the epimeric p-nitrobenzoate, m.p. 56.4–57.2°, was depressed when mixed with this material. The infrared spectrum of this derivative was indistinguishable from the spectrum of a p-nitrobenzoate, m.p. 62.8–63°, prepared from a pure isomer of 3-methylcyclohexanol.[14]

The α-naphthylurethan of XI was prepared in the usual way. After recrystallization from petroleum ether this material melted at 114.5–115° (lit.[7a] 118°).[32] The melting point of this derivative was depressed when mixed with the epimer, m.p. 128–130°. The melting point was not depressed when mixed with an α-naphthyl urethan, m.p. 116.8–117°, obtained from a pure isomer of 3-methylcyclohexanol.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Studies of Configuration. I. The Configurations of the 3-Methylcyclohexanols*

BY DONALD S. NOYCE AND DONALD B. DENNEY

RECEIVED JULY 3, 1952

Lithium aluminum hydride reduction of *cis*-3-hydroxycyclohexanecarboxylic acid to *cis*-3-hydroxycyclohexanemethanol, followed by conversion to the ω-monotosylate and reduction to *cis*-3-methylcyclohexanol has given the more stable isomer, previously assigned the "*trans*" configuration on the basis of the von Auwers–Skita rule. Similar reduction of *trans*-3-hydroxycyclohexanecarboxylic acid has afforded *trans*-3-methylcyclohexanol, confirming the stereospecificity of the reaction sequence. The isomeric 3-methylcyclohexanols thus show the same reversal of properties as the 1,3-dimethylcyclohexanes, and are in full accord with Pitzer's equatorial-polar concept with regard to relative stability.

Recent investigations of the stereochemistry of substituted cyclohexane derivatives have shown the usefulness and validity of the concept of equatorial and polar bonds in the cyclohexane ring system as developed by Pitzer[1] and Hassel.[2] Barton[3] has shown these concepts to be successful in the interpretation of the reactions of fused ring systems, including steroids and triterpenes. The structures of the hexachlorocyclohexanes[4] have also been correlated with these considerations.

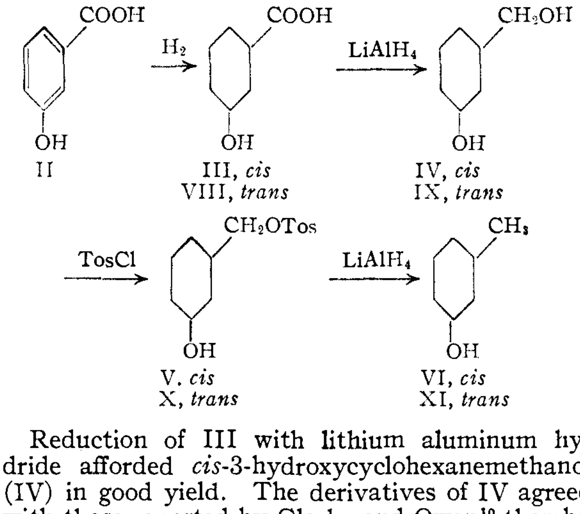
In a substituted cyclohexane the equatorial position tends to be preferred by a substituent,[5] and Pitzer and co-workers[1] have considered that the equatorial chair conformation is 1.8 kcal./mole more stable than the polar chair conformation for methylcyclohexane. In the case of the isomeric 1,3-dimethylcyclohexanes (I) it has been shown[1,6] that *cis*-I in which both methyl groups may be allocated to equatorial positions is more stable than *trans*-I. This is the reverse of the assignment on the basis of the von Auwers–Skita rule, in which it is proposed that the stereoisomer with the lower density and lower index of refraction is the *trans* isomer.

The reversal of the von Auwers–Skita rule for other 1,3-dialkylcyclohexane derivatives has most recently been shown for 1,3,5-trimethylcyclohexane[7] and 1,3,5-triethylcyclohexane. Further, Plattner[8] has pointed out that in 1,3-dimethylcyclohexan-2-one similar considerations apply.

