

The largest subfraction 5-3, chromatographically identical with cellobiose, was concentrated to an amber sirup, yielding 0.0265 g., $[\alpha]^{25D} +30.8^\circ$ (c 0.88, water); hydrolysis produced glucose only. Crystalline material formed in aqueous acetic acid

was removed by filtration, washed with acetone, and dried under vacuum and had m.p. 231–233°, unchanged upon admixture with authentic cellobiose. The infrared spectrum of the crystals was identical with that of authentic cellobiose.

Dissociation Constants of the Cyanohydrins of Some Methyl-Substituted Cyclobutanones, Cyclopentanones, and Cycloheptanones. Conformation of These Rings

OWEN H. WHEELER AND ELSIE GRANELL DE RODRIGUEZ

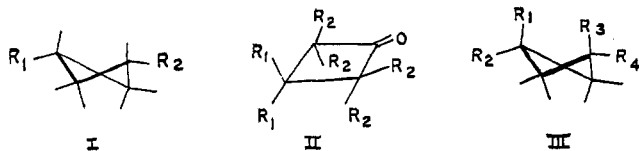
The Department of Chemistry and The Puerto Rico Nuclear Center,¹ University of Puerto Rico at Mayaguez College Station, Mayaguez, Puerto Rico

Received October 31, 1963

The dissociation constants of the cyanohydrins of a number of methyl-substituted cyclobutanones, cyclopentanones, and cycloheptanones have been determined in 95% ethanol at 23°. The results suggest that the cyclobutanone ring is slightly puckered, that cyclopentanone exists in a flexible half-chair or envelope conformation, and that the cycloheptanone ring is a flexible chair.

A study of the dissociation constants of the cyanohydrins of methyl-substituted cyclohexanones² has shown the large steric effect of this substituent in an axial position. The present study concerns ketones of smaller and larger rings, and the results are discussed in relation to the conformation of these rings.

Cyclobutanone.—A number of spectroscopic and thermodynamic studies of cyclobutane³ have shown that the ring is puckered (I). A recent study⁴ of the



isomeric methyl 3-methylcyclobutanecarboxylates has shown that the *cis* isomer (I, $R_1 = \text{CH}_3$; $R_2 = \text{CO}_2\text{CH}_3$) is more stable, and this is only consistent with a puckered ring conformation. The conformation of cyclobutanone is less certain. Its high infrared carbonyl stretching frequency⁵ has been interpreted^{5b} in terms of a "slightly puckered" ring with an internal ring carbonyl angle of only $82 \pm 9^\circ$. Recent measurements⁴ of the dipole moment, and ultraviolet and infrared spectra of α -bromocyclobutanone show that it exists largely with the carbon–bromine bond "axial" at an angle of 101° to the carbonyl dipole (*i.e.*, a near planar ring), although in polar solvents, this bond is partially "equatorial" (*i.e.*, a puckered ring as in I).

The value of the dissociation constant of cyclobutanone cyanohydrin (see Table I) determined in the present work is in good agreement with a previous value (0.84×10^{-2}) determined using carefully purified ketone,^{6a} but is smaller than the value (4.5×10^{-2}) reported by

(1) The Puerto Rico Nuclear Center is operated by the University of Puerto Rico for the Atomic Energy Commission under Contract No. AT-(40-1)-1833.

(2) O. H. Wheeler and J. Z. Zabiaky, *Chem. Ind. (London)*, 1388 (1956); *Can. J. Chem.*, **36**, 656 (1958).

(3) J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952); G. W. Rathjens, Jr., N. K. Freeman, W. D. Gwinn, and K. S. Pitzer, *J. Am. Chem. Soc.*, **75**, 5634 (1953); A. Almendinger, O. Bastiansen, and P. N. Skancke, *Acta Chem. Scand.*, **15**, 711 (1961).

