Work is in progress to extend the study of the chemical behavior of phosphonitrilic chloride toward ketoxime and amides.

### Experimental Section

**Materials.**—Hexachlorocyclotriphosphazatriene (1) was purchased from Albright and Wilson, England, and used after purification by crystallization from petroleum ether (bp 30–60°). The oximes were prepared by standard methods. The nitriles were identified by comparison of their ir spectra and glc retention times with those of authentic samples and by their melting points in the case of solids. Pure-grade solvents were used without further purification.

**General Procedure.**—Triethylamine ($3.0 \times 10^{-2}$ mol) was added to a solution of the oxime ($1.0 \times 10^{-2}$ mol) and compound 1 ($1.0 \times 10^{-2}$ mol). The solution was allowed to stand at room temperature and the reaction was followed by tlc analysis (silica gel and benzene or cyclohexane–ethyl acetate as eluents). When the aldoxime had almost completely disappeared, triethylamine hydrochloride was removed by filtration and the filtrate was concentrated under reduced pressure. The mixture was taken up in 20 ml of benzene and the resulting nitrile was purified by chromatography on a silica gel column using benzene as eluent. Typical preparations follow.

**Heptanenitrile.**—To a solution of heptanealdoxime (1.29 g, $1.0 \times 10^{-2}$ mol) and phosphonitrilic chloride (3.47 g, $1.0 \times 10^{-2}$ mol) in 50 ml of diethyl ether in a 100-ml flask was added triethylamine (3.03 g, $3.0 \times 10^{-2}$ mol) in 10 ml of diethyl ether. The solution was stirred for 8 hr at room temperature. The triethylamine hydrochloride was removed by filtration and the filtrate was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel using benzene as eluent. Heptanenitrile (1.3 g), bp 54° (8 mm), was obtained in 93% yield; spectroscopic data are in agreement with those recorded on an authentic sample.

*Anal.* Calcd for $C_7H_{13}N$: C, 75.61; H, 11.79; N, 12.60. Found: C, 75.84; H, 11.62; N, 12.52.

**3-Indolecarbonitrile.**—To a solution of 3-indolecarboaldoxime (1.6 g, $1.0 \times 10^{-2}$ mol) and phosphonitrilic chloride (3.47 g, $1.0 \times 10^{-2}$ mol) in 50 ml of tetrahydrofuran in a 100-ml flask was added triethylamine (3.03 g, $3.0 \times 10^{-2}$ mol). The solution was stirred for 2 hr at room temperature. The triethylamine hydrochloride was removed by filtration and the filtrate was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel using benzene–ethyl acetate (7:3) as eluent. 3-Indolecarbonitrile (1.25 g, 98% yield) had mp 180–182° (lit.[6] mp 182–184°): spectroscopic data are in agreement with those recorded on a sample independently prepared.[6]

*Anal.* Calcd for $C_9H_6N_2$: C, 76.04; H, 4.25; N, 19.71. Found: C, 75.89; H, 4.12; N, 19.54.

***O*-(Pentachlorocyclotriphosphazatriene)cyclohexanone Oxime (3).**—The reaction between cyclohexanone oxime and compound 1 was performed in diethyl ether as depicted in the general procedure and gave a compound (mp 74–75°, white crystals from pentane) in 63% yield, to which the structure of *O*-(pentachlorocyclotriphosphazatriene)cyclohexanone oxime (3) was assigned: ir (KBr) 2900 (w), 1470 (vw), 1430 (w), 1375 (m), 1360 (m), 1340 (m), 1325 (m), 1310 (m), 1280 (m), 1250 (s, shoulder), 1230 (vs, shoulder), 1200 (vs, broad), 1160 (vs, shoulder), 1122 (vs), 1095 (m), 1020 (w), 960 (m), 917 (m), 870 $cm^{-1}$ (m).

*Anal.* Calcd for $C_6H_{10}Cl_5N_4OP_3$: C, 16.95; H, 2.37; Cl, 41.77; N, 13.23. Found: C, 16.70; H, 2.47; Cl, 41.81; N, 13.12.