It would appear that such reversal should be common to all 1,3-disubstituted cyclohexanes, irrespective of whether or not the two substituent groups are the same. We wish to report evidence at the present time obtained in the course of other work to show that in the case of the isomeric 3-methylcyclohexanols a similar reversal occurs.

The sequence of reactions used is outlined in Chart I. Reduction of m-hydroxybenzoic acid (II) as its sodium salt with Raney nickel and hydrogen afforded good yields of the mixed *cis*- and *trans*-3-hydroxycyclohexanecarboxylic acid, from which, however, *cis*-3-hydroxycyclohexanecarboxylic acid (III) was isolated in rather poor yield by extended fractional crystallization from ethyl acetate. Reduction of II with platinum oxide and hydrogen in ethanol afforded a mixture containing appreciable amounts of cyclohexanecarboxylic acid, from which III could be isolated readily in satisfactory yield. That III has the *cis* configuration is shown by the formation of the lactone.[9]

CHART I



Reduction of III with lithium aluminum hydride afforded *cis*-3-hydroxycyclohexanemethanol (IV) in good yield. The derivatives of IV agreed with those reported by Clarke and Owen[10] thereby

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* This material was originally submitted as a Communication to the Editor, February 11, 1952.

(1) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

(2) O. Hassel, *Tids. Kjemi Bergvesen*, **3**, 32 (1943).

(3) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(4) J. M. Bijvoet, *Rec. trav. chim.*, **67**, 777 (1948); A. J. Kolka, H. D. Orloff and M. E. Griffing, Abstracts, 121st Meeting A.C.S., March, 1952, p. 5K.

(5) Other specific interactions may change this situation. See L. P. Kuhn, THIS JOURNAL, **74**, 2492 (1952).

(6) M. Mousseron and R. Granger, *Bull. soc. chim.*, **5**, 1618 (1938).

(7) G. Chirdoglu, *Bull. soc. chim. Belg.*, **60**, 39 (1951).

(8) Pl. A. Plattner, A. Furst and J. Hellerbach, *Helv. Chim. Acta*, **30**, 100 (1947).

(9) W. H. Perkin, Jr., and G. Tattersall, *J. Chem. Soc.*, **91**, 480 (1907); E. J. Boorman and R. P. Linstead, *ibid.*, 262 (1935).

(10) M. F. Clarke and L. N. Owen, *ibid.*, 2208 (1950).

confirming their assignment of configuration, since it has been shown that lithium aluminum hydride reduction does not racemize or invert asymmetric centers adjacent to carbonyl or carboxyl groups.[11] Similar reduction of (−)-3-hydroxycyclohexanecarboxylic acid ((−)-III) afforded (+)-IV. Treatment of (+)-IV with one mole of *p*-toluenesulfonyl chloride following the procedure of Clarke and Owen[10] afforded the crude oily ω-monotosylate (V), which was reduced directly with lithium aluminum hydride to give (−)-*cis*-3-methylcyclohexanol ((−)-VI) in 35% yield from (+)-IV.

The isomeric 3-methylcyclohexanols have been carefully studied by Macbeth and Mills,[12] and they have discussed the configurational assignment. The more accessible isomer (A) has been assigned the "*trans*" configuration. That this isomer is more stable is shown by the base-catalyzed equilibration studies of Claudon.[13] Macbeth and Mills[12] have reported derivatives of both the active and inactive forms of A.

The derivatives of (−)-VI, the *p*-nitrobenzoate, the 3,5-dinitrobenzoate, the α-naphthylurethan and the phenylurethan, all agreed with those reported for (−)-A. The infrared spectrum of (−)-VI agreed well with the infrared spectrum of isomer A isolated from the acid phthalate following the procedure of Macbeth and Mills.[12] The spectrum indicated the presence of a small amount of olefinic contamination (weak band at 1640 cm.$^{-1}$) which is a well-known by-product of lithium aluminum hydride reduction of tosylates.[14]