(4) J. M. Conia, J. L. Ripoll, L. A. Tushans, C. L. Neumann, and N. L. Allinger, *J. Am. Chem. Soc.*, **84**, 4983 (1962).

(5) (a) K. Frei and H. H. Gunthard, *Helv. Chim. Acta*, **43**, 649 (1960); (b) R. Zbinden and H. K. Hall, Jr., *J. Am. Chem. Soc.*, **82**, 1215 (1960).

TABLE I
DISSOCIATION CONSTANTS OF CYANOHYDRINS^a

	$K_D \times 10^2$
Cyclobutanone	0.922
3,3-Dimethyl-	21.2
2,2,4,4-Tetramethyl-	2.72
Cyclopentanone	2.98 ^b
2-Methyl-	3.15
3-Methyl-	3.71
2,4-Dimethyl-	3.90
2,5-Dimethyl-	4.71
2,2,4-Trimethyl-	1.92
2,4,4-Trimethyl-	6.71
2,2,4,4-Tetramethyl-	19.0
Cyclohexanone	0.059 ^c
Spiro[4.4]nonan-1-one (XIII)	12.3
Spiro[4.5]decan-6-one (XIV)	1.57
Cycloheptanone	8.77 ^d
2-Methyl-	17.8
3-Methyl-	8.56
4-Methyl-	10.8
3,3,5-Trimethyl-	25.3
3,5,5-Trimethyl-	10.3
3,3,5,5-Tetramethyl-	28.4

^a In 95% ethanol at $23 \pm 1^\circ$. ^b Ref. 2 gives 2.05 at 25° .

^c From ref. 2. ^d A. Lapworth and R. H. F. Manske [*J. Chem. Soc.*, 2533 (1923)] give $K_D \times 10^2 = 7.96$ at 20° , and V. Prelog and M. Kobelt [*Helv. Chim. Acta*, **32**, 1187 (1949)] give 13 at $22-23^\circ$.

Ruzicka and co-workers.^{6b} The two substituted cyclobutanones had cyanohydrin dissociation constants larger than the unsubstituted ketone, although the differences are smaller than for similarly substituted cyclohexanones.²

The two opposing factors of ring angle strain and nonbonded hydrogen interactions² are responsible for the nonplanar conformation of cyclobutane. In cyclobutanone the ring angle strain is considerably increased and any departure from a planar conformation will increase angle strain. However, the nonbonded hydrogen interactions are reduced from eight in a planar conformation of cyclobutane to only four in cyclobutanone. Although I-strain is relieved on forming the

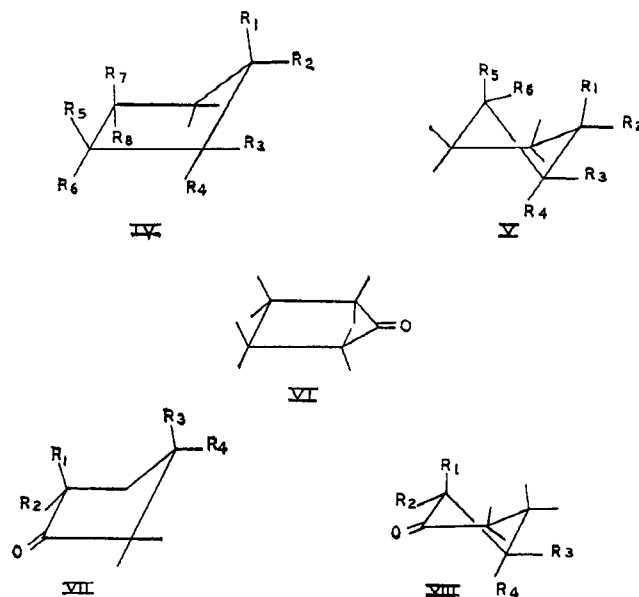
(6) (a) H. C. Brown and O. H. Wheeler, in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 238; (b) L. Ruzicka, P. A. Plattner, and H. Wild, *Helv. Chim. Acta*, **28**, 613 (1945).

cyanohydrin of cyclobutanone, unfavorable interactions are introduced between the hydroxyl and cyano groups and the ring hydrogen atoms. Consequently, the cyanohydrin dissociation constant of cyclobutanone is larger than that for cyclohexanone ($K_D = 0.059 \times 10^{-2}$, where I-strain is the principal factor²) but smaller than that for cyclopentanone (2.98×10^{-2} , where nonbonded interactions are the main factor⁷; see also below).

