[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Bicyclo[3.1.0]hexane Derivatives. I. Synthesis of Bicyclo[3.1.0]-2-hexanone and Methyl Bicyclo[3.1.0]hexane-1-carboxylate[1]

NORMAN A. NELSON AND GEORGE A. MORTIMER[2]

Received March 27, 1957

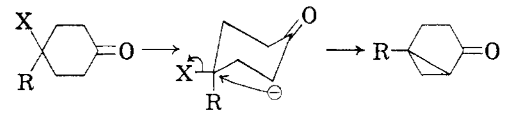
The reaction of 4-tosyloxycyclohexanone and 4-dimethylaminocyclohexanone methiodide with strong bases has been found to result in the formation of bicyclo[3.1.0]-2-hexanone. This type of intramolecular anionic displacement reaction was applied in the preparation of methyl bicyclo[3.1.0]hexane-1-carboxylate from methyl *cis*-3-brosyloxycyclohexanecarboxylate. Similar base catalyzed reactions of methyl 3,4-epoxycyclohexanecarboxylate resulted in transesterification reactions and intermolecular attack of the epoxide ring rather than an intramolecular displacement reaction. An attempted synthesis of sabina ketone is described.

The thujane terpenes[3] are unique among monoterpenes in their possession of the bicyclo[3.1.0]-hexane ring system. A number of methods of constructing this ring system have been developed which involve, in most instances, well known reactions for the preparation of substituted cyclopropanes. This paper will review briefly the known methods of preparing substituted bicyclo[3.1.0]-hexanes and will describe a study made in the preparation of new bicyclo[3.1.0]hexane derivatives involving methods which are extendable to the syntheses of thujane terpenes.

Of the numerous methods which have been described for the preparation of bicyclo[3.1.0]hexane derivatives, the following classifications can be made: the pyrolysis of substituted pyrazolines,[4] the dehalogenation of 1,3-dihalocyclohexanes[5] and related compounds[6] with zinc, internal free-radical coupling reaction[7] of iodomethylcyclopentane,[8] intramolecular anionic displacement reactions,[9] malonic ester synthesis,[10] solvolysis of cholesteryl derivatives,[11] and an intramolecular aldol condensation of a 1,2-diacylcyclopropane derivative.[12] The formation of the bicyclo[3.1.0]hexane derivatives in the present work involve intramolecular anionic displacement reactions.

The treatment of 4-tosyloxycyclohexanone (Ia) with a strong base can lead theoretically to a number of products. β-Elimination of the elements of *p*-toluenesulfonic acid would give 3-cyclohexenone (or 2-cyclohexenone by rearrangement of the double bond). An intermolecular S_N2 displacement reaction involving the base would give a 4-substituted cyclohexanone. If the strength of the base is such that enolization of the ketone can occur, the resulting enolate anion (II) could lead to the formation of bicyclo[3.1.0]-2-hexanone (IIIa) by an intramolecular anionic displacement reaction. This latter reaction is analogous to the conversion of 3-tosyloxy-6-cholestanone to *i*-cholestanone,[9a] and similar reactions have been used in the preparation of larger bicyclic ring systems.[13]

4-Tosyloxycyclohexanone was prepared by the



Ia, R = H
X = $OSO_2C_6H_4CH_3$
b, R = $CH(CH_3)_2$
X = Cl
c, R = H
X = $N(CH_3)_3^+I^-$

II

IIIa, R = H
b, R = $CH(CH_3)_2$

---

[1] This paper was abstracted from the thesis submitted by G. A. M. to the Graduate School of The Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1956.

[2] National Institutes of Health Fellow, 1955–1956.

[3] (a) D. H. R. Barton and S. H. Harper in E. H. Rodd's *Chemistry of Carbon Compounds*, Elsevier Publishing Co., New York, N.Y., 1953, Vol. IIB, pp. 546–556; (b) J. L. Simonsen, *The Terpenes*, 2nd ed., Cambridge University Press, Cambridge, Eng., 1949, Vol. II, pp. 5–60.

[4] (a) N. Kizhner, *J. Russ. Phys.-Chem. Soc.*, **44**, 849 (1912); *Chem. Abstr.*, **6**, 2915 (1912); (b) N. M. Kizhner and I. B. Losik, *Bull. acad. sci. U. R. S. S.*, *Classe sci. chim.*, 49 (1941); *Chem. Abstr.*, **37**, 2728 (1943).

[5] (a) N. D. Zelinsky and A. E. Uspensky, *Ber.*, **46**, 1466 (1913); (b) A. E. Uspensky, *J. Russ. Phys.-Chem. Soc.*, **51**, 245, 257 (1920); *Chem. Abstr.*, **18**, 1487 (1924); (c) A. Uspensky, *Arb. Inst. chem. reine Reagenzien*, **2**, 5 (1923); *Chem. Abstr.*, **19**, 3087 (1925); (d) R. Y. Levine, K. D. Geer, and E. G. Treshova, *Zhur. obsechei Khim.*, **26**, 920 (1956).

[6] (a) N. Zelinsky and M. Ouchakoff, *Bull. soc. chim. France*, **35**, 484 (1924); (b) N. D. Zelinsky and M. Ushakov, *J. Russ. Phys.-Chem. Soc.*, **56**, 67 (1925); *Chem. Abstr.*, **20**, 406 (1926).

[7] F. C. Whitmore, A. H. Popkin, H. I. Bernstein, and J. P. Wilkins, *J. Am. Chem. Soc.*, **63**, 124 (1941).

[8] N. D. Zelinsky, S. E. Michlina, and M. S. Eventowa, *Ber.*, **66**, 1422 (1933).

[9] (a) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 1786 (1952); (b) R. H. Eastman and A. Oken, *J. Am. Chem. Soc.*, **75**, 1029 (1953); (c) L. E. Smith and R. M. Scribner, *J. Am. Chem. Soc.*, **78**, 3412 (1956).

[10] R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 1803 (1953).

[11] (a) J. H. Beynon, I. M. Heilbron, and F. S. Spring, *J. Chem. Soc.*, 907 (1936); (b) E. S. Wallis, E. Fernholz, and F. T. Gephart, *J. Am. Chem. Soc.*, **59**, 137 (1937); (c) J. H. Beynon, I. M. Heilbron, and F. S. Spring, *J. Chem. Soc.*, 1459 (1937); (d) S. Winstein and R. Adams, *J. Am. Chem. Soc.*, **70**, 838 (1948); (e) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

[12] H. E. Smith and R. H. Eastman, *J. Org. Chem.*, **21**, 830 (1956).

hydrogenation of hydroquinone to a mixture of *cis*- and *trans*-1,4-cyclohexanediols (96%), formation of the corresponding monotosylates (79–82%) and oxidation of the monotosylates to the keto tosylate (Ia) (54%)[14] using chromium trioxide in an acetic acid-water-acetone medium.

Treatment of 4-tosyloxycyclohexanone with one equivalent of potassium *t*-butoxide in hot *t*-butyl alcohol gave a product which was isolated as the 2,4-dinitrophenylhydrazone in 87% yield. This dinitrophenylhydrazone was found to be isomeric with, but otherwise different from, 2- and 3-cyclohexenone 2,4-dinitrophenylhydrazones in melting point and infrared and ultraviolet spectra (see Table I). The ultraviolet spectrum of the product is in agreement with the presence of a conjugated three-membered ring. On the basis of these data, it is concluded that the ketone formed in this reaction is bicyclo[3.1.0]-2-hexanone (IIIa).