To more definitely confirm the stereospecificity of the latter steps of the reduction sequence, IV to VI, the ω-monotosylate of (−)-IV was converted to the iodide (VII), and VII was reduced with platinum oxide and hydrogen to (+)-VI. There was isolated from the reduction of VII in addition to (+)-VI an appreciable quantity of 1,3-endomethyleneoxycyclohexane, which can arise only from the *cis* isomer of 3-hydroxycyclohexylmethyl iodide. Further, *trans*-3-hydroxycyclohexanecarboxylic acid (VIII) was reduced to *trans*-3-hydroxycyclohexanemethanol (IX), characterized as the bis-*p*-nitrobenzoate and the bis-3,5-dinitrobenzoate. Conversion of IX to the ω-monotosylate (X) and reduction with lithium aluminum hydride afforded *trans*-3-methylcyclohexanol (XI). XI was characterized by infrared spectrum, which differed from that of (−)-VI, and the preparation of the *p*-nitrobenzoate, the 3,5-dinitrobenzoate and the α-naphthylurethan. These derivatives agreed with those reported by Macbeth and Mills [12a] for the less accessible, unstable isomer, (B), which has been assigned the "*cis*" configuration.

It is thus clearly shown that *cis*-3-methylcyclohexanol is the more stable isomer, in agreement with the polar-equatorial concept. It is, however, the isomer of lower index of refraction and lower density in contradiction to the predictions of the von Auwers–Skita rule.

Experimental[15]

Hydrogenation of *m*-Hydroxybenzoic Acid (II). (a) With Raney Nickel.—*m*-Hydroxybenzoic acid (II), 200 g., was dissolved in a solution of 58 g. of sodium hydroxide in 200 ml. of water. The resulting solution was diluted to a total volume of 375 ml.; commercial W-2 Raney nickel, 20 g., was added, and the acid was hydrogenated at 150° and an initial pressure of 3500 p.s.i. The hydrogenation was complete after two hours. The cooled, filtered solution was acidified with 18 *N* sulfuric acid to a *p*H of 3 and continuously extracted with ether for 48 hours. The ether extract was dried over magnesium sulfate, and the ether removed to give an oil which solidified on standing. The yield was 181.7 g. (87%). From 325 g. of acid obtained in the above fashion, 52.3 g. (13.8%) of *cis*-3-hydroxycyclohexanecarboxylic acid (III), was obtained by six crystallizations from ethyl acetate, m.p. 130.5–131.5° (lit.[9] 130–132°).

(b) With Platinum Oxide in Ethanol.—A solution of 75 g. of II in 200 ml. of 95% ethanol was hydrogenated at three atmospheres with platinum oxide (30 hours). Absorption of hydrogen slowed markedly after the theoretical amount of hydrogen had been absorbed. The catalyst was removed by filtration, and the ethanol was distilled under reduced pressure. To the residues obtained from two such runs 50 ml. of petroleum ether was added; the mixture crystallized with seeding to give 64.4 g. (41%) of product, m.p. 105–120°. From five runs 159 g. of solid material was obtained. Four crystallizations from ethyl acetate afforded 91 g. (23%) of III, m.p. 130.5–131.5°

Resolution of *cis*-3-Hydroxycyclohexanecarboxylic Acid (III).—Quinine trihydrate, 500 g. (1.30 moles), was dissolved in 1000 ml. of warm methanol; to this solution, a solution of 188.3 g. (1.30 moles) of III in 400 ml. of methanol was added in one portion. The combined solutions were placed in a large water-bath at 50° and allowed to cool slowly to room temperature. The solution was seeded and placed in an ice-bath for three hours. The resulting mixture was filtered to give 526 g. of crystals and mother liquor A. Recrystallization from 3 liters of methanol afforded 156 g. of salt, m.p. 193.4–194.2°. Further concentration of the mother liquor gave 128 g. of salt and mother liquor B. The mother liquors A and B were evaporated to dryness to yield 325 g. of the soluble salt. Fractional crystallization from methanol of the two head fractions afforded 162 g. (53%) of the quinine salt of (+) III, m.p. 197.1–198.1° (dec.), $[\alpha]^{25.6}\mathrm{D}$ −135° (*c* 1, in methanol).

Anal. Calcd. for $C_{27}H_{36}N_2O_5$. C, 69.20; H, 7.75; N, 5.97. Found: C, 69.08; H, 7.58; N, 5.94.