In the near-planar conformation of cyclobutanone (II, $R_1 = R_2 = H$; the carbonyl group is tipped slightly up) the introduction of two methyl groups in 3,3-dimethylcyclobutanone (II, $R_1 = CH_3$; $R_2 = H$) should produce little extra strain, and the four methyl groups in 2,2,4,4-tetramethylcyclobutanone (II, $R_1 = H$; $R_2 = CH_3$) also are staggered with respect to the hydrogen atoms and the carbonyl group. However, in the case of the cyanohydrin of 3,3-dimethylcyclobutanone (III, $R_1 = R_2 = CH_3$; R_3 and $R_4 = OH$ or CN) one of the two methyl groups ("axial" R_1 in III) will necessarily interfere with either the hydroxyl or cyano group, and reduce the stability of this cyanohydrin as compared to cyclobutanone. In 2,2,4,4-tetramethylcyclobutanone cyanohydrin, the two axial methyl groups are across the ring opposite to the axial hydroxyl or cyano group (R_3 in III) and the other pair are staggered in equatorial positions to the remaining cyanohydrin groups (R_4 in III). If the cyclobutane ring were planar, the dissociation constant of this compound would be considerably larger, since all four methyl groups would interfere with the cyanohydrin groups. (The inductive effect of the methyl group also will tend to increase K_D ; see below.)

Cyclopentanones.—The preferred conformation of a substituted five-membered ring is less certain⁸ than that of a cyclohexane ring.

The internal ring angle (108°) in a planar cyclopentane ring is little different from the carbon tetrahedral angle ($109^\circ 28'$). However, in a planar conformation there exist five pairs of unfavorable nonbonded hydrogen atom interactions. These interactions can be relieved without seriously changing the ring angles through puckering of the ring. Cyclopentane^{8c} itself assumes a mobile "envelope" conformation (IV, $R_{1-5} = H$) in which one carbon atom is above the others, and this alternates around the ring. Cyclopentanes substituted with small substituents adopt the same conformation, with the ring carbon atom carrying the substituent (R_2 in IV) above the general plane of the ring. Thus, cyclopentanone cyanohydrin exists in the envelope conformation^{8c} (IV, R_1 and $R_2 = OH$ or CN). Since there is no factor such as I-strain present in the ketone facilitating cyanohydrin formation (as in cyclohexanone,² $K_D = 0.59 \times 10^{-2}$), or nonbonded interactions in the cyanohydrin decreasing its stability (as in cycloheptanone, $K_D = 8.77 \times 10^{-2}$; see below), cyclopentanone shows moderate reactivity ($K_D = 2.98 \times 10^{-2}$). More highly substituted cyclopentanes adopt a more puckered envelope conformation or pass over to a half-chair conformation (V).^{8e} The dissociation con-



stants of the cyclopentanones covered a range of six-fold with dissociation constants larger than that of cyclopentanone itself. Part of the small increase in the dissociation constant for 2-methylcyclopentanone may be due to the inductive (+I) effect of the methyl group. However, the larger constant for the 3-methyl isomer can be due only to the steric effect of this group.⁹ While one α -methyl group (2-methylcyclopentanone; and compare 3-methyl- and 2,4-dimethylcyclopentanone, $K_D \times 10^2 = 3.71$ and 3.90, respectively) or two methyl groups on different α -carbon atoms (2,5-dimethylcyclopentanone, $K_D \times 10^2 = 4.71$) have little effect, two methyl groups on the same α -carbon atom have a large effect (cf. 3-methyl- and 2,2,4-trimethylcyclopentanone, $K_D \times 10^2 = 3.71$ and 19.2, respectively). Comparing 2-methyl- and 2,4,4-trimethylcyclopentanone ($K_D \times 10^2 = 3.15$ and 6.71), it can be seen that two β -substituents have a much smaller effect. The similarity of the dissociation constants of the cyanohydrins of 2,2,4-trimethyl- and 2,2,4,4-tetramethylcyclopentanone again illustrates the small effect resulting from β -substitution.