TABLE I

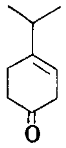
Comparison of 2,4-Dinitrophenylhydrazones

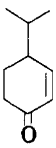
Dinitrophenylhydrazone of	M.P.	λ_{max} in mμ	ϵ
Bicyclo[3.1.0]-2-hexanone	175.5–176°	369[a]	23,750
2-Cyclohexenone[15]	167.5–168°	378[a]	27,400
3-Cyclohexenone[15]	133 –134°	362[a]	22,650
Dihydroumbellulone[16]	170.5–171°[b]	369[c]	23,600

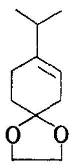
[a] In chloroform. [b] *Anal.* Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found. C, 57.86; H, 6.05; N, 16.56. [c] In ethanol.

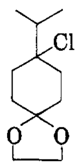
Although the dinitrophenylhydrazone of IIIa was obtained in good yield from this reaction, it was not possible to separate the ketone by distillation from the *t*-butyl alcohol used as the solvent. However, it was possible to prepare and isolate the pure ketone (IIIa) by using a different base and solvent. When an ethereal solution of 4-tosyloxycyclohexanone was treated with triphenylmethyl sodium and heated under reflux, no bicyclic ketone was isolated. By using a higher boiling solvent (benzene) with the same base, the bicyclic ketone (IIIa) was obtained in 12% yield. When the reaction was carried out in refluxing dioxane, the yield was increased to 57%. The best yield, 64%, was achieved using sodium hydride as the base and dioxane as the solvent. The infrared spectrum of bicyclo[3.1.0]-2-hexanone[17] is different from the spectra of the two cyclohexenones which are isomeric with it and contains bands at 3.24 and 3.32 μ which are characteristic for carbon–hydrogen stretching of the methylene hydrogens in a cyclopropane ring.[18a] The pure ketone was converted in 95% yield to the same dinitrophenylhydrazone obtained in the experiment using potassium *t*-butoxide as the base.

The preparation of 4-chloro-4-isopropylcyclohexanone (Ib) was undertaken next since, if a similar intramolecular displacement reaction could be effected, sabina ketone (IIIb)[3] would be formed. 4-Isopropylanisole was reduced to 2,5-dihydro-4-isopropylanisole in 88% yield by a modification of the Birch reduction.[15] The dihydroisopropylanisole was converted in 90% yield to 4-isopropyl-3-cyclohexenone (IV) by oxalic acid in an acetone-water-methanol medium. The presence of a single band at 5.83 μ in the infrared spectrum of the ketone excluded the possibility of appreciable double-bond migration during the hydrolysis.


IV


V


VI



VII

Direct addition of hydrogen chloride to IV to give the chloroketone Ib, was attempted, but no chlorine containing material was obtained. The product consisted of a mixture of unchanged starting material and its double bond isomer, 4-isopropyl-2-cyclohexenone (V). This result was not unexpected in view of the facile migration of β,γ-double bonds into conjugation with carbonyl groups under the influence of mineral acids.[15] To overcome the tendency for isomerization of the double bond during treatment with hydrogen chloride, the ketone function was converted to a ketal group. The ethylene ketal VI was obtained in 71% yield directly from dihydroisopropylanisole by treating it with ethylene glycol in the presence of *p*-toluenesulfonic acid, and removing the methanol formed in the reaction by distillation. The position of the double bond in the product was demonstrated by the conversion of VI in good yield into the known 2,4-dinitrophenylhydrazone of IV. Hydrogen chloride added smoothly to the unsaturated ketal to form the chloroketal VII in 78% yield. All attempts

---

(13) A. C. Cope and G. Holzman, *J. Am. Chem. Soc.*, **72**, 3062 (1950).

(14) R. Grewe, W. Lorenzen, and L. Vining, *Chem. Ber.*, **87**, 793 (1954), have reported higher yields for this oxidation; however, we were unable to obtain higher yields than reported here using their procedure.

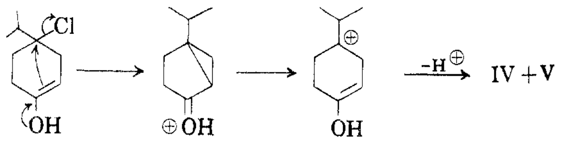
(15) (a) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5360 (1953); (b) A. J. Birch, *J. Chem. Soc.*, 593 (1946).

(16) R. H. Eastman and J. C. Selover, *J. Am. Chem. Soc.*, **76**, 4118 (1954). We are indebted to Dr. Eastman for a sample of dihydroumbellulone.

(17) The infrared spectrum of IIIa is identical with that of a sample prepared by another means by J. F. Brown, Jr.; private communication.

(18) (a) S. E. Wiberley and S. C. Bunce, *Anal. Chem.*, **24**, 623 (1952); (b) J. M. Derfer, E. E. Pickett, and C. E. Boord, *J. Am. Chem. Soc.*, **71**, 2482 (1949); (c) G. Herzberg, *Infrared and Raman Spectra of Polyatomic Molecules*, D. Van Nostrand Co., New York, N. Y., 1945, p. 352.

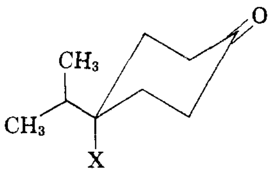
to convert VII to 4-chloro-4-isopropylcyclohexanone (Ib) were unsuccessful. Various methods of acid-catalyzed hydrolyses and ketal exchange reactions were investigated and in each case one of two results was observed; either the chloroketal was essentially unaffected or else a mixture of unsaturated ketones (IV and V) was obtained. The loss of hydrogen chloride in some of the reactions may have occurred by the usual E1 or E2 mechanism[19] or by an intramolecular displacement reaction of the enolized chloroketone (VIII) to the conjugate acid of sabina ketone (IX)[20] followed by acid-catalyzed cleavage of the three-membered ring[21] (as illustrated by X) and loss of a proton to give the observed products (after double bond migrations).



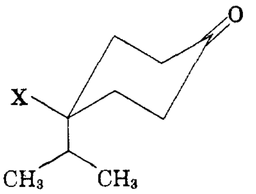
VIII IX X

It would appear that for the synthesis of sabina ketone by this type of synthetic approach to be successful, there must be placed in the tertiary 4-position of the 4-isopropylcyclohexanone molecule a group which is stable to mild conditions. This group should be sufficiently bulky to assume an equatorial configuration, and should be capable of being displaced by the enolate anion by the process illustrated in II.

It is known that the conformational arrangement of substituents on a disubstituted cyclohexane ring is controlled largely by the bulkier group, which will assume an equatorial configuration preferentially.[22] Therefore, the configuration of 4-chloro-4-isopropylcyclohexanone should be represented by structure XIa (X = axial chlorine) to a larger extent than structure XIb (X = equatorial chlorine).



