

washed with water, dried (Na_2SO_4), and evaporated at reduced pressure to give 1.40 g of the azide **4**, thick oil, ir (liquid film) 2130 cm^{-1} (azide).

The azide was warmed for 2 hr at 70° in 10 ml of anhydrous benzyl alcohol. The mixture was diluted with ethyl ether and extracted with 2 *N* sodium carbonate. The cooled alkaline solution was acidified with 2 *N* hydrochloric acid to pH 4 and reextracted with ether which was washed with water and dried (Na_2SO_4); solvent was evaporated off at reduced pressure. The oily residue was crystallized from ethanol-water to give 500 mg (28%) of *cis*- N,N' -dicarbobenzyloxy-5-amino-DL-proline, mp $141\text{--}142^\circ$.

Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_6$: C, 63.31; H, 5.57; N, 7.03. Found: C, 63.39; H, 5.65; N, 7.06.

Registry No.—**1**, 24377-91-1; **2**, 24377-92-2; **3**, 24377-93-3; **5**, 24377-94-4; α -keto- δ -acetylaminovaleric acid (2,4-dinitrophenylhydrazone), 24378-14-1.

A Facile Preparation of 3-Thujene from Thujone

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The bicyclic monoterpene 3-thujene (**1**) is much less readily available from natural sources than is thujone (**2**). The methods previously used^{1,2} for obtaining **1** from **2** involve reduction to the thujyl alcohols, separation of isomers, and eliminations. We have found that it is possible to obtain **1** from **2** in a rather simple procedure which is applicable to large-scale work by use of the Bamford-Stevens rearrangement.³

Thujone (**2**) was readily converted to the *p*-toluenesulfonylhydrazone which was initially decomposed with a solution of sodium in ethylene glycol. The hydrocarbon product was analyzed by preparative vpc and shown to contain 3-thujene (**1**, 42%), 2-thujene (**3**, 16%), γ -terpinene (**4**, 13%), a fourth unidentified compound, and a trace of *p*-cymene. Using acetamide as a solvent,⁴ the hydrocarbon product (97% yield) consisted of **1** (80%) and **4** (20%), **4** being slightly contaminated with an unidentified isomer. 3-Thujene was characterized by its spectral properties and by conversion to terpinene dihydrochloride.⁵ This procedure therefore represents a simple process for obtaining 3-thujene from readily available thujone.

Experimental Section⁶

***p*-Toluenesulfonylhydrazone.**⁷—Hydrazine hydrate (40 g, 85%) was slowly added to a benzene solution of 60 g of *p*-toluene-

sulfonyl chloride (recrystallized from an ether-ligroin mixture) at 5° through the condenser into a 500-ml flask. After 2 hr the solid was filtered and recrystallized from hot water. The yield was 42.6 g (72%), mp $110\text{--}112^\circ$ (lit.⁷ 112°).

Thujone *p*-Toluenesulfonylhydrazone.—*p*-Toluenesulfonylhydrazone (42.6 g) and 40 g of **2**, $[\alpha]_D^{20} +20.13^\circ$, were dissolved in 200 ml of ethanol and refluxed in a 500-ml flask for 3.5 hr until the reaction was complete as indicated by thin layer chromatography. Following reflux, the ethanol was removed under reduced pressure until a precipitate formed, and then the mixture was heated on a steam bath to effect solution. The solution was cooled to effect crystallization; the crystals were filtered, recrystallized from ethanol, and dried. The yield was 25.6 g (35%), mp $126\text{--}129^\circ$, $[\alpha]_D^{20} +105.7^\circ$; ir (CHCl_3) 3310 (NH), 2980, 1610, 1170 cm^{-1} .

Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{SO}_2$: C, 63.75; H, 7.50; N, 8.75. Found: C, 63.99; H, 7.74; N, 8.63.

3-Thujene (1). I. **Ethylene Glycol as Solvent.**—The hydrazone (**5** g) and 50 ml of 1.5 *N* sodium in ethylene glycol were placed in a 100-ml flask. Most of the solid dissolved immediately and the remainder dissolved on the application of heat. Nitrogen evolution continued steadily for 15 min and the resulting organic layer was then distilled off at $141\text{--}175^\circ$ yielding 1.5 ml of product. The vpc analysis indicated four products: 3-thujene (**1**, 42%), 2-thujene (**3**, 16%), contaminated slightly with another compound γ -terpinene (**4**, 13%), and 20% of an unidentified mixture.