These results are clearly not consistent with a planar conformation (VI) for cyclopentanone, since this would result in a large α -substituent effect and an appreciable effect for β -substitution in the opposed cyanohydrin.

The two conformations of cyclopentanone based on the envelope (IV) and half-chair (V) conformation of cyclopentane will be as in VII and VIII. The keto group in VII is placed on one of the lower carbon atoms, rather than at the apex, since this relieves the nonbonded hydrogen interactions of the opposed atoms in IV. Similarly, the carbonyl group in the half-chair conformation (VIII) is located as shown and not on one of the other carbon atoms.

Considering the envelope conformation for cyclopentanone (VII), one or two methyl groups can be accommodated on either of the two α -positions (R_1 and R_2 in VII) or on the β -position (R_3 and R_4 in VII) without interfering with either the keto group or the neighboring hydrogen atoms. However, in the case of the

(7) H. C. Brown, *J. Chem. Soc.*, 1248 (1956).

(8) (a) C. G. Le Fevre and R. J. W. Le Fevre, *ibid.*, 3549 (1956); (b) F. V. Brutcher, Jr., T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959); (c) K. S. Pitzer and W. E. Donath, *ibid.*, **81**, 3213 (1959); (d) M. Low, *Tetrahedron Letters*, **1**, 3 (1960); (e) J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961); (f) F. V. Brutcher, Jr., and W. Bauer, Jr., *ibid.*, **84**, 2233 (1962).

(9) Both cyclopentanone and its cyanohydrin have about the same entropy,^{8c} since the pseudorotation of the ring is restricted in both compounds and entropy differences cannot account for the differences in K_D .

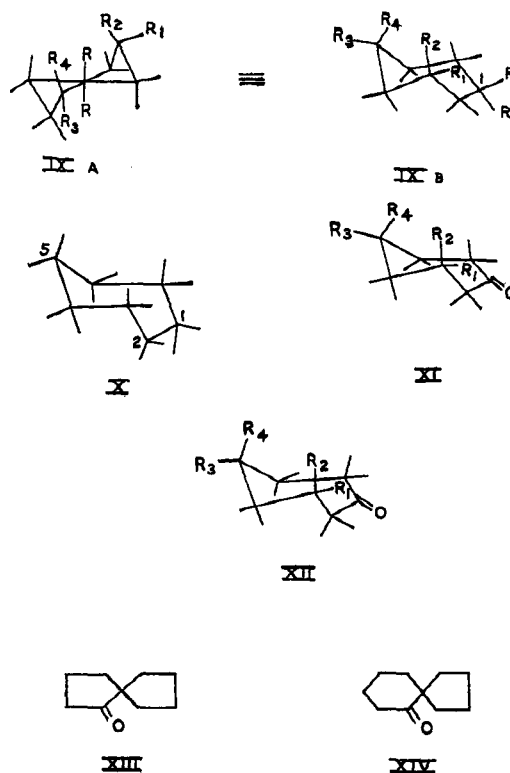
cyanohydrin (IV, R_1 and $R_2 = \text{OH}, \text{CN}$) where one α -methyl group (R_4 in IV) or two α -methyl groups on different carbon atoms can be accommodated, two methyl groups on the same α -carbon atom (R_3 and R_4 in IV) will reduce necessarily the stability of the cyanohydrin (interaction between "equatorial" R_2 and R_3 in IV). One β -methyl group will not interfere (R_5 in IV), and a second β -methyl group (R_6 in IV) will have only a small additional effect. If the cyanohydrin were to adopt the twist-chair conformation (V), then two β -methyl groups would considerably increase the cyanohydrin dissociation constant (interference between R_5 and R_1 in V).