XIa



XIb

Structure XIa is undesirable for the preparation of a bicyclic ketone from two standpoints. The axial leaving group is oriented *trans* to β-axial hydrogen atoms and is therefore susceptible to elimination reactions. The leaving group X is not oriented properly for a backside displacement from the potential anion across the ring (as in II). Structure XIb, on the other hand, should be less susceptible to elimination reactions and the molecular orbitals are aligned for easy bond formation in an intramolecular displacement reaction. Therefore, if the leaving group in structure XI is bulkier than an isopropyl group, it would be expected that the larger percentage of molecules would have structure XIb and a displacement reaction could occur to give sabina ketone.

An example of a group which fulfills the requirement of bulkiness is the trimethylammonium ion. This group could be generated from the dimethylamino group in the last stages of a synthesis, and the latter group should exhibit no tendency to be displaced or eliminated under mild conditions as was the chloro group in the work just described.

Since the base-catalyzed decomposition of alkyltrimethylammonium ions usually goes by way of a Hofmann elimination (rather than a displacement reaction),[23] it was decided to evaluate the usefulness of the trimethylammonium ion in intramolecular displacement reactions using a readily available compound rather than XI (X = $(CH_3)_3N^+-$). The model chosen was 4-dimethylaminocyclohexanone methiodide (Ic).

The high pressure hydrogenation of *p*-dimethylaminophenol in the presence of Raney nickel gave 4-dimethylaminocyclohexanol in 19% yield. This compound was also prepared from *p*-aminophenol through the intermediates, *p*-acetamidophenol (76%), 4-acetamidocyclohexanol (*ca.* 100%) and 4-aminocyclohexanol. The latter compound was converted to 4-dimethylaminocyclohexanol in 46% yield using formaldehyde and formic acid. Oxidation of the aminoalcohol to 4-dimethylaminocyclohexanone was accomplished in 37% yield using potassium dichromate in aqueous sulfuric acid. The amino ketone was converted to the methiodide (Ic) in 97% yield.

When 4-dimethylaminocyclohexanone methiodide was treated with potassium *t*-butoxide in refluxing *t*-butyl alcohol, evolution of trimethyl amine occurred and, from the reaction mixture, bicyclo[3.1.0]-2-hexanone could be isolated as its 2,4-dinitrophenylhydrazone in 42% yield (crude product). Identification of the ketone derivative was made on the basis of its infrared and ultraviolet spectra and mixed melting point determinations. Because of the insolubility of the methiodide in nonhydroxylic solvents, the reaction could not be attempted under the other conditions described for 4-tosyloxycyclohexanone. The Hofmann pyrolysis

---

(19) E. R. Alexander, *Ionic Organic Reactions*, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 104.

(20) For a similar reaction, see H. L. Goering, A. C. Olson, and H. H. Espy, *J. Am. Chem. Soc.*, **78**, 5371 (1956).

(21) O. Wallach, *Ann.*, **359**, 265 (1908), has reported the acid-catalyzed conversion of sabina ketone to a mixture of IV and V.

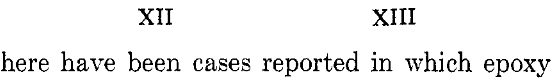
(22) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(23) Displacement reactions yielding cyclopropanes have been observed in cases where a relatively stable anion can be formed in a position γ to the trimethylammonium group. See, for example, (a) H. Rinderknecht and C. Niemann, *J. Am. Chem. Soc.*, **73**, 4259 (1951); (b) J. Weinstock, *J. Org. Chem.*, **21**, 541 (1956).

of the quaternary ammonium hydroxide obtained from the methiodide Ic by the usual method[24] gave only polymeric material. In summary, the displacement reaction of Ic was not clean and was limited to hydroxylic solvents because of solubility problems. In view of these results, it has been concluded that although the trimethylammonium group can be displaced with the formation of a three-membered ring, it is not a good leaving group. Therefore, the synthesis of sabina ketone by a similar approach was not attempted.

Attention was turned next to the possibility of synthesizing bicyclo[3.1.0]hexane derivatives in which the carbonyl function would not be part of the ring system itself, but adjacent to the ring. This possibility, if reailized, would widen the scope of possible syntheses of thujane terpenes and could provide a handle for the introduction of an isopropyl group at the bridgehead position (the position it occupies in all terpenes of the thujane type). The synthesis of methyl bicyclo[3.1.0]hexane-1-carboxylate was therefore undertaken.

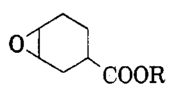
Catalytic hydrogenation of methyl *m*-hydroxybenzoate over Raney nickel gave mainly methyl *cis*-3-hydroxycyclohexanecarboxylate in 71% yield. The hydroxy ester was converted to methyl *cis*-3-brosyloxycyclohexanecarboxylate (XII) in 71% yield. When the brosylate was treated with potassium *t*-butoxide in *t*-butyl alcohol solution, a white precipitate formed quickly and the solution became neutral. The methyl bicyclo[3.1.0]hexane-1-carboxylate (XIII) isolated from the reaction mixture (83% yield) is inert to potassium permanganate solution and has bands characteristic of a cyclopropane ring[18] in the infrared spectrum. The corresponding amide was prepared by an ammonolysis reaction and was found to be different from all of the possible cyclohexenecarboxamides (as expected).



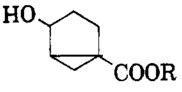
XII XIII

There have been cases reported in which epoxy ketones have undergone base-catalyzed intramolecular displacement reactions with the formation of new ring systems.[25] As an extension to our work we undertook the synthesis of the epoxy ester XIVa and a study of its reactions with base. If an intramolecular displacement reaction occurred to give XV, the product would have utility in the preparation of substituted bicyclohexanones.

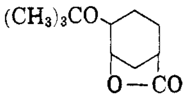
Methyl 3,4-epoxycyclohexanecarboxylate (XIVa) was prepared from methyl 3-cyclohexenecarboxylate by oxidation with peracetic acid. Treatment of the epoxy ester with sodium hydride or triphenylmethyl sodium in dioxane gave polymeric material. When compound XIVa was treated with potassium *t*-butoxide in a refluxing solution of *t*-butyl alcohol for 1 hour, transesterification occurred and *t*-butyl 3,4-epoxycyclohexanecarboxylate (XIVb) was obtained in 71% yield. The infrared spectrum of the product excludes isomeric structures for the product, such as XVI. When the epoxy ester XIVa was treated with potassium *t*-butoxide in a refluxing solution of *t*-butyl alcohol for a longer period of time (about 8 hr.), the *t*-butyl ester (XIVb) was obtained again in addition to 22% of a higher boiling alcohol. The infrared spectrum of the alcohol did not contain bands characteristic of a three-membered ring (thus excluding structure XV) and on the basis of other evidence, structure XVII is proposed. No attempt was made to establish the relative positions of the hydroxyl and methoxyl groups in the product since it is likely that a mixture of isomers was formed.