Decomposition of the Soluble Quinine Salt.—The soluble quinine salt, 309 g. (0.694 mole) was suspended in a stirred solution of 40 g. (1.0 mole) of sodium hydroxide in 750 ml. of water. The mixture was stirred and heated on a steam-bath for two hours at which time 100 ml. of water was added as the mixture became very thick and heavy. After 30 minutes more, 150 ml. of water was added, and the stirring and heating were continued for an additional 1.5 hours, and then the mixture was allowed to stand at room temperature for 12 hours. The suspension was filtered, and the aqueous solution was acidified to *p*H 3 with ice-cold 18 *N* sulfuric acid. The acidic solution was continuously extracted with ether for 36 hours. The ether extract was not dried as this caused precipitation of the acid. The ethereal solution was evaporated to dryness to afford 78 g. of partially resolved (−)-III. The recovered quinine was dissolved in chloroform and extracted with 100 ml. of 1.5 *N* sodium hydroxide solution. The basic extract was acidified with ice-cold 18 *N* sulfuric acid and continuously extracted with ether for six hours. Evaporation of the ether extract yielded 17 g. of partially resolved (−)-III. The total yield of crude (−)-III was 95 g. (100%), m.p. 122–128°, $[\alpha]^{16.5}\mathrm{D}$ −6.2° (*c* 2, in methanol).

Resolution of Partially Resolved (−)-III with Cinchonidine.—Crude (−)-III, 106 g. (0.736 mole), m.p. 123–129°, $[\alpha]^{25°}\mathrm{D}$ −6.2° (*c* 2, in methanol), was dissolved in 250 ml. of 95% ethanol. The above solution was added to a warm solution of 217 g. (0.736 mole) of cinchonidine in 1500 ml. of 95% ethanol. After the solution had cooled to room temperature, it was seeded and placed in an ice-bath for 12

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[11] D. S. Noyce and D. B. Denney, THIS JOURNAL, **72**, 5743 (1950).

[12] (a) A. K. Macbeth and J. A. Mills, *J. Chem. Soc.*, 709 (1945); (b) 205 (1947).

[13] M. M. Claudon, *Bull. soc. chim. France*, **17**, 627 (1950).

[14] P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

[15] All melting points are corrected; boiling points are uncorrected. Microanalyses are by the Microanalytical Laboratory of the University of California.

hours. The resultant mixture was filtered and the crystals were dried. The yield of the cinchonidine salt was 217 g., m.p. 175–181°. Fractional crystallization of the first crop and material from its mother liquor afforded 170 g. of the cinchonidine salt of (–)-*cis*-3-hydroxycyclohexanecarboxylic acid (III). The yield was 57%, and the salt had the following properties: m.p. 179.5–180.3° (dec.), $[\alpha]^{25}\mathrm{D}$ –91.5° (*c* 1, in 95% ethanol).

Anal. Calcd. for $C_{28}H_{34}N_2O_4$: C, 71.20; H, 7.81; N, 6.39. Found: C, 71.00; H, 7.89; N, 6.50.

Decomposition of the Quinine Salt of (+) III.—In a 2000-ml. round-bottomed three-necked flask equipped with a stirrer and a reflux condenser, there were placed 20 g. (0.50 mole) of sodium hydroxide and 750 ml. of water. The solution was stirred and warmed on a steam-bath, and to it was added 161.4 g. (0.344 mole) of the quinine salt of (+) III. The solution was stirred and warmed on the steam-bath for one hour. After stirring the mixture at room temperature for four hours, it was filtered and the quinine was dissolved in 300 ml. of chloroform. The chloroform solution was extracted with 80 ml. of 1.25 *N* sodium hydroxide solution. The combined basic extracts were acidified with ice-cold 18 *N* sulfuric acid, and the acidic solution was continuously extracted with ether for 36 hours. The ether extract was evaporated to yield 49.4 g. (100%) of (+)-*cis*-3-hydroxycyclohexanecarboxylic acid. One crystallization from ethyl acetate afforded 45 g. (91%) of (+)-III, m.p. 131.0–131.5°, $[\alpha]^{23.6}\mathrm{D}$ +9.82° (*c* 4, in methanol), $[\alpha]^{23.6}\mathrm{D}$ +9.75° (*c* 4, in 95% ethanol).

