[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Some Observations on the Reported "Isomers" of 4-Methyl-1,1-cyclohexanedicarboxylic Acid

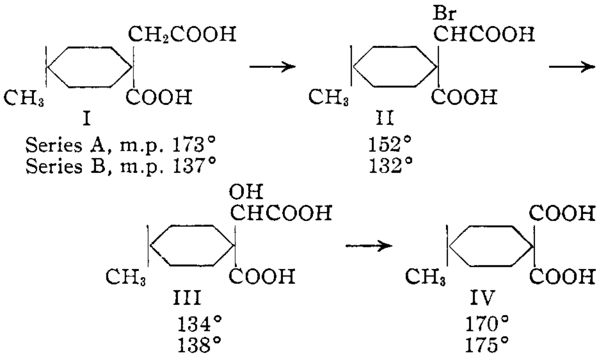
BY CHARLES C. PRICE, WING-YAO CHEN[1] AND ROBERT J. CONVERY

RECEIVED DECEMBER 28, 1953

Repetition of the work by Desai, Hunter and Sahariya, who reported the isolation of two isomeric forms of 4-methyl-1,1-cyclohexanedicarboxylic acid, has produced compounds with melting points similar to those they reported but with different structures. An authentic sample of 4-methyl-1,1-cyclohexanedicarboxylic acid was prepared by an independent synthesis establishing its identity.

In 1942 Desai and Hunter[2] reported the isolation of two compounds, m.p. 175° and m.p. 170°, to both of which they assigned the structure of 4-methyl-1,1-cyclohexanedicarboxylic acid (IVA and IVB). Since it is not possible to account for two such isomers on the basis of the classical stereochemistry of the cyclohexane ring system, they proposed that these isomers differed in the conformation of the cyclohexane ring, being "boat" and "chair" forms.

Since so many claims for such isomers have been proved incorrect,[3] we have repeated the conversions of Desai and Hunter, outlined below.



They reported the mixed melting point of IVA and IVB to be 148°.

Experimental[4]

4-Methylcyclohexanone was condensed[2] with ethyl cyanoacetate to yield **ethyl *p*-methylcyclohexylidenecyanoacetate,** b.p. 165° (12 mm.), n^{20}_D 1.4889, d^{20}_4 1.027 (82%). Reaction with potassium cyanide, followed by hydrolysis and decarboxylation, afforded a 50% yield of mixed **1-carboxy-4-methylcyclohexyl-1-acetic acids** (I), m.p. 120–150°. This mixture was most effectively separated by recrystallization from benzene affording the less-soluble isomer IA, m.p. 173°, readily but the more-soluble isomer IB, m.p. 134°, in pure form only after repeated recrystallization.

Bromination with bromine and phosphorus pentachloride was carried out initially in the cold but finally for 36 hours at 60°. The bromoacid chloride was hydrolyzed in boiling 98% formic acid and recrystallized from 90 to 98% formic acid: IIA, m.p. 152–153° (84%); IIB, m.p. 132°. If the isomer B product was worked up in warm formic acid, the product was the cyclic anhydride, m.p. 81–82°.

Anal. Calcd. for $C_{10}H_{13}BrO_3$: C, 45.99; H, 5.02; Br, 30.62. Found: C, 46.11; H, 5.09; Br, 31.45.

Hydrolysis by refluxing in aqueous sodium carbonate, followed by ether extraction and recrystallization from benzene gave IIIA, m.p. 134° (87%). From IIB, the acid obtained melted at 144–145° and analysis showed it to be the lactone (VI) of IIIB.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.52; H, 7.41.

Oxidation of the barium salt of the glycolic acid IIIA with permanganate at room temperature or at 50–60° afforded only a very small amount of ether-extractable acid, m.p. 170° dec., after recrystallization from benzene. Analytical data and identity of infrared spectra demonstrated that this material was not the expected malonic acid derivative, but was the original acid, IA, presumably present as an impurity in the starting material.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.97; H, 8.06. Found: C, 59.84; H, 8.25.

The *p*-toluidide (VA) prepared by treating the acid above with thionyl chloride and then with *p*-toluidine, melted at 150° after recrystallization either from benzene or from aqueous ethanol.

Anal. Calcd. for $C_{17}H_{23}NO_3$: C, 70.59; H, 7.96; N, 4.84. Found: C, 70.69; H, 8.03; N, 4.98.

Oxidation of the glycolic lactone (IIIB) by the same procedure as for IIIA yielded an acid, m.p. 175–176°, after recrystallization from benzene. When mixed either with authentic IA or a sample of IA isolated from the oxidation of IIIA, the mixture melted at 148°. Analysis, however, showed that this material was actually the **glycolic acid IIIB.**

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.56; H, 7.41. Found: C, 56.00, 55.85; H, 7.71, 7.65.