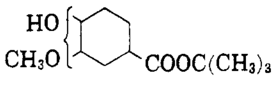
XIVa, R = CH_3
b, R = $C(CH_3)_3$



XV

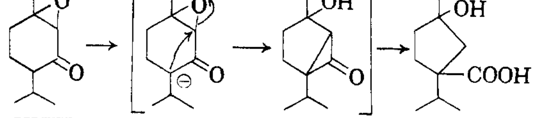


XVI



XVII

The formation of XVII undoubtedly takes place *via* compound XIVb. The methoxide ion formed in the transesterification reaction, being a weaker base than the *t*-butoxide ion, is probably the predominant basic species in the reaction mixture and, in addition, being a less bulky entity, the methoxide ion is not as sterically hindered in its approach toward the epoxide ring. The failure to obtain any of the expected bicyclic compound XV is surprising in view of the fact that similar reactions have been reported before. For example, the rearrangement of piperitone oxide (XVIII) to the hydroxy acid XIX on treatment with methanolic potassium hydroxide solution[26] can be rationalized as proceeding through an intramolecular displacement reaction as shown.



XVIII XIX

The reactions leading to bicyclic ring systems reported in this work have occurred by a backside attack of the enolate anion on the leaving

---

[24] A. C. Cope, D. C. McLean, and N. A. Nelson, *J. Am. Chem. Soc.*, **77**, 1628 (1955).

[25] See, for example, D. H. R. Barton and A. S. Lindsay, *J. Chem. Soc.*, **1951**, 2988.

[26] (a) W. Treibs, *Ber.*, **64B**, 2545 (1931); (b) R. H. Reitsema and V. J. Varnis, *J. Am. Chem. Soc.*, **78**, 3792 (1956).

group. The configuration of the epoxides (XIVa and b) may be such that the molecular orbital of the epoxide ring is not aligned properly for bond displacement with the enolate anion. The importance of the orientation of molecular orbitals for electron interaction across a ring has been discussed recently.[27]

EXPERIMENTAL[28]

4-Tosyloxycyclohexanone (Ia). A mixture of 611 g. of hydroquinone, 700 ml. of 95% ethanol and 6 teaspoonfuls of Raney nickel[29] was shaken in a hydrogen atmosphere (initial pressure, 1800 p.s.i.) at 140° until the hydrogen uptake ceased (4.5 hr.). The catalyst was separated by filtration from the hot reaction mixture and on cooling the filtrate, 257 g. (40%) of a mixture of 1,4-cyclohexanediols was deposited which consisted of about 90% *trans*- and 10% *cis*-diol as estimated from its melting point range of 131–141.5°.[30] Distillation of the filtrate gave an additional 363 g. (56%) of a mixture of isomers, m.p. 100.5–116°, which contained approximately 60% *trans*- and 40% *cis*-1,4-cyclohexanediol.

Eighty-two grams (0.43 mole) of *p*-toluenesulfonyl chloride was added in one portion to a solution of 50 g. (0.43 mole) of 1,4-cyclohexanediol (m.p. 100.5–116°) in 400 ml. of anhydrous pyridine. After stirring the mixture for 1 hr., it was placed in the refrigerator for 18 hr. The solid material was removed by suction filtration and the filtrate was diluted with water and extracted with ether (the ditosylate is relatively insoluble in ether and water, while the unchanged starting material is relatively insoluble in ether, but soluble in water). The ether extract was filtered and washed with dilute hydrochloric acid, water and dried.[31] Concentration of the ether, finally at reduced pressure, gave 95.8 g. (82%) of the crude semicrystalline 4-tosyloxycyclohexanol. The two isomers of this compound have been described.[32]

A solution of 38.8 g. of the crude 4-tosyloxycyclohexanol, 38 ml. of acetone, and 80 ml. of acetic acid was cooled in an ice bath to 10° and a solution of 21.0 g. of chromium trioxide in 17 ml. of water and 35 ml. of acetic acid was added dropwise with stirring over a period of 13 min. while maintaining the temperature below 20°. After 30 min. the mixture was poured into ether (1 l.) and the ether layer was washed several times with water, sodium bicarbonate solution, water, and then dried.[31] Most of the ether was removed by distillation, and crystallization of the product was induced by cooling the resulting solution with Dry Ice. Additional crops of crystals were obtained by further concentration of the mother liquor and by addition of pentane. The crude 4-tosyloxycyclohexanone (20.7 g., 54%, m.p. 90–95°) was recrystallized from ether-hexane before use, m.p. 97.2–97.8° (reported,[14] 94–95°).

Anal. Calcd. for $C_{13}H_{16}O_4S$: C, 58.19; H, 6.01. Found: C, 58.15; H, 6.21.

4-Tosyloxycyclohexanone 2,4-dinitrophenylhydrazone was prepared at 0° from an ethanolic solution of 2,4-dinitrophenylhydrazine hydrochloride and was recrystallized from an ethanol-chloroform solution, m.p. 150.4–150.6°, $\lambda_{max}^{CHCl_3}$ 361 mμ, ϵ 23,500.

Anal. Calcd. for $C_{19}H_{20}N_4O_7S$: C, 50.88; H, 4.50; N, 12.49. Found: C, 50.67; H, 4.50; N, 12.41.

4-Tosyloxycyclohexanone semicarbazone was prepared by treating the ketone with an ethanolic solution of semicarbazide hydrochloride and pyridine. Recrystallization from absolute ethanol afforded an analytical sample, m.p. 140.3–140.7° (dec.), λ_{max}^{EtOH} 227.5 mμ, ϵ 26,300 [reported,[14] m.p. 145° (dec.)].

Anal. Calcd. for $C_{14}H_{19}N_3O_4S$: C, 51.68; H, 5.89; N, 12.91. Found: C, 52.05; H, 5.93; N, 12.98.

Bicyclo[3.1.0]-2-hexanone (IIIa) *from 4-tosyloxycyclohexanone.* (a) *Using sodium hydride as the base.* The reaction was carried out under a nitrogen atmosphere in a dry 200-ml. 3 necked flask equipped with a Hershberg stirrer and reflux condenser. In the flask were placed 3.8 g. of dried 4-tosyloxycyclohexanone, 0.36 g. of sodium hydride, 50 ml. of anhydrous dioxane[33] and 1 drop of absolute ethanol. The mixture was stirred and heated under reflux for 2.5 hr. and allowed to cool. The reaction mixture was diluted with 50 ml. of water and sufficient potassium carbonate was added to saturate the aqueous layer before extracting with ether. The ether extract was dried.[31] The bulk of the solvent was removed by distillation and the concentrate was distilled through a semimicro column giving 0.87 g. (64%) of bicyclo[3.1.0]-2-hexanone (IIIa), b.p. 58° (13 mm.), n_D^{25} 1.4706. An analytical sample of IIIa had b.p. 69° (20 mm.), n_D^{25} 1.4747; $\lambda_{max}^{CCl_4}$ 3.24 and 3.32μ (CaF_2 prism).

Anal. Calcd. for C_6H_8O: C, 74.97; H, 8.39. Found: C, 74.70; H, 8.45.

Bicyclo[3.1.0]-2-hexanone 2,4-dinitrophenylhydrazone was prepared from the pure ketone in 95% yield using an ethanolic solution of dinitrophenylhydrazine hydrochloride at 0°, m.p. 170.6–171.9°. An analytical sample, recrystallized from ethanol-benzene, melted at 175.5–176.1°, $\lambda_{max}^{CHCl_3}$ 369 mμ, ϵ 23,750.