**Registry No.**—1, 940-71-6; 3, 37709-15-2; heptanenitrile, 629-08-3; heptanealdoxime, 629-31-2; 3-indolecarbonitrile, 5457-28-3; 3-indolecarboaldoxime, 2592-05-4; cyclohexanone oxime, 100-64-1.

**Acknowledgment.**—The authors express their appreciation to Professor Luciano Caglioti for his interest in this project.

(6) H. M. Blatter, H. Lukaszewski, and G. de Stevens, *J. Amer. Chem. Soc.*, **83**, 2203 (1961); *Org. Syn.*, **43**, 58 (1963).



## The Synthesis of 1,3,5-Trimethylbicyclo[4.4.1]undecan-11-one by Intramolecular Alkylation[1]

IRVING J. BOROWITZ* AND NAUSICAA SUCIU

*Department of Chemistry, Belfer Graduate School of Science, Yeshiva University, New York, New York 10033*

*Received October 31, 1972*

In our approach toward the synthesis of molecules resembling the methymycin antibiotics, we recently reported the low yields found thus far in the acid-catalyzed cyclization–dehydration of 2,4,6-trimethyl-7-(4′-hydroxybutyl)cycloheptanone (**1**) to **2**.[2]

In an attempt to overcome this problem, the following alternate pathway to **2** was developed. The alkylation of *cis,cis*-2,4,6-trimethyl-7-carbethoxycycloheptanone (**3**)[2] *via* its sodium enolate with 1,4-dibromobutane (**4**) gives a 60:40 mixture of the desired 2,4,6-trimethyl-7-carbethoxy-7-(4′-bromobutyl)cycloheptanone (**5**, as a mixture of stereoisomers) and the O-alkylated product **6**. Since **3** is a highly hindered β-keto ester,[2] it had been anticipated that some O-alkylation might occur.[3] The corresponding alkylation of the sodium enolate of carbethoxycycloheptanone (**7**) with **4** occurs mainly on carbon.[4] Treatment with acid results in the hydrolysis of **6** to leave **5**, which is then internally alkylated (with sodium hydride in hexamethylphosphoramide) to give a 60:40 mixture of the desired enol ether **9** and the bridged keto ester **8**. Decarboxylation of this mixture with lithium iodide–collidine gives 1,3,5-trimethylbicyclo[4.4.1]undecan-11-one (**10**), a mixture of the enol ethers **2**, and a small amount of 2,4,6-trimethyl-7-(3′-butenyl)cycloheptanone (**11**, derived from **2** with lithium iodide). Ketone **10** (and a minor amount of **11**) is obtained by acid hydrolysis, which converts **2** to the easily separable **1**.

The intramolecular alkylation of **5a** had been expected to occur at the presumably less hindered oxygen site of the enolate ion, especially in highly polar hexamethylphosphoramide as solvent. Indeed, the sodium enolate of 2-carbethoxy-2-(4′-bromobutyl)cycloheptanone (i) gives 9:1 O/C intramolecular alkylation (ii, iii) in the less polar medium toluene–dimethylformamide.[4] The unexpected C-alkylation in **5a** may be due to enhancement of the normally greater nucleophilicity of the enolate carbon by the 2-methyl[5a] and possibly by inhibition of solvation at the crowded enolate carbon.[6]

(1) This investigation was supported by Public Health Service Research Grant AI 07455 from the National Institute of Allergy and Infectious Diseases.

(2) I. J. Borowitz, G. J. Williams, L. Gross, H. Beller, D. Kurland, N. Suciu, V. Bandurco, and R. D. G. Rigby, *J. Org. Chem.*, **37**, 581 (1972).