II. **Acetamide as Solvent.**—The acetamide (200 g) was melted in a 500-ml three-necked flask and purged with oxygen-free nitrogen. The acetamide was cooled to 100° and 6.0 g of sodium was added in small quantities under a nitrogen atmosphere (extreme care must be taken to avoid combustion). The hydrazone (**38.6** g) was added and the temperature held at $140\text{--}150^\circ$. Nitrogen evolution ceased after 25 min and the reaction mixture was cooled slightly. Water (200 ml) was added and the organic layer was extracted into petroleum ether. The ethereal solution was dried (MgSO_4), filtered, concentrated, and distilled giving 15.9 g (97%) of mixed hydrocarbon product. The mixture was readily separated *via* preparative vpc and **1** was characterized as follows: n_D^{20} 1.4471, $[\alpha]_D^{20} -32.05^\circ$, bp $150\text{--}151^\circ$; ir (neat) 2985, 2881, 3057 cm^{-1} ; nmr (neat) δ 0.02 (t, 1, $J = 3$ Hz), 0.90 (m, 2), 0.98 (d, 6, $J = 3$ Hz), 1.35 (m, 1), 1.76 (q, 3, $J = 2$ Hz), 2.30 (m, 2), 4.90 (m, 1); mass spectrum (70 eV) m/e 136, 93 (lit.⁸).

Terpinene Dihydrochloride.⁵—To 5 ml of glacial acetic acid was added 0.20 g of **1** and the solution was saturated with gaseous HCl. The mixture developed a red color after 9 hr of standing and was then poured over ice. The resulting solid was filtered and recrystallized from methanol: mp $47\text{--}49^\circ$; nmr (CDCl_3) δ 1.68 (s, 3), 1.90 (d, 6, $J = 6$ Hz), 1.98 (s, 9).

The absolute configurations of 3-thujene (**1**), thujone (**2**), and 2-thujene (**3**) are those verified by Norin.^{9,10}

Registry No.—**1**, 3917-48-4; **2**, 546-80-5; **2** *p*-toluenesulfonylhydrazone, 18791-12-3.

Acknowledgment.—We thank the U. S. Public Health Service (A108862-01) and the Alfred P. Sloan Foundation for their support of this research.

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Alkaline Cleavage of Phosphetane Oxides

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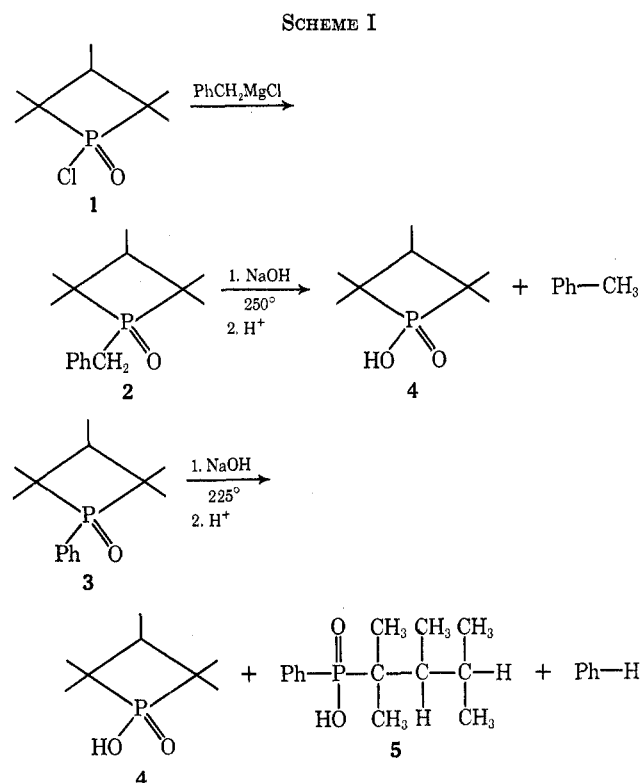
Recently, we reported the alkaline cleavage of several heterocyclic phosphine oxides.¹ In all but one