Anal. Calcd. for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.35; H, 4.58; N, 20.35.

(b) *Using triphenylmethyl sodium as the base.* The reaction was carried out under a nitrogen atmosphere in a dry 200-ml. 3 necked flask equipped with a Hershberg stirrer, dropping funnel, and a distillation head which could be used for total reflux. To a solution of 7.1 g. of dried 4-tosyloxycyclohexanone and 100 ml. of purified dioxane[33] was added dropwise 49.5 ml. of $0.53N$ triphenylmethyl sodium in ether. The red color of the base was discharged immediately and a yellow-green precipitate formed. The solvent was distilled slowly until the boiling point reached 99° (about 2.3 hr.). The reaction mixture was cooled and 100 ml. each of water and ether were added. The aqueous layer was saturated with potassium carbonate and extracted with ether. The combined organic layers were dried.[31] The ether was removed by distillation and the residue was distilled rapidly under reduced pressure until triphenylmethane began to distil, the distillate being collected in a Dry Ice-cooled trap. The distillate was concentrated through a 20-cm. helix-packed column until most of the dioxane had been removed. The material remaining in the flask and column was dissolved in ether, the solution was concentrated, and the concentrate was distilled through a semimicro column giving 1.44 g. (57%) of bicyclo[3.1.0]-2-hexanone, b.p. 60–64° (14–15 mm.), n_D^{25} 1.4717.

(c) *Using potassium t-butoxide as the base.* The apparatus was set up as in (a). To a solution of 4.6 g. of 4-tosyloxycyclohexanone in 75 ml. of anhydrous *t*-butyl alcohol was added

---

(27) (a) M. Simonetta and S. Winstein, *J. Am. Chem. Soc.*, **76**, 18 (1954); (b) E. E. van Tamelen, *J. Am. Chem. Soc.*, **77**, 1704 (1955).

(28) Melting points are corrected and boiling points are uncorrected. Ultraviolet spectra were determined with a Cary Ultraviolet Recording Spectrophotometer, Model 11MS. Infrared spectra were determined with a Baird (Model B) or Perkin-Elmer (Model 21) Double Beam Infrared Recording Spectrophotometer fitted with a sodium chloride prism unless otherwise noted. We are indebted to Dr. S. M. Nagy and his associates for analyses.

(29) Obtained from Raney Catalyst Co., Chattanooga, Tenn.

(30) R. C. Olberg, H. Pines, and V. N. Ipatieff, *J. Am. Chem. Soc.*, **66**, 1096 (1944).

(31) Drying agent, anhydrous magnesium sulfate.

(32) L. N. Owen and P. A. Robbins, *J. Chem. Soc.*, 320 (1949).

(33) L. F. Fieser, *Experiments in Organic Chemistry*, 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 284.

over a 5-min. period 0.017 mole of potassium *t*-butoxide in 25 ml. of *t*-butyl alcohol. A white precipitate formed almost immediately. The mixture was stirred and heated under reflux for 2.5 hr., at which time the reaction mixture was neutral. Water (65 ml.) and potassium carbonate were added to the flask and the organic material was extracted with ether and dried.[31] The ether was removed by distillation through a 40-cm. Vigreux column. An aliquot of the remaining solution gave 87% of bicyclo[3.1.0]-2-hexanone 2,4-dinitrophenylhydrazone, identical in m.p., mixed m.p. and ultraviolet spectrum with the sample obtained from the pure ketone. The ketone (IIIa) azeotropes (or codistils) with *t*-butyl alcohol and could not be obtained by fractional distillation.

4-Isopropyl-3-cyclohexenone (IV). The procedure described below gives higher yields than reported previously.[34] To an insulated 1-l. 3 necked flask fitted with a Hershberg stirrer and dropping funnel was added 20 g. of 4-isopropylanisole (b.p. 95–96.5° at 21 mm.; n_{D}^{25} 1.5004; $\lambda_{\max}^{\mathrm{EtOH}}$ 223 mμ, ϵ 9,650, 277 mμ, ϵ 1,810, 284 mμ, ϵ 1,550: reported,[34] b.p. 81–82° at 10 mm.; n_{D}^{20} 1.5038) and 50 ml. of anhydrous ether. With stirring, 500 ml. of liquid ammonia was added, followed by 5.1 g. of lithium wire[15a] added in small pieces over a 5-min. period. After 10 min., 55 ml. of absolute ethanol was added dropwise over a 3-min. period. When the blue color of the reaction mixture had been discharged, 2.7 g. of lithium wire was added as before and stirred for 5 min. before 30 ml. of absolute ethanol was added dropwise. The product was isolated in the usual way[15] and gave 17.5 g. (86%) of 2,5-dihydro-4-isopropylanisole, b.p. 98–99° (21 mm.), n_{D}^{25} 1.4748. The ultraviolet spectrum of the distillate between 277 and 284 mμ indicated the virtual absence of unchanged starting material.

A sample of the dihydro compound was converted[15a] to *4-isopropyl-3-cyclohexenone 2,4-dinitrophenylhydrazone* in 91% yield, m.p. 114.2–117°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 364 mμ, ϵ 23,150 [reported, m.p. 107–108°,[15b,34] $\lambda_{\max}^{\mathrm{ETOH}}$ 263 mμ,[34b] ϵ 22,400].

A mixture of 1.0 g. of oxalic acid, 40 ml. of water, 90 ml. of acetone, 50 ml. of methanol, and 10.0 g. of 2,5-dihydro-4-isopropylanisole was stirred at room temperature for 75 min. The reaction mixture was diluted with 600 ml. of water and extracted continuously with ether overnight. The ether solution was dried[31] and the solution concentrated. Distillation of the residue through a semimicro column gave 8.2 g. (90%) of 4-isopropyl-3-cyclohexenone, b.p. 73–75° (9 mm.) [reported,[34] b.p. 77–78° (7 mm.)]. The infrared spectrum has a single band at 5.83 μ indicating the absence of 4-isopropyl-2-cyclohexenone.

4-Isopropyl-3-cyclohexenone ethylene ketal (VI). The reaction was carried out in a distillation apparatus having a partial-reflux distillation head. A solution of 300 ml. of dry benzene, 36.7 g. of 2,5-dihydro-4-isopropylanisole, 38.1 g. of ethylene glycol, and 0.5 g. of *p*-toluenesulfonic acid was boiled gently for 2.5 hr., during which time 75 ml. of liquid distilled. The benzene solution was cooled and shaken vigorously with an excess of aqueous sodium carbonate solution. The aqueous layer was extracted with ether and the combined organic layers were washed with saturated sodium chloride solution and dried.[31] Removal of the solvents at reduced pressure and fractional distillation of the residue through a 30-cm. Podbielniak wire-spiral column gave 31.1 g. (71%) of 4-isopropyl-3-cyclohexenone ethylene ketal, b.p. 114.5–118° (20 mm.). An analytical sample had b.p. 115–115.5° (18 mm.), n_{D}^{25} 1.4733.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.38; H, 9.95.

A sample of the ketal was converted at 0° to *4-isopropyl-3-cyclohexenone 2,4-dinitrophenylhydrazone* in 70% yield, m.p. 110–111°.

