recrystallized from water. It should be noted, however, that a number of workers have questioned the validity of much of Plets's work; *cf.* L. D. Freedman and G. O. Doak, *Chem. Rev.*, **57**, 479 (1957), and F. A. Cotton, *ibid.*, **55**, 551 (1955). P. Haake, M. J. Frearson, and C. E. Diebert, *J. Org. Chem.*, **34**, 788 (1969), have described the mass spectrum of di-*o*-tolylphosphinic acid but have not reported its synthesis.

[16] H. E. Ramsden, A. E. Balint, W. R. Whitford, J. J. Walburn, and R. Cserr, *ibid.*, **22**, 1202 (1957).

[17] P. C. Crofts, I. M. Downie, and K. Williamson, *J. Chem. Soc.*, 1240 (1964).

A Novel Catalytic Effect in the Diaxial–Diequatorial Rearrangement of 5,6-Dibromocholesteryl Benzoate[1a]

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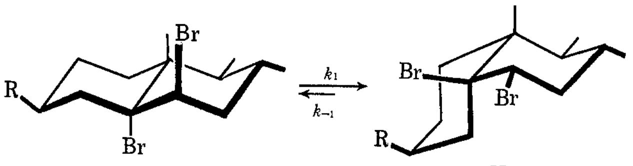
Received February 23, 1971

In connection with a specific project in the steroid field, we became interested in the rate of the diaxial–diequatorial rearrangement of 5α,6β-dibromocholesterol and its esters to the corresponding 5β,6α stereoisomers. This rearrangement is typical for 2,3 and 5,6 axially disubstituted steroids. It has been reviewed recently.[2] Although, in general, the reaction reaches an equilibrium, in the case of the 5,6-dibromides the thermodynamically favored 5β,6α isomers constitute not less than 80% of the rearranged product and the reaction can be utilized for preparative purposes. In their detailed studies on 5,6-dibromocholestane, partial structure **1**, Grob and Winstein[3] attempted to discern a rate-influencing species that would be helpful in elucidating the rearrangement mechanism. The lack of a common ion effect and the insensitivity of the rate toward the addition of nucleophiles like CH_3COONa and LiBr were two of the main reasons that led them to



1, R = H
3, R = $OCOC_6H_5$

2, R = H
4, R = $OCOC_6H_5$

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[1] (a) This work was supported, in part, by the National Research Council of Canada. (b) Department of Chemistry, University of British Columbia, Canada.

[2] D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier, Amsterdam, 1968, p 373 ff.

[3] C. A. Grob and S. Winstein, *Helv. Chim. Acta*, **35**, 782 (1952).