In the case of the tri- and tetramethylcyclopentanones, adoption of the "half-chair" conformation (VIII) relieves the nonbonded interactions between the α - and β -methyl groups (R_1 and R_2 , and R_3 and R_4 in VIII). The structure is less crowded than the alternate "envelope" conformation (VII) in which the methyl groups will interfere in 2,2,4,4-tetramethylcyclopentanone (VII, $R_1 = R_2 = R_3 = R_4 = \text{Me}$; opposition R_1 and R_2). The cyanohydrin of these ketones must adopt conformation IV. Assuming that the bulkier cyanohydrin groups occupy the apex (R_1 and R_2), the three methyl groups in 2,4,4-trimethylcyclopentanone can be accommodated (on R_4 , R_7 , and R_8) with little interference, but for 2,2,4-trimethyl- and 2,2,4,4-tetramethylcyclopentanone, oppositions are introduced between an α -methyl group (R_3) and the cyanohydrin.

Comparing the dissociation constants for 2-methylcyclopentanone and 2,4,4-trimethylcyclopentanone, the free energy of interaction [from $\Delta(\Delta F) = -RT \ln (K_1/K_2)$] of the two β -methyl groups with the cyanohydrin function was -0.4 kcal./mole. In 2,4,4-trimethylcyclopentanone and 2,2,4,4-tetramethylcyclopentanone one additional α -methyl group produced a free energy difference of -0.6 kcal./mole. The axial nonbonded methyl-cyanohydrin interaction in cyclohexanone was found² to be -1.55 kcal./mole. However, in the cyclopentanones the conformation of the ketone changes with substitution and in the case of the two β -methyl groups these are not conformationally equivalent.

Cycloheptanones.—The conformations of cycloheptane and cycloheptanone rings have been considered recently.¹⁰

The most stable conformation of cycloheptane seems to be the twist-chair conformation, illustrated "end-on" in structure IXa and "side-view" in structure IXb. This conformation has been estimated^{10c} to be 2.16 kcal./mole more stable than the chair conformation (X). There is some interference between the hydrogen atoms on the axis carbon atom^{10c,d} (atom 1) of the twist-chair conformation (IXa,b) and the hydrogen atoms on the α -carbon atoms. However, the two pairs of equatorial and axial hydrogen atoms on the two carbon atoms (atoms 1 and 2) at the "base" of the chair conformation (X) are opposed, and this probably is largely responsible for the high energy of this conformation. The replacement of two geminal hydrogen atoms by an oxygen atom in cycloheptanone can result in relief of these nonbonded interactions. In the twist-



chair conformation (IXa,b) of cycloheptanone the reduction in these interactions is greatest if the keto group is placed on C-1 as in XI. Positioning of the keto group on C-1 in the chair conformation (X) eliminates the opposed hydrogen interactions, as is illustrated in structure XVI. An alternative suggestion^{10a} that the keto group may be on the apex C-5 of X seems unlikely since these hydrogen oppositions are not relieved. There would seem to be little difference in the energies of the twist-chair and chair conformation (XI and XII) for cycloheptanone.

The cyanohydrin dissociation constants of the methyl substituted cycloheptanones were only a little larger than cycloheptanone itself (see Table I). The higher dissociation constant of cycloheptanone cyanohydrin (*cf.* cyclohexanone and cyclopentanone cyanohydrins, $K_D \times 10^2 = 0.59$ and 2.98, respectively) is consistent with the suggestion that no large ring angle strain (I-strain) effects are present in either the ketone or its addition product but are due to steric effects resulting from the introduction of two large groups (OH and CN) into the cycloheptane ring.