The *p*-toluidide (VB), prepared as above, melted at 150° but the analysis and mixed melting point with VA (140°) proved their separate identity.

Anal. Calcd. for $C_{17}H_{23}NO_4 \cdot {}^1/_2H_2O$: C, 64.97; H, 7.64; N, 4.46. Found: C, 64.74; H, 7.17; N, 4.70.

4-Methyl-1,1-cyclohexanedicarboxylic Acid (IV) (R.J.C.).—To establish unequivocally that neither of the acids obtained above following Desai and Hunter[2] had in fact the structure they claimed, an authentic specimen was prepared by condensing malonic ester with 1,5-dibromo-3-methylpentane.[5,6]

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.57; neut. equiv., 95.5. Found: C, 57.97; H, 7.53; neut. equiv., 93.1.

The melting point of a mixture with the acid IIIB (m.p. 175–176°) was around 150° dec. The infrared spectra of four of the acids are summarized in Table I.

3-Methyl-1,1-cyclohexanedicarboxylic Acid (R.J.C.).—Although we were unable to duplicate the experimental observation of Desai and Hunter[2] on an analogous series of conversions for the 3-methyl isomers of IA and IB, we did prepare an authentic sample of 3-methyl-1,1-cyclohexane-

---

[1] Abstracted from part of the Ph.D. dissertation of W.-Y. C.

[2] R. D. Desai, R. F. Hunter and G. S. Sahariya, *Proc. Indian Acad. Sci.*, **15A**, 168 (1942).

[3] W. Hückel and O. Neunhoeffer, *Ann.*, **477**, 106 (1930); M. Vavon and M. Mitschovitch, *Bull. soc. chim.*, **43**, 429, 808 (1928); S. Goldschmidt and G. Grafinger, *Ber.*, **68**, 279 (1935); R. D. Desai, R. F. Hunter and G. S. Sahariya, *J. Chem. Soc.*, 416 (1936); R. F. Miller and R. Adams, THIS JOURNAL, **58**, 787, 2659 (1936); A. N. Dey and R. P. Linstead, *J. Chem. Soc.*, 1063 (1935); C. C. Price, THIS JOURNAL, **61**, 1847 (1939).

[4] Microanalyses by Micro-Tech Laboratories, Skokie, Illinois.

[5] N. J. Leonard and Z. W. Wicks, THIS JOURNAL, **68**, 2402 (1946).

[6] In the reduction of γ-picoline by sodium in alcohol, the resulting γ-pipecoline was found to contain considerable unsaturation, presumably due to tetrahydropicoline (see S. Wawzonek, M. F. Nelson, Jr., and P. J. Thelen, *ibid.*, **74**, 2894 (1952)). Catalytic hydrogenation of the mixed N-benzoyl amides in glacial acetic acid over platinum gave N-benzoyl-γ-pipecoline of suitable purity.

dicarboxylic acid by hydrolysis of the corresponding barbituric acid.[7] Hydrolysis by refluxing in aqueous alkali yielded an acid, m.p. 180° dec., after recrystallization from water.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.57. Found: C, 58.15; H, 7.79.

This may correspond to the acid, m.p. 185°, reported by Desai and Hunter,[2] but which we were unable to obtain by their procedure.

TABLE I

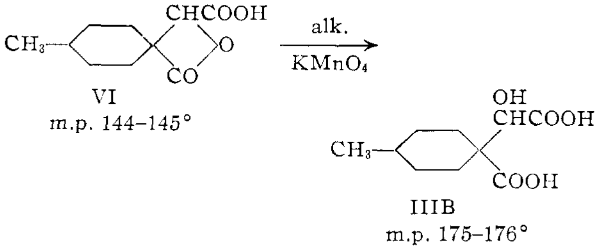
INFRARED ABSORPTION, 2 TO 12 μ[a]

IA (m.p. 173°)	IB (m.p. 134°)	III (m.p. 176°)	IV (m.p. 177.5°)
		2.96 st.	
3.4–3.5 v. st.	3.4–3.5 v. st.	3.4–3.55 v. st.	3.4–3.5 v. st.
		3.90 st.	
5.90 st.	5.90 st.	5.92 v. st.	5.93 st.
6.83 v. st.	6.86 st.	6.87 v. st.	6.85 v. st.
7.06 v. w.			
7.23 med.	7.26 med.	7.28 st.	7.22 st.
7.40 v. w.	7.50 med.	7.55 med.	
7.70 med. –	7.70 med.	7.64 med. –	7.75 med.
7.90 med.	7.85 med.	7.93 med.	7.95 w.
8.18 med. +	8.02 med. +	7.99 med. +	8.14 med.
8.47 v. w.	8.12 med. +	8.10 med.	8.59 v. w.
8.62 w.	8.33 med. +	8.38 med.	
8.78 w.	8.77 med.	8.80 med. +	8.72 med.
9.08 med. –		8.90 w.	9.10 w.
9.45 w.		9.66 w.	
9.92 w.	9.85 w.	9.90 med.	
10.70 st.	10.70 st.	10.30 med.	10.90 v. st.
		10.62 st.	
		11.25 med.	
		11.64 med.	