4-Chloro-4-isopropylcyclohexanone ethylene ketal (VII). In a 200-ml. flask equipped with a gas-inlet tube and an outlet protected with a calcium chloride-drying tube were placed 10.0 g. of 4-isopropyl-3-cyclohexenone ethylene ketal and 50 ml. of anhydrous ether. Anhydrous hydrogen chloride was bubbled through the solution at 0° until the ether was saturated (about 45 min.). The mixture was allowed to stand at room temperature overnight. The ether and hydrogen chloride were removed at reduced pressure in a dry nitrogen atmosphere. Distillation of the residue through a semimicro column (nitrogen atmosphere) yielded 9.4 g. (78%) of 4-chloro-4-isopropylcyclohexanone ethylene ketal, b.p. 63–67° (0.08 mm.). An analytical sample had b.p. 90–90.5° (0.73 mm.), n_{D}^{25} 1.4813.

Anal. Calcd. for $C_{11}H_{19}ClO_2$: C, 60.40; H, 8.76; Cl, 16.21. Found: C, 60.65; H, 8.82; Cl, 15.94.

This ketal did not form a dinitrophenylhydrazone at 0° when treated in the usual way.[15a] At higher temperatures (45° and above), *4-isopropyl-2-cyclohexenone 2,4-dinitrophenylhydrazone* was formed, m.p. 132–132.4°, $\lambda_{\max}^{\mathrm{CHCL_3}}$ 379 mμ, ϵ 27,300 (reported m.p. 135–136°, $\lambda_{\max}^{\mathrm{EtOH}}$ 376 mμ, ϵ 28,100;[34] m.p. 136°, $\lambda_{\max}^{\mathrm{EtOH}}$ 376 mμ, ϵ 29,300[35]).

Attempted preparation of 4-chloro-4-isopropylcyclohexanone. (a) *From 4-isopropyl-3-cyclohexenone.* The attempted Markownikoff addition of hydrogen chloride to the β,γ-unsaturated ketone in benzene solution at 10° gave a liquid (b.p. 90–91° at 14 mm.) which exhibited strong bands of equal intensity at 5.83 μ and 5.95 μ These results indicated that the product was a mixture of 4-isopropyl-2-cyclohexenone and starting material.

(b) *From 4-chloro-4-isopropylcyclohexanone ethylene ketal.* A series of experiments involving the direct hydrolysis of the chloroketal were carried out in solutions of aqueous acetone and *p*-toluenesulfonic acid, cold concentrated hydrochloric acid (short contact time), and aqueous alcoholic hydrochloric acid. Acid catalyzed transketalization reactions using acetone and pyruvic acid as acceptors were also investigated. In no instance was any of the desired product detected. Usually unchanged starting material or a mixture of unsaturated ketones was isolated.

4-Dimethylaminocyclohexanol. *p*-Aminophenol (500 g.) in 600 ml. of water and 100 ml. of acetic acid was acetylated by the dropwise addition of 600 ml. of acetic anhydride at 60°. The reaction mixture was heated on the steam bath for 1 hr., allowed to stand overnight at room temperature, then cooled. The *p-acetamidophenol* was collected on a filter, washed with water and dried to yield 524 g. (76%), m.p. 168–170° (reported,[36] m.p. 166°, 169°). An ethanol solution of *p*-acetamidophenol (322 g.) was hydrogenated over Raney nickel[29] at 180° and an initial pressure of 2000 p.s.i. Filtration of the reaction mixture and distillation of the solvent gave 334 g. of crystalline *4-acetamidocyclohexanol.* No attempt was made to separate the known *cis* and *trans* isomers of this compound.[37] The infrared spectrum of the product did not contain the characteristic bands of the starting phenol.

4-Acetamidocyclohexanol (50 g., 0.32 mole), potassium hydroxide (29.5 g., 0.45 mole) and 100 ml. of water were combined and heated under reflux for 18.5 hr. The solution was concentrated to a syrup and extracted with tetrahydrofuran. The solvent was then removed by distillation at reduced pressure, and to the residue were added 43 ml. (1 mole) of 98–100% formic acid and 49 ml. (0.65 mole) of 37% formaldehyde. The reaction mixture was warmed carefully until the vigorous effervescence subsided and then heated under reflux for 23 hr. Following the addition of 27 ml. (0.32 mole) of concentrated hydrochloric acid, the reaction mixture was concentrated under reduced pressure to a sirupy consistency. With cooling, the reaction mixture was made alkaline with 50% sodium hydroxide solution, ex-

---

[34] (a) M. D. Soffer and M. A. Jevnik, *J. Am. Chem. Soc.*, **77**, 1003 (1955); (b) Presumably this $\lambda_{\max}$ should be 363 mμ.

[35] K. G. Lewis, *J. Chem. Soc.*, 2765 (1951).

[36] (a) P. Friedlaender, *Ber.*, **26**, 172 (1893); (b) H. E. Fierz-David and W. Kuster, *Helv. Chim. Acta*, **22**, 82 (1939).

[37] E. Ferber and H. Bruckner, *Ber.*, **72**, 995 (1939).

tracted with tetrahydrofuran and the extracts dried.[31] Distillation of the product under nitrogen and through a 10-cm. Vigreux column gave 18.9 g. (41%) of 4-dimethylaminocyclohexanol, b.p. 121–123° (14 mm.) (reported,[38] b.p. 126° at 19 mm.). The infrared spectra of this material and another sample prepared in 19% yield by catalytic reduction of *p*-dimethylaminophenol (using Raney nickel) were essentially the same.

4-Dimethylaminocyclohexanone. The procedure employed is similar to that of Baker and McEvoy.[39] In a 500-ml. 3 necked flask equipped with a thermometer, stirrer, and dropping funnel were placed (with cooling) 40.0 g. of 4-dimethylaminocyclohexanol, 165 ml. of ice and water and 43 ml. of concentrated sulfuric acid. When the temperature was 20°, 32.2 g. of potassium dichromate was added in one portion. The cooling bath was used as required to keep the temperature below 35°. After 30 min., stirring was discontinued, a few seeds of hydrated chromic sulfate were added, and the reaction mixture was cooled in the refrigerator for 2 days. Solids were removed by filtration and the filtrate was poured slowly, with stirring and cooling, into a solution of 300 g. of potassium hydroxide and 300 ml. of water. The mixture was shaken with 200 ml. of ether and filtered through a pad of Celite (545) to break the emulsion. The filter cake was washed with ether and the aqueous layer was separated and extracted with ether. The combined extracts were washed with saturated sodium chloride solution and dried.[31] Distillation of the product in a nitrogen atmosphere through a Vigreux column gave 12.2 g. of 4-dimethylaminocyclohexanone, b.p. 104–111° (16 mm.), n_D^{25} 1.4712 and 7.3 g. of material which was largely unchanged starting material, b.p. above 116° (16 mm.). The amino ketone darkens within a few hours when exposed to air. An analytical sample had b.p. 95° (12 mm.), n_D^{25} 1.4706.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 68.34; H, 10.80; N, 10.20.