Decomposition of the Cinchonidine Salt of (–)-III.—The cinchonidine salt of (–)-III, 168 g. (0.383 mole), was suspended in a solution of 22 g. (0.55 mole) of sodium hydroxide in 750 ml. of water. The suspension was stirred and heated on the steam-bath for one hour and then stirred at room temperature for four hours. The suspension was filtered, and the cinchonidine was dissolved in 800 ml. of 1.25 *N* sodium hydroxide solution. The combined basic extracts were acidified with ice-cold 18 *N* sulfuric acid, and the acidic solution was continuously extracted with ether for 36 hours. The ether extract was evaporated to give 53.1 g. of (–) III. One crystallization from ethyl acetate afforded 48.7 g. (88%) of pure (–) III, m.p. 130.9–131.3°, $[\alpha]^{19.6}\mathrm{D}$ –9.93° (*c* 4, in methanol), $[\alpha]^{19.7}\mathrm{D}$ –9.84° (*c* 4, in 95% ethanol).

Isolation of *trans* 3-Hydroxycyclohexanecarboxylic Acid (VIII).—The *trans* acid, VIII, was obtained from the mother liquors of the fractional crystallization of the Raney nickel hydrogenation products. Distillation of these residues yielded some of the lactone of the *cis* acid b.p. 131–135° (28 mm.) and the crude *trans* acid, b.p. 150–170° (18 mm.). Some crude *trans* acid could also be obtained by saponifying the pot residue from the distillation. The crude acid was purified by crystallization from ether, m.p. 117.8–119.6°, lit.[9] 119–120°. The benzylisothiouronium salt was prepared in the usual manner. After crystallization from dioxane, it had m.p. 130.0–130.7°.

Anal. Calcd. for $C_{15}H_{22}SN_2O_3$: C, 58.04; H, 7.14. Found: C, 57.87; H, 6.97.

Conversion of (+)-III to (–)-*cis*-3-Hydroxycyclohexanemethanol (IV).—In a 2000-ml. three-necked flask equipped with a stirrer, reflux condenser and calcium chloride drying tube, there were placed 30.4 g. (0.80 mole) of lithium aluminum hydride and 1000 ml. of anhydrous ether. The mixture was refluxed with stirring for 45 minutes and then allowed to cool to room temperature. The flask was fitted with a soxhlet extractor which contained 57.7 g. (0.40 mole) of (+) III. The solution was refluxed with stirring; after three hours 200 ml. of dry ether was added, and refluxing and stirring were continued for 33 hours. The flask was cooled in an ice-bath, and 100 ml. of ice-cold water was added dropwise. The inorganic hydroxides were dissolved in 750 ml. of ice-cold 10% sulfuric acid. The two layers were separated, and the aqueous phase was continuously extracted with ether for 48 hours. Methanol was added to the ether extract as some of the diol separated out of the ether. The combined organic extracts were concentrated to a volume of 400 ml. and then dried over magnesium sulfate. Distillation afforded 44.6 g. (86%) of (–)-IV, b.p. 132–134° (4 mm.), $[\alpha]^{25.2}\mathrm{D}$ –2.4° (*c* 4, in methanol), $n^{24}\mathrm{D}$ 1.4910.

The bis-3,5-dinitrobenzoate prepared in the usual manner and crystallized three times from acetone had m.p. 186.0–186.6°, $[\alpha]^{23°}\mathrm{D}$ –13.2° (*c* 2, in chloroform).

Anal. Calcd. for $C_{21}H_{18}N_4O_{12}$: C, 48.65; H, 3.50; N, 10.81. Found: C, 48.48; H, 3.52; N, 10.67.