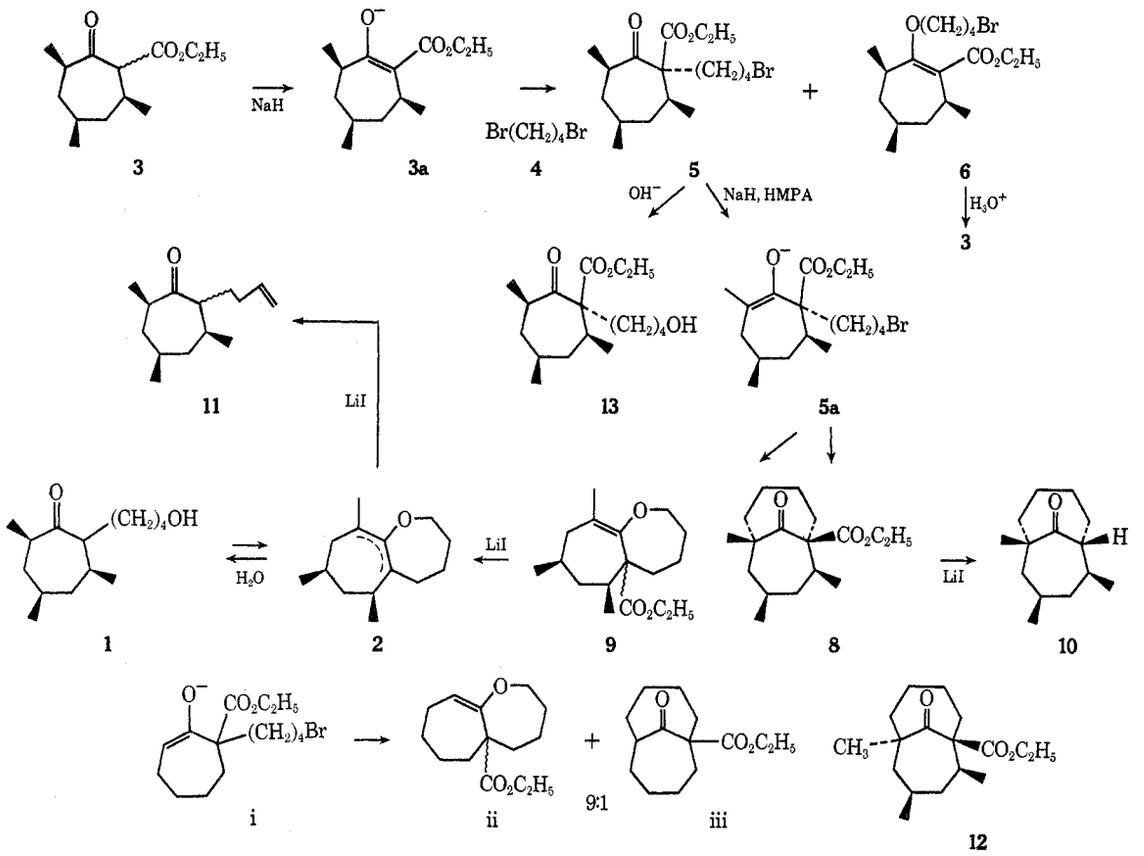
(3) The related alkylation of the sodium enolate of **3** with 1-bromo-4-acetoxybutane also gives some O-alkylation.[2]

(4) Professor John Wiseman, University of Michigan, private communication.

(5) (a) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 560; (b) pp 586–595.

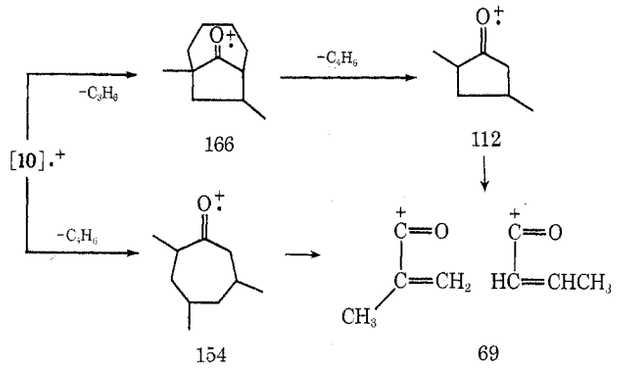
(6) Keto ester **5** may represent a borderline system wherein various factors can cause C- or O-intramolecular alkylation to predominate. The sodium enolate of 2-carbethoxy-2-(4′-bromobutyl)cyclododecanone (a large ring system approaching the behavior of acyclic enolates) gives intramolecular C-alkylation only.[7]

(7) H. Nozaki, H. Yamamoto, and T. Mori, *Can. J. Chem.*, **47**, 1107 (1969).