The small differences found between the cyanohydrin dissociation constants of the substituted cycloheptanones, which cover a range of only 3.2 (*cf.* range of 800 in similarly substituted cyclohexanones²), are due probably to the operation of a number of factors. However, the following interpretation would seem reasonable and consistent.

Of the monomethylcycloheptanones, the 2-methyl isomer showed the largest effect. As for 2-alkylcyclohexanone an α -methyl group could occupy both equatorial and axial positions and would exert steric hindrance to formation of the cyanohydrin in an equatorial position in either conformation XI or XII. The small decrease in the dissociation constant for 3-methylcycloheptanone and the increase in 4-methylcycloheptanone probably are not significant, but may be due to minor changes in the ring conformations on substitution.

(10) (a) C. G. LeFevre, R. J. W. LeFevre, and R. P. Rao, *J. Chem. Soc.*, 2340 (1959); (b) R. Paunez and D. Ginsburg, *Tetrahedron*, **9**, 40 (1960); (c) J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961); (d) J. B. Hendrickson, *ibid.*, **84**, 3355 (1962).

However, the differences between the two trimethyl- and tetramethylcycloheptanones are important. The methyl groups are accommodated in the ketones without any serious interference in either conformation XI or XII (at R₁, R₂, R₃, or R₄). Considering the corresponding cyanohydrins, the three methyl groups in 3,5,5-trimethylcycloheptanone cyanohydrin can be accommodated (on R₁, R₃, and R₄ in IXa,b) without interfering with the cyanohydrin function (R, R in IX). However, in both 3,3,5-trimethyl- and 3,3,5,5-tetramethylcycloheptanone, the second β -methyl (R₂ in IXa,b) interferes with either the cyano or hydroxyl group (best seen in IXa).

Comparing the K_D values of 3,5,5- and 3,3,5-trimethylcycloheptanone cyanohydrins, changing a methyl to the β -position results in an increase in free energy [$\Delta(\Delta F) = -RT \ln (K_D^1/K_D^2)$] of -0.5 kcal./mole. For 3,5,5-trimethyl- and 3,3,5,5-tetramethylcycloheptanone cyanohydrins, the effect of the extra β -methyl group in the later is -0.6 kcal./mole. These small differences may be compared with the corresponding value of $\Delta(\Delta F) = -1.55$ kcal./mole for a methyl-cyanohydrin group repulsion in cyclohexane² (the ratio of K_D values for 3,3,5-trimethyl- and 3,3,5,5-tetramethylcyclohexanone cyanohydrins was 1:21).

Conclusions

Comparison of the present data with the previous measurements on cyclohexanones,² emphasizes the unique nature of a six-membered carbon ring, both in regard to its high reactivity and the very large effects of methyl substitution. This also is reflected in the cyanohydrin dissociation constants of spiro[4.5]decan-6-one (XIV, five-membered ring in α -position of cyclohexanone) as compared to cyclohexanone (ratio 27:1) and spiro[4.4]nonan-1-one (XIII, five-membered ring α to cyclopentanone) as compared to cyclopentanone (ratio 4:1).

The general conclusions are that a cyclobutanone ring adopts a near-planar conformation, that a substituted cyclopentanone assumes a "half-chair" conformation passing to an envelope conformation on further substitution, and that the cycloheptanone ring exists in flexible-chair conformation. In the cases of all three rings two β -methyl groups have a large effect, and this is more pronounced for the less flexible cyclobutanone ring.

Experimental

Ketones-Cyclobutanones.—Cyclobutanone was purchased from the Aldrich Chemical Company. 3,3-Dimethylcyclobutanone was synthesized¹¹ by treating dimethyl ketone in ethyl acetate¹² with diazomethane in a nitrogen atmosphere. 2,2,4,4-Tetramethylcyclobutanone was prepared by Wolf-Kishner reduction of 2,2,4,4-tetramethylcyclobutanedione disemicarbazone,¹³ and was purified *via* its semicarbazone (m.p. 197–198°, lit.^{13a} m.p. 193–194°), being regenerated by steam distillation with oxalic acid.