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- (2) D. V. Banthorpe and H. F. S. Davies, *J. Chem. Soc. B*, 1339 (1968).
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- (4) J. W. Powell and M. L. Whiting, *Tetrahedron*, **7**, 305 (1959).
- (5) A. J. Birch and J. C. Earl, *J. Proc. Roy. Soc. N. S. W.*, **72**, 55 (1938).
- (6) Melting points were measured on a Kofler hot stage and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrophotometer, nuclear magnetic resonance spectra on Varian A-60 and HA-100 spectrometers with tetramethylsilane as an internal reference, and mass spectra on an AEI MS 9 mass spectrometer. Refractive indices were determined on a Bausch and Lomb ABBE-3L refractometer and optical rotations on the Perkin-Elmer P22 spectropolarimeter. Analytical and preparative vpc analyses were made on a Varian Aerograph Model 700 using a 30% Carbowax column on 45-60 Chromosorb W support at 180° . Thujone was kindly supplied by Fritzsche Bros. Inc., New York, N. Y. Elemental analysis was performed by the Midwest Microlab, Inc., Indianapolis, Ind.
- (7) K. Freudenberg and F. Blümmel, *Justus Liebig's Ann. Chem.*, **440**, 51 (1924).

case, the reactions gave the products corresponding to cleavage of the group capable of forming the more stable carbanion. We suggested^{1b} that the general cleavage reaction normally proceeds via a trigonal-bipyramidal intermediate with the oxygen atoms occupying the apical positions. For heterocyclic phosphine oxides, in cases where a large amount of ring strain would be involved in placing the heterocyclic ring in diequatorial positions, some other pathway would seem necessary. We suggested, in the case of 5-benzylidibenzophosphole 5-oxide where ring cleavage predominates over cleavage of the more stable benzyl carbanion,^{1a} that, owing to ring strain, the reaction proceeds by an S_N2-type process. The present paper offers additional information on the cleavage of heterocycles involving ring-strain considerations.

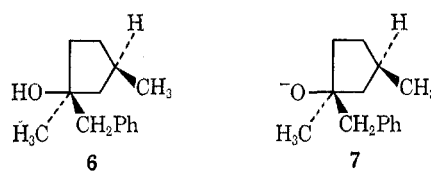
The reactions involved in this study are shown in Scheme I. The acid chloride 1 was prepared by the



method of McBride and coworkers,² and the phosphetane oxide 3 was prepared by the method of Cremer and Chorvat.³ The reaction of benzylmagnesium chloride with 1 to form the phosphetane oxide 2 proceeded smoothly without interference from ring-opening reactions as was observed with phenyllithium.^{3,4} The preparation of 2 by the same method employed here was recently cited, without detail, in a communication.⁵ Fusion of 2 with sodium hydroxide gave only 1-hydroxy-2,2,3,4,4-pentamethylphosphetane 1-oxide (4)

corresponding to exclusive cleavage of the more stable benzyl carbanion. Fusion of 3 with sodium hydroxide led to both 4 and phenyl (2,3,4,4-tetramethylbutyl)-phosphinic acid (5) in approximately a 1:4 ratio. This result corresponds to preferential ring cleavage even though this means cleavage of the least stable carbanion. Clearly, the direction of cleavage for this four-membered ring is influenced by both the ring and the stability of the leaving carbanion. The fact that the ring influences the direction of cleavage is in contrast to the saturated five-membered ring,^{1b} but in agreement with the unsaturated five-membered ring.^{1a}

Historically, trigonal-bipyramidal intermediates have received prime attention in the field of organophosphorus chemistry. Considerable attention has recently been given to the position of the leaving group in the trigonal-bipyramidal intermediates formed during alkaline cleavage of phosphonium salts.⁶ Apical departure has been shown to take precedence over cleavage of groups capable of forming more stable carbanions in certain small-ring heterocyclic phosphoniums.⁷ In other cases, where exocyclic benzyl groups have cleaved in preference to small heterocyclic rings,^{1a,8} it is questionable whether the benzyl group leaves from an equatorial position of the initially formed intermediate or from an apical position of a new intermediate derived from pseudorotation. Marsi,^{8b} after showing that the benzyl group was cleaved from both isomers of 1-benzyl-1,3-dimethylphospholanium bromide with retention of configuration at phosphorus, suggested equatorial benzyl departure. His argument was based on the energetically unfavorable pseudorotation of intermediate 6 to an intermediate containing the electronegative hydroxyl group in an equatorial position. He further suggests that if such a pseudorotation process did occur, then intermediates that would give rise to inversion of configuration would also be reasonable. Since, as Marsi shows in his kinetic scheme, intermediate 7



would also be expected in the reaction process, pseudorotation should have been considered for this intermediate also. Replacement of 6 by 7 in the pseudorotation scheme given by Marsi results in a reversal of the energetics. Pseudorotation of 7 to an intermediate with the oxygen atom in an equatorial position is energetically favorable since this means moving the least electronegative group (the negative oxygen) from an