The stereochemistry suggested for the major isomer of **5**, for **8**, and for **10** (as illustrated) is based on the following assumptions. Introduction of the alkyl group from the less hindered side in **3a** *via* a transition state resembling the starting enolate[5b] should give **5**. Intramolecular cyclization of **5a** should give the all-cis isomer **8** as the less strained product (in comparison to the trans isomer **12**). Decarboxylation of **8** should give the all-cis **10**, again as the less strained isomer when compared to the alternate isomer with trans bridgehead methyl and proton groups.

Ketone **10** represents one of the few available examples of the bicyclo[4.4.1]undecane system.[8] Support for its structure is found in its mass spectrum, which includes peaks at *m/e* 112, 154, and 166. The latter two (among others) are not found in the mass spectra of the enol ether isomers of **2**. Suggested structures are as follows.



(8) See T. L. Westman and R. D. Stevens, *Chem. Commun.*, 459 (1965), and references cited therein.

It is interesting to note that intramolecular acid-catalyzed aldol condensation in cyclohexanones, leading to the bicyclo[3.3.1]nonane system, is favored by 2,6-dimethyl substitution.[9] The reasons for this "methyl group effect" differ, however, from those pertaining to enolate alkylation.

## Experimental Section[10]

**Alkylation of β-Keto Ester 3.**—Alkylation of the sodium enolate of 2,4,6-trimethyl-7-carbethoxycycloheptanone [from **3** and sodium hydride in toluene–dimethylformamide (4–5:1) at reflux for 30 min] with 1,4-dibromobutane (**4**, 1 equiv, at reflux for 24 hr) gave a neutral solution which was filtered, concentrated, and treated with 1 *N* HCl in methanol–water (6:1) for 24 hr at 25°. Neutralization with $NaHCO_3$, evaporation of the methanol, and extraction of the organic layer into diethyl ether, followed by drying ($MgSO_4$) and evaporation *in vacuo*, gave 2,4,6-trimethyl-7-carbethoxy-7-(4′-bromobutyl)cycloheptanone (**5**, 26%): bp 150–160° (0.15 mm); ir ($CCl_4$) 1710, 1700 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 5.83 (m, 2, $CO_2CH_2CH_3$), 6.67 (t, 2, $CH_2Br$), 7.9–9.1 (m, 16), 8.7 (t, 3, $CH_3CH_2$), and 8.95 (broad d, 6, $CH_3CH$); vpc (10% SE-30 at 200°) two peaks with close retention times (*ca.* 12 min).

*Anal.* Calcd for $C_{17}H_{29}O_3Br$: C, 56.51; H, 8.10; Br, 22.12. Found: C, 56.26; H, 7.92; Br, 21.86.

Similar alkylation of **3** with NaH and **4** in toluene–DMF without acid treatment gave a mixture of **5** and **6** in 60:40 ratio (28–38%), vpc (1% SE-30 at 165°) retention time 11 and 7 min, respectively. The use of toluene–DMF in 2 or 3:1 ratio gave a C-

(9) J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965).

(10) Infrared spectra were recorded on Perkin-Elmer 257 and 700 spectrophotometers. Nmr spectra were recorded on a Varian A-60A spectrometer with TMS as an internal standard. Boiling points are uncorrected. Mass spectra were done on a Varian Atlas CH-5 vpc-inlet mass spectrometer by Mr. Jack Landis, City University of New York. Solvents were dried by distillation from phosphorus pentoxide, calcium hydride, or lithium aluminum hydride. Reactions involving carbanions were conducted under prepurified nitrogen. Gas chromatograms were done on a Varian Aerograph A-700 employing columns packed with 5 or 10% SE-30 on Chromosorb W (5 or 10 ft × 0.25 in.).