Cyclopentanones.—The cyclopentanones generally were prepared by oxidation of the appropriate cyclohexanones with nitric acid and cyclizing the resulting adipic acids by distillation from barium hydroxide.^{14,15} 2-Methylcyclopentanone was prepared by methylation of ethyl cyclopentanone-2-carboxylate,¹⁶ and 2,2,4-trimethylcyclopentanone also was prepared by Clemmensen

reduction of dimedone.¹⁷ The spiro ketones were prepared from cyclopentanone pinacol.¹⁸

Cycloheptanones.—The cycloheptanones generally were prepared by ring expansion of the appropriate cyclohexanone with diazomethane in methanol.^{19–21} 2-Methylcycloheptanone was prepared similarly from cyclohexanone and diazoethane.²¹

3,3,5,5-Tetramethylcycloheptanone.—3,3,5,5-Tetramethylcyclohexanone²² in methanol (10 ml.) and 30% aqueous sodium hydroxide (15 ml.) was cooled to below 0°, and N-nitrosomethylurea (7.5 g.) was added in portions with stirring over 0.5 hr.²⁴ The reaction mixture was stirred at room temperature overnight and was extracted with ether. The ether extract was washed with dilute hydrochloric acid and water and dried. Distillation of the residue, left after evaporating the ether through a short column, gave the ketone (4.2 g.), b.p. 87° (20 mm.), n_D^{25} 1.4515.

Anal. Calcd. for C₁₁H₂₀O: C, 78.45; H, 12.0. Found C, 78.2; H, 12.2.

All the ketones were purified by fractional distillation and were used immediately. Only fractions showing a single sharp peak on gas chromatography (Craig polyester succinate at 150°) were used. Their physical constants are given in Table II.

TABLE II
PHYSICAL CONSTANTS OF KETONES

	B.p., °C. (mm.) ^a	n_D^{25}
Cyclobutanone	98 [98–100] ^b	1.4174 ²⁸ (1.4189 ²⁸)
3,3-Dimethyl-	119 [122–124 (770)] ^c	1.4177 ²⁸
2,2,4,4-Tetramethyl-	128 [128.5–129 (745)] ^d	1.4190 ²⁸
Cyclopentanone		1.4325 ²⁷
2-Methyl-	140 [139] ^e	1.4341 ²⁸ (1.4364 ²⁸) ^e
3-Methyl-	144 [143 (756)] ^f	1.4291 ²⁸ (1.433 ²⁸) ^f
2,2,4-Trimethyl-	155–156 [156.1] ^g	1.4242 ²⁸ (1.4293 ²⁸) ^g
2,4,4-Trimethyl-	159–160 [161.29] ^h	1.4254 ²⁸ (1.4312 ²⁸) ^h
2,2,4,4-Tetramethyl-	80 (35) [165.38] ^g	1.4309 ²⁸ (1.4305 ²⁸) ^g
Spiro[4.4]non-1-one	88 (18) [90 (22)] ^h	1.4725 ²⁷ (1.4737 ²⁸) ^h
Spiro[4.5]decan-6-one	103–105 (18) [105–110 (20)] ^h	1.4863 ²⁷ (1.4869 ²⁸) ^h
Cycloheptanone	85 (45)	1.4574 ²⁸
2-Methyl-	61 (13) [178–183] ⁱ	1.4585 ²⁷ (1.4528 ²⁸) ⁱ
3-Methyl-	105 (68) [84–85 (20)] ^j	1.4526 ²⁸ (1.4561 ²⁴) ^j
4-Methyl-	69–70 (20) [84.5 (25)] ^k	1.4540 ²⁸ (1.4560 ²⁸) ^k
3,3,5-Trimethyl-	95 (36) [86–88 (12)] ^l	1.4520 ²⁷ (1.4594 ^{16,45}) ^l
3,5,5-Trimethyl-	108 (36) [87–88 (12.5)] ^l	1.4515 ²⁸ (1.4590 ^{16,45}) ^l
3,3,5,5-Tetramethyl-	87 (20)	1.4515 ²⁸