(2) J. J. McBride, E. Jungermann, J. V. Killheffer, and R. J. Clutter, *J. Org. Chem.*, **27**, 1833 (1962).

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(6) A survey of both the phosphine oxide and phosphonium cleavage reactions is given in ref 1a and references therein.

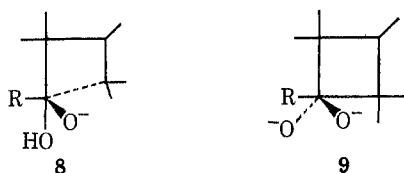
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(8) (a) D. W. Allen and I. T. Millar, *J. Chem. Soc. C*, 252 (1969); (b) K. L. Marsi, *J. Amer. Chem. Soc.*, **91**, 4724 (1969); (c) W. Hawes and S. Trippett, *Chem. Commun.*, 295 (1968).

(9) R. Kluger, F. Covitz, E. Dennis, L. D. Williams, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **91**, 6066 (1969).

apical to an equatorial position. Also, pseudorotation to intermediates that would result in inversion of configuration is now unlikely in this scheme since one step requires the energetically unfavorable process of moving the negative oxygen from an equatorial to an apical position. Thus, depending on the intermediate chosen, arguments for either apical or equatorial departure can be supported by the same pseudorotation scheme.

If an intermediate is formed in the cleavage reactions of the phosphetane oxides, structure **8** seems most reasonable. The four-membered ring occupies apical-equatorial positions and the position-*vs.*-electronegativity requirements are best satisfied. It seems unreasonable that the coulombic repulsion between the oxide oxygen and the hydroxide ion would be sufficient to cause formation of an intermediate with the ring in diequatorial positions.^{1,10} If **8** was formed, it is possible,



considering the extreme alkaline conditions employed for the reactions, that a second equivalent of hydroxide ion would react to form the conjugate base. Pseudorotation could then lead to a more stable intermediate, **9**, if the rate of the cleavage step was slower than that of pseudorotation. As in the case with the phosphonium reactions, apical or equatorial departure for an exocyclic group would depend on the intermediate. Regardless of whether **8** or some conjugate base was the key intermediate, the influence of the ring on the direction of cleavage would have to be explained by the reaction process leading from intermediate to product. Whether this influence would be associated with a preference for apical departure as seems to be the case with phosphonium cleavage reactions⁶ or a ring strain factor is not obvious. Although a comparison between the cleavage reactions of phosphetanium salts^{7,8c} and the phosphetane oxides presented here suggest a strong similarity in factors determining direction of cleavage, a similar comparison for the dibenzophosphole ring system shows definite differences. The latter comparison prompted us to previously suggest an S_N2-type mechanism.^{1a,11}

The detailed mechanism for cleavage of phosphine oxides with sodium hydroxide is far from being established. The results, to date, are insufficient for a prediction of the direction of cleavage for small ring compounds. It is clear, however, from the results presented here and in previous papers,¹ that ring size and relative carbanion stabilities have a definite influence on the direction of cleavage. The effect of ring size is best demonstrated by a comparison of the cleavage of 1-phenyl-2,5-dicyclohexylphospholane 1-oxide^{1b} and the

phosphetane oxide **3**. The exocyclic phenyl group is common to both compounds and the carbanions derived from ring cleavage are of comparable stabilities. No ring cleavage is observed with the five-membered ring, whereas ring cleavage predominates with the four-membered ring. The effect of relative carbanion stability is best demonstrated by a comparison between 5-benzylidibenzophosphole 5-oxide^{1a} and the phosphetane oxide **2**. The exocyclic benzyl group is common to both compounds, but the carbanion derived from cleavage of the dibenzophosphole ring is considerably more stable than the tertiary aliphatic carbanion derived from cleavage of the phosphetane ring. Even though any strain factor should be more significant for the four-membered ring, exclusive exocyclic cleavage occurs for **2** while preferential ring cleavage is observed for the dibenzophosphole ring.

