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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

2,6-Dimethylcyclohexanecarboxylic Acids[1]

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2,6-Dimethylcyclohexanecarboxylic acid exists as four stereoisomers: *meso cis*, *meso trans* and two enantiomers. The racemic modification was obtained from 2,6-dimethylbenzoic acid by reduction with sodium and isoamyl alcohol and identified by resolution. The *meso cis* isomer was obtained by reduction of the aromatic acid with hydrogen and platinum. Its configuration was assigned on the basis of this synthesis and the ease of isomerization to the *meso trans* compound. Other methods of synthesis of these compounds are given, and a number of reactions described. The *meso trans* isomer was converted through 1-bromo-2,6-dimethylcyclohexanecarboxylic acid to 2,6-dimethyl-1-cyclohexenecarboxylic acid, previously obtained from the racemic modification.

The synthesis and certain reactions of the stereoisomeric 2,5-dimethylcyclopentanecarboxylic acids were reported recently.[2] As a continuation of that study of steric hindrance, this paper describes the synthesis of the 2,6-dimethylcyclohexanecarboxylic acids and qualitative experiments on their reactivity.

2,6-Dimethylcyclohexanecarboxylic acid exists in four stereoisomeric forms, Ia, Ib, II and III, as does 2,5-dimethylcyclopentanecarboxylic acid. Several acids believed to have the structure of the cyclohexane acid have been reported in the literature without indication of their configurations. One isomer melting at 75.5–75.8° was prepared by reduction of 2,6-xylic acid with sodium and isoamyl alcohol.[3,4] We have repeated this synthesis and obtained in low yield an acid melting at 80.8–81.3° which has been shown to be racemic modification Iab by partial resolution through the methocinchoninium salt.

An isomer, melting point 77–78°, believed to be the same as the acid prepared by Noyes was obtained[5] by reduction of a 2,6-dimethyl-3-cyclohexene-1-carboxylic acid, melting point 86–87°, synthesized by the Diels–Alder reaction between piperylene and crotonic acid. In our hands this reaction has given a cyclohexene acid of about the melting point indicated, but with some softening as low as 81°. Hydrogenation of the product gave an acid of melting range 78.5–89.5° from which a low yield of III, melting point 103–104°, was obtained by fractional recrystallization. These experiments on the Diels–Alder synthesis will be reported later.

Another isomer melting at 87.5–88° was obtained by reduction of 2,6-xylic acid in acetic acid with Adams platinum catalyst.[6] We have carried out the same reduction and obtained the same isomer in essentially quantitative yield. This isomer was also isolated as the principal product of a similar hydrogenation of 2,6-dimethyl-1-cyclohexenecarboxylic acid. These hydrogenation experiments are evidence that this isomer is *meso cis* acid II; the configuration is confirmed by rearrangement to a higher melting form by heating with hydrochloric acid in acetic acid. The new acid melts at 103–104° and is assigned structure III.

A variety of other methods of synthesis of 2,6-dimethylcyclohexanecarboxylic acid are easily formulated, but when 2,6-dimethylaniline is available commercially, the reduction of the aromatic acid is the best source of II and hence of III. An alternative synthesis which was very useful during the first part of our work when the xylidine could not be obtained on the market, is outlined in the equations (IV→VIII). None of the racemic

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[1] This paper contains material from the Ph.D. thesis of Russell Reed (August, 1950) and the M.S. thesis of Eva Pacovska (February, 1946). A preliminary report of the work was presented before the Organic Division of the American Chemical Society at the 112th Meeting, New York City, September, 1947.