Conversion of (–)-III to (+)-IV.—Reduction of (–)-III, 11 g. (0.0764 mole), was carried out using the same general procedure reported above. The reaction afforded 8.5 g. (86%) of (+)-IV, b.p. 136–137° (5 mm.), $[\alpha]^{20}\mathrm{D}$ +2.8° (*c* 1.6, in methanol), $n^{22}\mathrm{D}$ 1.4899.

Conversion of VIII to *trans*-3-Hydroxycyclohexanemethanol (IX).—Reduction of 8.5 g. (0.059 mole) of VIII with lithium aluminum hydride afforded 5.62 g. (73%) of IX, b.p. 132–134° (6 mm.), $n^{22}\mathrm{D}$ 1.4930.

The bis-*p*-nitrobenzoate prepared in the usual manner and crystallized three times from acetone had m.p. 160.5–161.5° (lit.[10] 162°).

The bis-3,5-dinitrobenzoate was also prepared; after two crystallizations from ethanol–acetone, it had m.p. 167.3–169.1°.

Anal. Calcd. for $C_{21}H_{18}N_4O_{12}$: C, 48.65; H, 3.50; N, 10.81. Found: C, 48.97; H, 3.67; N, 10.53.

Conversion of III to IV.—In a preliminary experiment III was reduced to IV, and the bis-3,5-dinitrobenzoate was prepared. After two crystallizations from ethyl acetate, it had m.p. 180.5–181.5° (lit.[10] 181°).

Formation of the ω-Tosylate of (–)-IV.—Following the procedure of Clarke and Owen,[10] 40.6 g. of (–) was converted to the ω-tosylate.

Similar conditions were used to convert (+)-IV and IX to their tosylates.

Reduction of the ω-Tosylate of IX to *trans*-3-Methylcyclohexanol (XI).—The general procedure of Rapoport and Bonner[16] was followed. It was found that the reduction of the ω-tosylate was unsatisfactory in *n*-butyl ether, and experimentally more satisfactory in *n*-propyl ether as solvent rather than tetrahydrofuran. The reduction at 70–80° of 12.1 g. of X in *n*-propyl ether with lithium aluminum hydride afforded, after isolation in the usual manner, 2.50 g. (54% based on IX) of *trans*-3-methylcyclohexanol, b.p. 166–168°, $n^{20}\mathrm{D}$ 1.4587.

The *p*-nitrobenzoate, prepared in the usual manner and crystallized from methanol–water, had m.p. 62.1–62.5° (lit.[12a] 63°).

The α-naphthylurethan, prepared in the usual manner and crystallized four times from petroleum ether, had m.p. 116.8–117.3° (lit.[12a] 118°).

The 3,5-dinitrobenzoate, crystallized from methanol, melted sharply at 102.5–103.5° (lit.[12a] 111°).[17]

Anal. Calcd. for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.22; N, 9.09. Found: C, 54.39; H, 5.14; N, 9.25.

Reduction of the ω-Monotosylate of (+)-IV to (–)-*cis*-3-Methylcyclohexanol (VI).—The ω-monotosylate of (+)-IV, 16.1 g., was reduced in the same manner to give 2.6 g. (36% yield based on (+)-(IV)) of (–)-*cis*-3-methylcyclohexanol, b.p. 167–170°, $n^{26}\mathrm{D}$ 1.4555, $\alpha\mathrm{D}$ +5.13° (homog. in a 1-dm. tube). The alcohol was contaminated with a small amount of highly dextrorotatory alkene as the derivatives were prepared in good yield, and had negative rotations.

The 3,5-dinitrobenzoate, prepared in the usual manner and crystallized four times from ethanol, had m.p. 96.5–97.1°, $[\alpha]^{23.6}\mathrm{D}$ –3.1° (*c* 2, in chloroform) (lit.[12b] 97–98°).

The *p*-nitrobenzoate, crystallized twice from methanol–water, had m.p. 45–46° (lit.[12b] 46–47°).

The α-naphthylurethan was also prepared and after two crystallizations from petroleum ether it had m.p. 146.4–147.0° (lit.[12b] 147–148°).