4-Dimethylaminocyclohexanone 2,4-dinitrophenylhydrazone was prepared from ethanolic 2,4-dinitrophenylhydrazine hydrochloride and precipitated by the addition of sodium bicarbonate solution. An analytical sample was recrystallized from methanol, m.p. 117.5–118°, $\lambda_{max}^{CHCl_3}$ 365 mμ, ε 21,050.

Anal. Calcd. for $C_{14}H_{19}N_5O_4$: C, 52.33; H, 5.96; N, 21.80. Found: C, 52.60; H, 6.13; N, 21.92.

The *p-toluenesulfonic acid salt* was prepared by combining equimolar quantities of 4-dimethylaminocyclohexanone and *p*-toluenesulfonic acid in ethyl acetate. The pure derivative, recrystallized from ethyl acetate, melted at 114.2–115.6°.

Anal. Calcd. for $C_{15}H_{23}NO_4S$: C, 57.48; H, 7.40; N, 4.47. Found: C, 57.40; H, 7.32; N, 4.57.

4-Dimethylaminocyclohexanone methiodide (Ic) was prepared in 97% yield by allowing a solution of 3.4 g. of the amino ketone, 7 g. of methyl iodide and 25 ml. of anhydrous ether to stand in the refrigerator overnight. A sample was recrystallized from absolute ethanol for analysis, m.p. 274° (hot stage).

Anal. Calcd. for $C_9H_{18}INO$: C, 38.17; H, 6.41; I, 44.82; N, 4.95. Found: C, 38.03; H, 6.49; I, 44.75; N, 4.96.

Bicyclo[3.1.0]-2-hexanone 2,4-dinitrophenylhydrazone from 4-dimethylaminocyclohexanone methiodide. To a mixture of 3.90 g. of the methiodide (Ic) and 100 ml. of anhydrous *t*-butyl alcohol contained in a 200-ml. 3 necked flask equipped with a stirrer, dropping funnel, and condenser, was added a solution of 0.0135 mole of potassium *t*-butoxide in 25 ml. of *t*-butyl alcohol over a 5-min. period. The reaction mixture was heated under reflux for 2.5 hr. at which time the alkalinity of the solution had dropped to about *p*H 8. Water (50 ml.), potassium carbonate and ether were added to the reaction mixture and the organic layer was dried.[31] Distillation of the ether gave a solution, an aliquot of which on treatment with 2,4-dinitrophenylhydrazine reagent at 0° gave a 42% yield of crude bicyclo[3.1.0]-2-hexanone 2,4-dinitrophenylhydrazone, m.p. 151–160°, $\lambda_{max}^{CHCl_3}$ 371 mμ, ε 21,000. The mixed m.p. (155–165°) was not depressed with an authentic sample, but the mixed m.p. with 2-cyclohexenone 2,4-dinitrophenylhydrazone (m.p. 162–163.5°)[15] was depressed (135–147°). A recrystallized sample (good recovery) had m.p. 160–169° and an infrared spectrum essentially identical with the spectrum of the pure derivative of IIIa.

Methyl cis-3-brosyloxycyclohexanecarboxylate (XII). A methanolic solution of methyl *m*-hydroxybenzoate was hydrogenated with a Raney nickel catalyst[29] at 180° and 1800 p.s.i. to give 71% of crude *methyl cis-3-hydroxycyclohexanecarboxylate,* b.p. 103–110° (1–2 mm.), containing a small amount of the corresponding cyclic lactone as an impurity. The product was shown to be chiefly one isomer by its conversion (below) to a crystalline brosylate in 71% yield and by saponification of a sample to the known *cis*-3-hydroxycyclohexanecarboxylic acid (m.p. of crude sample, 121.5–125.5°) (reported,[40] m.p. 130–132°, 132°).

A mixture of 15.4 g. of methyl *cis*-3-hydroxycyclohexanecarboxylate, 100 ml. of anhydrous pyridine, and 25 g. of *p*-bromobenzenesulfonyl chloride was stirred for 1 hr. and then placed in the refrigerator overnight. The reaction mixture was filtered, the filtrate was shaken with dilute sodium carbonate solution and extracted with ether. The ether extract was washed with dilute hydrochloric acid, saturated sodium chloride solution and dried.[31] Removal of the ether at reduced pressure and recrystallization of the residue from ether-hexane gave 25.5 g. (71%) of methyl *cis*-3-brosyloxycyclohexanecarboxylate, m.p. 80–85° which was used in the next experiment. An analytical sample, recrystallized from benzene-pentane, had m.p. 89.5–90.0°.

Anal. Calcd. for $C_{14}H_{17}BrO_5S$: C, 44.57; H, 4.54; Br, 21.18; S, 8.50. Found: C, 44.82; H, 4.61; Br, 21.34; S, 8.52.

Methyl bicyclo[3.1.0]hexane-1-carboxylate (XIII). To a warm solution of 38.1 g. of dry methyl *cis*-3-brosyloxycyclohexanecarboxylate and 300 ml. of anhydrous *t*-butyl alcohol contained in a 3-necked flask equipped with a stirrer, dropping funnel, and condenser was added over a 5-min. period 0.101 mole of potassium *t*-butoxide in 100 ml. of *t*-butyl alcohol. The reaction mixture was heated under reflux for 25 min., at which time it was neutral. (The reaction mixture is nearly neutral within a few minutes after the addition of base). Water (100 ml.) and saturated sodium chloride solution (200 ml.) were added to the cooled reaction mixture and the mixture was extracted with ether. After drying the extract,[31] the solvents were removed by distillation through a Vigreux column. Distillation of the residue gave 11.72 g. (83%) of methyl bicyclo[3.1.0]hexane-1-carboxylate, b.p. 77–80° (21 mm.), n_D^{25} 1.4616. An analytical sample had b.p. 79° (22 mm.), n_D^{25} 1.4615.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.81; H, 8.71.

The product does not decolorize a 2% potassium permanganate solution in 2 min. The infrared spectrum shows two bands at 3.24 and 3.32 μ (calcium fluoride prism) attributable to the carbon-hydrogen stretching of the methylene hydrogens on a cyclopropane ring[18a] and a strong band at 9.65 μ[18a,b] attributable to the cyclopropane symmetric vibration.[18c] The vapor phase chromatogram (silicone column) shows a single sharp band, indicating the absence of olefinic isomers.

Bicyclo[3.1.0]hexane-1-carboxamide was prepared by heating 0.56 g. of the ester and 10 ml. of a saturated methanolic-ammonia solution in a sealed tube at 100° for 4 days. Removal of the solvent gave 0.33 g. (66%) of crude material which was crystallized from cyclohexane–benzene (nearly

---

[38] H. Heckel and R. Adams, *J. Am. Chem. Soc.*, **47**, 1712 (1925).

[39] B. R. Baker and F. J. McEvoy, *J. Org. Chem.*, **20**, 136 (1955).