*vs.* O-alkylated product ratio of 1:1 (35%). Reaction in toluene gave **5** in 8% yield. Reaction of **5** with aqueous NaOH gave 2,4,6-trimethyl-7-carbethoxy-7-(4′-hydroxybutyl)cycloheptanone (**13**) identical (by vpc, ir, and nmr) with a genuine sample [from the base hydrolysis of 2,4,6-trimethyl-7-carbethoxy-7-(4′-acetoxybutyl)]cycloheptanone].[2]

**Intramolecular Alkylation of 5.**—To a suspension of 52% NaH (washed with hexane, 1.31 g, 0.028 mol) in hexamethylphosphoramide (75 ml), **5** (10 g, 0.028 mol) was added with stirring at room temperature. The resultant mixture was stirred for 24 hr at 140° to give a neutral solution which was filtered and distilled to give a mixture containing **8** and **9** in 40:60 ratio (2.94 g, 0.011 mol, 39% if only **8**, **9**): bp 130–150° (0.15 mm); ir ($CCl_4$) 1680 (vinyl ether), 1725 (ketone), and 1740 $cm^{-1}$ (ester); nmr ($CCl_4$) $\tau$ 5.88 (2, m, $CO_2CH_2CH_3$), 6.40 (m, $CH_2O$), 8.33 (s, vinyl $CH_3$), 8.8 (t, 3, $CH_2CH_3$), 8.2–8.8 (m), 8.95–9.2 (m, 6, $CH_3$); vpc–mass spectrum (5% SE-30, 75 eV) *m/e* peak 1 (minor isomer of **8**) 280, peak 2 (major isomer of **8**) 280, peak 3 (minor isomer of **9**) 280, peak 4 (major isomer of **9**) 280, peak 5 (minor amount, **1**) 298. Preparative tlc (on silica, extracted with $CHCl_3$) gave a mixture of fractions 1–4 (**1** was left behind) which was analyzed. *Anal.* Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.62; H, 10.03.

**Decarboxylation of 8 and 9.**—A mixture of lithium iodide dihydrate (4.4 g, 0.026 mol) and the above mixture of **8** and **9** (5.20 g, 0.019 mol) in dry collidine (25 ml) was heated at reflux for 30 hr. The cooled mixture was then poured into ice water (40 ml)–diethyl ether (40 ml) and carefully acidified with cold 1 *N* HCl. The resultant organic layer was then washed with 2 *N* $Na_2CO_3$ (30 ml) and saturated NaCl (2 × 30 ml), dried ($Na_2SO_4$), and distilled to give **2** and **10** in 60:40 ratio (0.7 g, 0.0034 mol, 18%): bp 75° (0.15 mm); ir (neat) 1700 $cm^{-1}$, no OH; nmr ($CCl_4$) $\tau$ 6.45 (m, $CH_2O$), 8.0–8.8 (m, $CH_2$, CH), 8.4 (s, vinyl $CH_3$), 8.95–9.2 (m, 6, $CH_3CH$); vpc–mass spectrum (5% SE-30, 70 eV) *m/e* (rel intensity) peak 1 (**10**) 208 ($M\cdot^+$, 27), 193 (25), 166 (28), 155 (38), 154 (98), 139 (98), 126 (34), 125 (48), 112 (98), 111 (100), 109 (35), 97 (40), 95 (60), 84 (42), 83 (98), 69 (98), 55 (98), M + 1 = 16.1 (calcd for $C_{14}H_{24}O$, M + 1 = 15.6),[11] peak 3 (isomer of **2**) 208 ($M\cdot^+$, 60), 193 (62), 179 (10), 165 (68), 151 (37), 139 (34), 137 (35), 126 (98), 112 (67), 111 (73), 109 (52), 95 (78), 81 (65), 69 (93), 55 (100), and similar fragmentation for peak 4 (isomer of **2**). Also obtained was a fraction consisting mainly of **1** (identical vpc, ir, and nmr with those of a genuine sample)[2] and small amounts of **2** and **10** (0.6 g, 0.0027 mol, 14% if all 1), bp 125° (0.15 mm). Peak 2 (*m/e* 208) is probably **11** (see below).