Experimental Section¹²

1-Benzyl-2,2,3,4,4-pentamethylphosphetane 1-Oxide (2).—1-Chloro-2,2,3,4,4-pentamethylphosphetane 1-oxide² (25.2 g, 0.13 mol) in ether was added dropwise to a stirred ethereal solution of benzylmagnesium chloride prepared from magnesium (0.15 g-atom) and benzyl chloride (0.15 mol). The solution was heated and stirred 1 hr after the addition. The solution was then cooled and 300 ml of 5% hydrochloric acid was added dropwise. The organic layer was separated and washed with 5% sodium hydroxide solution and then water. The ether was evaporated and the solid residue recrystallized from benzene: yield 14.5 g (45%); mp 180–182°; nmr τ 8.5–9.2 (m, 15, -CH₃), 7.9–8.2 (m, 1, methine H), 6.74 (d, J_{P-H} = 11.5 Hz, P-CH₂-Ph), 2.4–2.9 (m, 5, aromatic H).

Anal. Calcd for C₁₅H₂₅OP: C, 71.97; H, 9.26; P, 12.37. Found: C, 72.10; H, 9.24; P, 12.19.

Cleavage of 1-Benzyl-2,2,3,4,4-pentamethylphosphetane 1-Oxide (2).—This phosphine oxide (4.7 g, 0.019 mol) was cleaved with sodium hydroxide (0.08 mol) at 250° for 1 hr. About 2 ml of toluene (identified by glpc and ir), essentially the calculated amount for exclusive benzyl cleavage, distilled during this time. The usual isolation procedure,¹ except that the acid was extracted from the acidic aqueous solution with chloroform, gave 1-hydroxy-2,2,3,4,4-pentamethylphosphetane 1-oxide (**4**): yield 2.8 g (85%); mp (after drying in a vacuum desiccator over phosphorus pentoxide) 71–73° (lit.² mp 72–74°). The acid was identical (ir and mixture melting point) with an authentic sample prepared by hydrolysis of the acid chloride **1**.

Cleavage of 1-Phenyl-2,2,3,4,4-pentamethylphosphetane 1-Oxide (3).⁸—This compound (5.9 g, 0.025 mol) was cleaved with sodium hydroxide (0.1 mol) at 225° for 1 hr. Several drops of benzene (identified by glpc) distilled during this time. The reaction mixture was dissolved in water and then acidified with hydrochloric acid. The aqueous solution, which contained a viscous oil, was extracted with chloroform. Evaporation of the chloroform gave an oily mixture of **4** and phenyl (2,3,4,4-tetramethylbutyl)phosphinic acid (**5**) in a ratio of approximately 1:4 as determined by nmr, yield 5.6 g (94% based on the above ratio). The acid **5** could be separated from **4** by repeatedly dissolving the mixture in a dilute sodium hydroxide solution and precipitating with hydrochloric acid. The first material precipitated was taken. The solid was recrystallized from aqueous ethanol and dried in a vacuum desiccator over phosphorus pentoxide: mp 100–103°; nmr τ 8.8–9.4 (m, 15, -CH₃), 7.6–8.5 (m, 2, methine H), 2.1–2.7 (m, 5, aromatic H).

Anal. Calcd for C₁₄H₂₅O₂P: C, 66.12; H, 9.11; P, 12.17. Found: C, 65.96; H, 8.95; P, 12.10.

Registry No.—**2**, 24655-74-1; **5**, 24655-75-2.

(10) Our suggestion (ref 2b) that acyclic phosphine oxides cleaved from a trigonal-bipyramidal intermediate with the oxygen atoms in the apical positions was based on coulombic repulsion and did not consider the competing factor of having the negative oxygen in an equatorial position.

(11) It is possible that the rate of exocyclic cleavage is slow because of an increase in ring strain in going from an intermediate (**8** or **9**) to a cyclic product.

(12) Melting points were taken with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 221 spectrophotometer. Nmr spectra were taken with a Varian A-60 instrument; deuteriochloroform was used as a solvent with tetramethylsilane as an internal standard. Elemental analysis were performed by Spang Microanalytical Laboratory.