Conversion of the ω-Monotosylate of (–)-IV to 3-Iodomethylcyclohexanol (VII).—In a one-liter three-necked flask, equipped with a stirrer and reflux condenser, there were placed 113 g. (0.75 mole) of sodium iodide and 420 ml. of anhydrous acetone. The mixture was stirred until all of the sodium iodide had dissolved. To this solution there was added dropwise a solution of 89 g. of the ω-tosylate of (–)-IV in 180 ml. of acetone. The resulting solution was refluxed with stirring for 24 hours; during this time the solution became very highly colored because of the iodine formation. Attempts to filter the resulting solution met with little success, consequently, water was added until the sodium *p*-toluenesulfonate had dissolved. Sodium thio-

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[16] H. Rapoport and R. Bonner, THIS JOURNAL, **73**, 2872 (1951).

[17] This undoubtedly represents another case of dimorphism, which is common in this series.

sulfate was also added until the iodine color had been discharged. The resulting solution was extracted with three 100-ml. portions of ether, and dried over magnesium sulfate. Distillation of the solvents afforded 42.7 g. of the crude iodo compound, VII. Attempted distillation of the crude iodo compound resulted in much decomposition; however, a fairly good boiling sample could be obtained b.p. 106–110° (0.3 mm.).

Hydrogenation of VII to Give (+)-*cis*-3-Methylcyclohexanol.—Crude VII, 39.8 g. (0.165 mole) was dissolved in anhydrous methanol; 48.4 g. (0.35 mole) of potassium carbonate was added to the methanolic solution, and the volume was adjusted to 250 ml. by the addition of methanol. Platinum oxide, 2 g., was added to the mixture, and it was hydrogenated on a Parr low pressure hydrogenation apparatus. The compound absorbed 14.1 pounds of hydrogen (calculated, 14.2 pounds) in 75 minutes. The mixture from the hydrogenation was filtered, and the methanol was distilled through a short column. The cooled residue from the distillation contained a large quantity of potassium iodide. The liquid residue was taken up in ether, and the potassium iodide was washed with three 50-ml. portions of ether. The combined ether washes were dried over magnesium sulfate, and distilled through a short column. The product was distilled through a short column to give two fractions No. 1, b.p. 168–174°, $n^{25}\text{D}$ 1.4580, 7.65 g.; No. 2, b.p. 174–178°, $n^{25}\text{D}$ 1.4587, 1.33 g. Redistillation of these two fractions afforded 7.1 g. of crude (+)-*cis*-3-methylcyclohexanol, b.p. 170–173°, $[\alpha]_{\text{obsd.}}$ +20.91 (homog. in a 1-dm. tube).

The alcohol obtained above was used to prepare derivatives without further purification. The **α-naphthylurethan** after three crystallizations from petroleum ether had m.p. 146.7–147.5° (lit.[12b] 147–148°).

The **3,5-dinitrobenzoate** was prepared, and after 4 crystallizations from 95% ethanol it had m.p. 96.4–97.4° (lit.[12b] 97–98°).

The **phenylurethan** after two crystallizations from petroleum ether had m.p. 116.4–117.2° (lit.[12b] 117–118°).

Further purification of the crude alcohol was carried out by conversion of 6.8 g. to the acid phthalate in the usual manner. After removal of neutral impurities, regeneration of the alcohol by hydrolysis afforded 3.16 g. of (+)-*cis*-3-methylcyclohexanol, b.p. 173–175°, $n^{18}\text{D}$ 1.4620, $\alpha^{18}\text{D}$ +1.76° (homog. in a 1-dm. tube).

Isolation and Properties of 1,3-Endomethyleneoxycyclohexane.—During the distillation of the (+)-*cis*-3-methylcyclohexanol, a fairly large quantity of solid material came over as a forerun. This material was sublimed twice; after this treatment it had m.p. 94–97.5° (sealed tube), $\alpha^{19.4}\text{D}$ +81.7° (*c* 1.8, in 95% ethanol). A satisfactory analysis of the compound could not be obtained because of its extremely high volatility. The melting point of the oxide and its general properties agreed quite well with those reported for the optically inactive oxide.[10]

Acknowledgments.—We wish to thank Dr. N. K. Freeman for his assistance in the determination and interpretation of the infrared spectra, and the Graduate Fellowship Committee of the University of California for the award of the Abraham Rosenberg Fellowship to one of us (D. B. D.).