Treatment of the mixture of **2**, **10**, and **11** (0.4 g, *ca.* 0.002 mol) with 1 *N* HCl (2 ml) in methanol (5 ml) gave a mixture of **1**, **10**, and **11** (minor amount). Distillation gave 1,3,5-trimethylbicyclo[4.4.1]undecan-11-one (**10**, *ca.* 0.15 g, 0.0007 mol, 35%): bp 70° (0.15 mm); ir (film) 1700 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 7.0–8.8 (m, 15), 9.02 [s, 3, bridgehead $CH_3$, shifted downfield by Eu(DPM)$_3$], 9.01 (d, 6, $CH_3CH$, $J$ = 7 Hz); vpc retention time for **10** as in above sample. About 10% (by vpc area of a separate peak) of **11** was present: ir 1640 $cm^{-1}$; nmr $\tau$ 4–4.5, 5.05 (br d), 5.3 ($CH=CH_2$).[2]

**Registry No**—**2** (10-ene), 33015-94-0; **2** (5a-ene), 37931-56-9; **3**, 37931-57-0; **4**, 110-52-1; **5**, 37931-58-1; **8** (major isomer), 37931-59-2; **8** (minor isomer), 37931-60-5; **9** (major isomer), 37931-61-6; **9** (minor isomer), 37931-62-7; **10**, 37931-63-8.

(11) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," Wiley, New York, N. Y., 1963, p 37.

# *Communications*

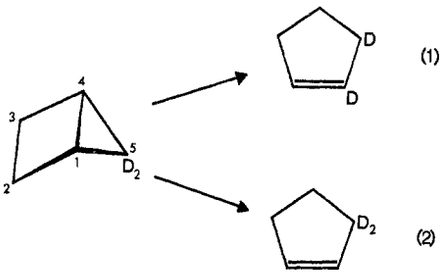
See Editorial, *J. Org. Chem.*, **38**, No. 19, 4A (1972)

## Thermal Rearrangement of 5,5-Dideuteriobicyclo[2.1.0]pentane[1]

*Summary:* Through a deuterium-labeling study the thermal rearrangement of bicyclo[2.1.0]pentane to cyclopentene has been shown to involve a hydrogen rather than a carbon migration.

*Sir:* 5,5-Dideuteriobicyclo[2.1.0]pentane has been prepared and employed by Gassman, Atkins, and Lumb[2] in their investigations of the rhodium dicarbonyl chloride dimer catalyzed isomerization of that bicyclic system to cyclopentene. The rearrangement product indicated extensive scrambling of deuterium label at some stage of the reaction.

We have used this dideuterio compound to study the gas phase thermal isomerization of bicyclopentane to cyclopentene.[3–5] The results obtained provide the first experimental distinction between mechanistic options requiring C(1)–C(4) bond cleavage and C(5)–H hydrogen migration (eq 1), and others postulating C(1)–C(5) bond cleavage with C(3) carbon migration (eq 2).




Isomerizations analogous to each of these alternatives, and others consistent with either, have been observed in some acetyl- and ethoxycarbonyl-substituted bicyclopentanes.[6–9]

The deuterated substrate was prepared through reaction of cyclobutene[10] with 60% deuterated benzylmercuriiodomethane,[11] secured in turn from partially

(1) Supported by the National Science Foundation through Grant GP-31415.

(2) P. G. Gassman, T. J. Atkins, and J. T. Lumb, *Tetrahedron Lett.*, 1643 (1971); *J. Amer. Chem. Soc.*, **94**, 7757 (1972).

(3) R. Criegee and A. Rimmelin, *Chem. Ber.*, **90**, 414 (1957).

(4) M. L. Halberstadt and J. P. Chesick, *J. Amer. Chem. Soc.*, **84**, 2688 (1962).

(5) C. Steel, R. Zand, P. Hurwitz, and S. G. Cohen, *ibid.*, **86**, 679 (1964).

(6) T. H. Kinstle, R. L. Welch, and R. W. Exley, *ibid.*, **89**, 3660 (1967).

(7) M. J. Jorgenson and T. J. Clark, *ibid.*, **90**, 2188 (1968).

(8) M. J. Jorgenson and A. F. Thatcher, *Chem. Commun.*, 1030 (1969).

(9) E. Baggiolini, K. Schaffner, and O. Jeger, *ibid.*, 1103 (1969).

(10) A. C. Cope, A. C. Haven, Jr., F. L. Ramp, and E. R. Trumbull, *J. Amer. Chem. Soc.*, **74**, 4867 (1952).

(11) R. Scheffold and U. Michel, *Angew. Chem., Int. Ed. Engl.*, **11**, 231 (1972).