[40] (a) H. L. Goering and C. Serres, Jr., *J. Am. Chem. Soc.*, **74**, 5908 (1952) (b) W. H. Perkin, Jr., and G. Tattersall, *J. Chem. Soc.*, 91, 486 (1907); (c) E. J. Boorman and R. P. Linstead, *J. Chem. Soc.*, 258 (1935).

quantitative recovery) to give pure bicyclo[3.1.0]hexane-1-carboxamide having the same melting point as a sample sublimed for analysis, m.p. 161–162°, with softening at 155°. The infrared spectrum (potassium bromide pellet) contains an inflection at 3.32 μ and a band at 3.23 μ (calcium fluoride prism) as well as a strong band at 9.94 μ, characteristic of the three-membered ring.[18]

Anal. Calcd. for $C_7H_{11}NO$: C, 67.16; H, 8.86; N, 11.19. Found: C, 67.29; H, 8.98; N, 11.37.

Methyl 3-cyclohexenecarboxylate. Butadiene and methyl acrylate were condensed in a Diels-Alder reaction by a published procedure[41] to give a 91% yield of methyl 3-cyclohexenecarboxylate, b.p. 80° (20 mm.), n_D^{25} 1.4589 (reported,[41] b.p. 70° at 13 mm.).

3-Cyclohexenecarboxamide was prepared by heating 0.69 g. of the ester and 10 ml. of a saturated methanolic-ammonia solution in a sealed tube at 100° for 2 days. Removal of the solvent and crystallization of the crude product from cyclohexane-benzene gave 0.48 g. (78%) of 3-cyclohexenecarboxamide having the same melting point as a sample sublimed for analysis, m.p. 155.5–156.5°.

Anal. Calcd. for $C_7H_{11}NO$: C, 67.16; H, 8.86; N, 11.19. Found: C, 67.43; H, 9.00; N, 11.34.

Methyl 3,4-epoxycyclohexanecarboxylate (XIVa). A solution of 0.10 mole of commercial peracetic acid in 30 ml. of methylene chloride was shaken with 4.0 g. of sodium acetate trihydrate, separated, and added dropwise with stirring over a 10-min. period to a cold solution of 7.0 g. (0.05 mole) of methyl 3-cyclohexenecarboxylate in 28 ml. of methylene chloride. When the addition was complete, the reaction mixture was allowed to stand at room temperature for 2 days. A 40% solution of sodium hydroxide was added dropwise, with cooling, to neutralize the excess acid. The solid material was separated, dissolved in water and extracted with methylene chloride. The combined methylene chloride solutions (which gave a negative starch-iodide test) were dried.[31] Distillation of the product through a semimicro column gave 2.8 g. of unchanged ester, b.p. 80–82° (22 mm.), and 3.6 g. (77%, based on recovered starting material) of methyl 3,4-epoxycyclohexanecarboxylate, b.p. 115–117° (22 mm.), n_D^{25} 1.4626. Large scale preparations gave comparable yields. An analytical sample had b. p. 109.5–110.5° (17 mm.), n_D^{25} 1.4625.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.49; H, 7.56.

Reaction of methyl 3,4-epoxycyclohexanecarboxylate with potassium t-butoxide. (a) *Short reaction time.* A solution of 0.047 mole of potassium *t*-butoxide in 50 ml. of *t*-butyl alcohol was added dropwise, with stirring, over a 5-min. period to a solution of 7.41 g. (0.047 mole) of methyl 3,4-epoxycyclohexanecarboxylate and 50 ml. of *t*-butyl alcohol. The reaction mixture was heated under reflux for 1 hr., cooled, treated with sodium chloride solution, and extracted with ether. The dried ether solution was concentrated on the steam bath and the residue was distilled through a semimicro column giving 6.63 g. (71%) of *t-butyl 3,4-epoxycyclohexanecarboxylate* (XIVb), b.p. 82.5–85.5° (1.3 mm.), n_D^{25} 1.4525–1.4534. An analytical sample had b.p. 80.5–81.5° (1.4 mm.), n_D^{25} 1.4525.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.91; H, 9.09.

The infrared spectrum of the product contains the bands characteristic of a *t*-butyl group (7.22 and 7.33 μ)[42] and does not contain bands characteristic for a hydroxyl group or a cyclopropane ring. Lithium aluminum hydride reduction gave as a product a viscous oil whose infrared spectrum did not contain the characteristic bands of a *t*-butyl group. This demonstrates that the *t*-butyl group must be present in an ester rather than an ether function.

(b) *Long reaction time.* The reaction was carried out as in part (a) using 7.91 g. (0.051 mole) of methyl 3,4-epoxycyclohexanecarboxylate in 100 ml. of anhydrous *t*-butyl alcohol and a solution of 0.052 mole of potassium *t*-butoxide in 50 ml. of *t*-butyl alcohol. The reaction mixture was stirred and heated under reflux for 8.5 hr., then worked up as in part (a). Fractional distillation through a semimicro column gave 4.38 g. (44%) of *t*-butyl 3,4-epoxycyclohexanecarboxylate, b.p. 75–105° (1.2 mm.), n_D^{25} 1.4533–1.4559 and 2.54 g. (22%) of a fraction distilling mostly at 113–114° (1.2 mm.), n_D^{25} 1.4577 which was identified as *t-butyl 3,4-methoxyhydroxycyclohexanecarboxylate* (XVII). An analytical sample had b.p. 74° (0.03 mm.), n_D^{25} 1.4575.

Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63; OCH_3, 13.47. Found: C, 62.60; H, 9.63; OCH_3, 15.15.

The infrared spectrum (calcium fluoride prism) of the *t*-butyl 3,4-methoxyhydroxycyclohexanecarboxylate contains the characteristic bands for associated (2.88 μ, broad) and unassociated hydroxyl (2.78 μ, sharp) and for the *t*-butyl group[42] (7.22 μ and 7.34 μ).

CAMBRIDGE, MASS.

---

(41) K. Alder and W. Vogt, *Ann.*, **564**, 109 (1949).

(42) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 13, 22.

[CONTRIBUTION FROM THE INSTITUTO DE QUÍMICA, UNIVERSIDAD NACIONAL AUTÓNOMA DE MEXICO]

Structure and Properties of Cyclic Compounds. X.[1] Dissociation Constants of Cyanohydrins of Some Bridged-Ring Ketones

O. H. WHEELER,[2a] R. CETINA, AND J. Z. ZABICKY[2b]

Received March 4, 1957

The dissociation constants of the cyanohydrins of norcamphor (XIII) and dehydronorcamphor (XIV) and of a number of methyl derivatives (XV–XVII) of the former have been measured. Methyl groups have a very large effect on reactivity in this system.

The bicyclo[2.2.1]heptane system of norcamphane (I) contains a cyclohexane ring (III) rigidly held in a boat form.[3] The one-carbon bridge distorts the ring and introduces considerable strain which has been estimated to amount to about 6 kcal.[4] In forming this ring from the boat form of cyclo-

---

(1) Part IX, *J. Am. Chem. Soc.*, **79**, 4191 (1957).

(2a) Present address, Department of Chemistry, Dalhousie University, Halifax, N. S. (2b) Department of Organic Chemistry, Hebrew University, Jerusalem, Israel.

(3) (a) C. W. Shoppee, *Chemistry & Industry*, 86 (1952); (b) D. H. R. Barton, *J. Chem. Soc.*, **1953**, 1027.

(4) R. P. Linstead, *Ann. Rep. Chem. Soc.*, **32**, 315 (1935).