BERKELEY 4, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DEPAUL UNIVERSITY]

Unsymmetrical Quaternary Carbon Compounds. I. The Alkylation of Ethyl 2-Cyano-3-methyl-2-pentenoate with Aliphatic Grignard Reagents

BY FRANKLIN S. PROUT

RECEIVED JULY 21, 1952

The reaction of several aliphatic Grignard reagents with ethyl 2-cyano-3-methyl-2-pentenoate has been studied. The normal Grignard reagents *added* to this conjugated system to give *t*-alkylcyanoacetic esters in 34–51% yields and *reduced* this conjugated system to furnish ethyl 2-cyano-3-methylpentanoate in 20–30% yields. The other propyl and butyl Grignard reagents have also been evaluated. The alkylated cyanoacetic esters have been hydrolyzed and decarboxylated to form the 3-ethyl-3-methyl substituted nitriles and acids, further confirming the character of the addition.

This work extends the findings of Alexander, McCollum and Paul[1] and Kohler and Reimer[2] showing that Grignard reagents add to ethyl alkylidenecyanoacetates, $R_2C{=}C(CN)COOC_2H_5$, to furnish ethyl *t*-alkylcyanoacetates, $R_3C{-}CH(CN)\text{-}COOC_2H_5$, with little or no interference by reaction of the Grignard reagents with the ester or cyano groups. Several other examples of analogous alkylations of similar conjugated systems occur in the literature.[3]

In our extension of this work with the cyanoacetates, the alkylidene group was *s*-butylidene and the Grignard reagents were propyl, butyl, pentyl, hexyl, isobutyl, isopropyl, *s*-butyl, *t*-butyl and neopentyl. Yields were 34–51% with the *n*-alkylmagnesium bromides. Alexander, McCollum and Paul[1] have reported a yield of 42% on the comparable reaction of *n*-butylmagnesium bromide on ethyl 2-cyano-3-methyl-2-butenoate (*s*-propylidene homolog). A variety of changes in alkylation procedure led to no better method than the one given by these authors.[1] Isobutylmagnesium bromide, however, gave only an 8% yield and neopentylmagnesium bromide gave 0% yield. The *s*-butyl and *t*-butyl analogs gave 8 and 3% yields, respectively. Oddly enough, isopropylmagnesium bromide furnished a 38% yield of the desired product, an observation which conflicts with the findings of Alexander and his colleagues.[1]

Ethyl 2-cyano-3-methylpentanoate, $C_2H_5\text{-}CH(CH_3)\text{-}CH(CN)\text{-}COOC_2H_5$, and olefins (propylene from *n*-propylmagnesium bromide) were obtained in a reaction concurrent with the addition. This reduction product was much more important in the reactions with isobutyl- and *s*-butylmagnesium bromides and *t*-butylmagnesium chloride than with the normal isomers.

The highly hindered character of these *t*-alkylcyanoacetic esters has led to a convenient alkaline hydrolysis furnishing the *t*-alkylacetonitriles, R_3C-

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[1] E. R. Alexander, J. D. McCollum and D. E. Paul, THIS JOURNAL, **72**, 4791 (1950).

[2] E. P. Kohler and M. Reimer, *Am. Chem. J.*, **33**, 333 (1905).

[3] (a) E. P. Kohler, *ibid.*, **34**, 132 (1905); (b) S. Wideqvist, *Arkiv. Kemi, Mineral. Geol.*, **B23**, No. 4 (1946); (c) B. Riegel, S. Siegel and W. M. Lilienfeld, THIS JOURNAL, **68**, 984 (1946); (d) B. Riegel, S. Siegel and D. Kritchevsky, *ibid.*, **70**, 2950 (1948); (e) J. H. Wotiz and J. S. Matthews, *ibid.*, **74**, 2559 (1952). *Cf.* also H. Gilman, "Organic Chemistry, An Advanced Treatise," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 511, 673, 674.