^a Literature values in brackets; unless otherwise stated, the pressure is 760 mm. ^b J. D. Roberts and C. W. Sauer, *J. Am. Chem. Soc.*, **71**, 3925 (1949). ^c Ref. 11. ^d Ref. 13. ^e Ref. 16. ^f Ref. 15. ^g Ref. 14. ^h Ref. 18. ⁱ Ref. 22. ^j Ref. 19. ^k Ref. 21. ^l Ref. 20.

Dissociation Constants.—The ketones (0.3–0.5 g.) were dissolved in purified 95% ethanol (d_{25}^{25} 0.8051, ca. 30 ml.), and hydrogen cyanide in ethanol (0.1 M, 10 ml.) and 2% tri-*n*-propylamine in ethanol (2 ml.) were added. The volume was brought to 50 ml. and allowed to equilibrate at 23 ± 1° for at least 24 hr. Aliquots (10 ml.) were titrated after 24 hr. and again after 48 hr. with 0.05 N aqueous mercuric nitrate containing 5% nitric acid, using a freshly prepared saturated ethanol solution of diphenylcarbazide as indicator²⁵ and titrating to the first indication of blue coloration. The determinations were carried out at least in triplicate, and the mean values which had average errors of ± 5% are given in Table I.

Acknowledgment.—The authors are grateful to Dr. K. W. Greenlee for generous gifts of a number of cyclopentanones. The work was supported in part by a grant from the National Science Foundation.

(14) G. Stomp, Jr., M. Inatome, C. E. Bowers, J. M. Derfer, K. W. Greenlee, and C. E. Board, *J. Org. Chem.*, **25**, 514 (1960).

(15) A. I. Vogel, *J. Chem. Soc.*, 907 (1931).

(16) P. D. Bartlett and A. Bavley, *J. Am. Chem. Soc.*, **60**, 2416 (1938).

(17) A. N. Day and R. P. Linstead, *J. Chem. Soc.*, 1065 (1935).

(18) D. J. Cram and H. Steinberg, *J. Am. Chem. Soc.*, **76**, 2753 (1954).

(19) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

(20) M. Stoll and W. Scherrer, *Helv. Chim. Acta*, **23**, 941 (1940).

(21) C. Djerassi and G. W. Krakower, *J. Am. Chem. Soc.*, **81**, 237 (1959);

C. Djerassi, B. F. Burrows, C. G. Overburger, T. Takekoshi, C. D. Gutsche, and C. T. Chang, *ibid.*, **85**, 949 (1963).

(22) G. Stork and I. J. Borowitz, *ibid.*, **82**, 4307 (1960).

(23) M. S. Kharasch and P. O. Tawney, *ibid.*, **63**, 2308 (1941).

(24) Cf. D. W. von E. Doering and D. B. Denney, *ibid.*, **77**, 4619 (1955).

(25) V. Prelog and M. Kobelt, *Helv. Chim. Acta*, **32**, 1187 (1949); O. H. Wheeler and V. S. Gains, *Can. J. Chem.*, **36**, 1735 (1958).

(11) M. D. Owen, G. R. Ramage, and J. L. Simanse, *J. Chem. Soc.*, 1208 (1938).

(12) C. W. Smith and D. G. Norton, *Org. Syn.*, **33**, 29 (1953).

(13) (a) H. L. Herzog and E. R. Buchman, *J. Org. Chem.*, **16**, 99 (1951); (b) F. Lauten-Schlaeger and G. F. Wright, *Can. J. Chem.*, **41**, 863 (1963).