[a] st. = strong; med. = medium; w. = weak; v. = very.

Discussion

The agreement in melting point between the products we isolated and those of Desai and Hunter[2] are excellent for every case except that of the acid, m.p. 138°, to which they assigned the structure of the glycolic acid IIIB. Our sample of acid isolated at this stage proved to be a lactone. It seems likely that their acid, m.p. 138°, was actually an impure sample of the lactone VI since, like our sample of VI, "oxidation" with alkaline permanganate gave an acid, m.p. 175–176°. Our identification of this material as the glycolic acid IIIB and not the malonic acid IVB is based not only on analysis but on the strong hydroxyl bands in the infrared spectra, a sharp band at 2.96μ for the free hydroxyl group and a broad band at 3.90 μ for the associated hydroxyl group (see Table I).



VI
m.p. 144–145°

IIIB
m.p. 175–176°

It would appear from our experience that permanganate oxidation of the glycolic acids IIIA or IIIB leads to their complete degradation to water-soluble fragments which we did not isolate by simple extractive procedures, leaving behind traces of starting acid IA or unreacted glycolic acid IIIB.

It would therefore appear that the evidence offered by Desai and Hunter cannot be accepted as demonstrating the existence of stable "chair" and "boat" isomers in a cyclohexane ring compound.

NOTRE DAME, INDIANA

---

[7] This acid was kindly supplied to us by Dr. E. H. Van Heyningen of the Eli Lilly Laboratories, m.p. 248–250°, dec *Anal.* Calcd. for $C_{10}H_{14}N_2O_3$: N, 13.32. Found: N, 13.43 (private communication).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE UNIVERSITY]

Addition of Hydrogen Bromide to *trans*-4-Heptenoic Acid

BY HARRY D. ZOOK AND JAMES A. KNIGHT[1]

RECEIVED DECEMBER 12, 1953

trans-4-Heptenoic, 4-bromoheptanoic and 5-bromoheptanoic acids have been synthesized in high purity. The addition of anhydrous hydrogen bromide to *trans*-4-heptenoic acid gives an equal mixture of 4- and 5-bromoheptanoic acids. This addition appears to be the first to give a statistical ratio of products from an olefinic acid in which the double bond is closer to the carboxyl group than the 9,10-position.

The influence of the carboxyl group on the mode of addition of unsymmetrical reagents to a double bond in several remote positions in a carbon chain is still an unsettled question. When the double bond is in the terminal position, $CH_2{=}CH(CH_2)_nCO_2H$, addition of hydrogen bromide according to the Markownikoff rule and reverse addition in the presence of peroxides are well established.[2] Non-terminal double bonds in the β,γ-position, $RCH{=}CHCH_2CO_2H$, appear to add the negative parts of hydrogen halides,[3,4] sulfuric acid[4] and hypochlorous acid[5] predominately to the γ-carbon atom, although the evidence in all cases is not convincing. This mode of addition is predicted by the strong positive inductive effect of the carboxyl group. Finally, although the randomness of additions of hydrogen

---

[1] This work was taken from the Ph.D. thesis of James A. Knight, Procter and Gamble Fellow, The Pennsylvania State College, 1948–1949.

[2] R. Ashton and J. C. Smith, *J. Chem. Soc.*, 435 (1934); M. S. Kharasch and M. C. McNab, *Chemistry and Industry*, **54**, 989 (1935); A. Michael and H. S. Mason, THIS JOURNAL, **65**, 683 (1943). The last two papers refute the so-called solvent effect in these additions. See, for example, A. W. Ralston, "Fatty Acids and Their Derivatives " John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 444–450, and K. S. Markley, "Fatty Acids," Interscience Publishers, Inc., New York, N. Y., 1947, pp. 340–342.

[3] E. Schjanberg, *Ber.*, **70**, 2386 (1937); A. Eckert and O. Halla, *Monatsh.*, **34**, 1815 (1913); E. J. Boorman, R. P. Linstead and H. N. Rydon, *J. Chem. Soc.*, 568 (1933).

[4] R. Fittig and co-workers, *Ann.*, **255**, 30, 77 (1889).

[5] G. F. Bloomfield and E. H. Farmer, *J. Chem. Soc.*, 2062 (1932).