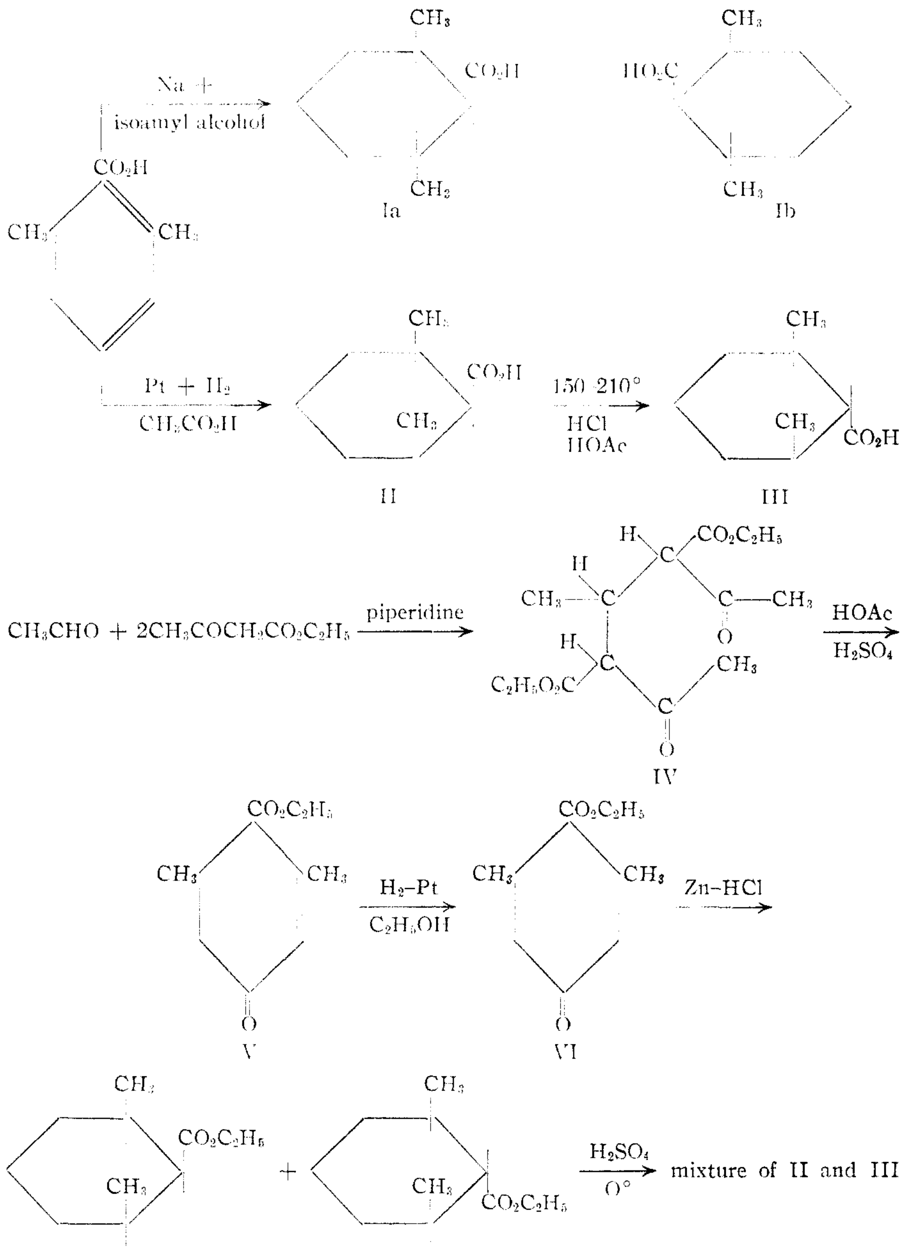
[2] Jacobs and Florsheim, THIS JOURNAL, **72**, 256, 261 (1950).

[3] Noyes, *Am. Chem. J.*, **20**, 789 (1898); **22**, 1 (1899).

[4] Hufferd and Noyes, THIS JOURNAL, **43**, 925 (1921).

[5] Meek, Merrow, Poon, Lane and Cristol, Abstracts of Papers presented at the Atlantic City Meeting of the American Chemical Society, September, 1949, p. 18 M. A sample of the isomer, m.p. 80.8–81.3°, which we obtained by Noyes' method was sent to Dr. Meek who found that it gave no depression of m.p. when mixed with his compound. Further recrystallization raised the m.p. of his sample.

[6] Smith and Stanfield, THIS JOURNAL, **71**, 81 (1949).



isomer Iab could be isolated in this synthesis, presumably because the catalytic reduction of ethyl 2,6-dimethyl-2-cyclohexen-4-one-1-carboxylate V to the saturated keto ester VI is stereospecific at least to the extent that both methyl groups in VI are on the same side of the ring. However, small amounts of Iab might escape detection because it is the most soluble isomer.

Hydrolysis of the ester mixture, VII and VIII, was accomplished in high yield by solution in 97.5% sulfuric acid at 0°. Alkaline hydrolysis was slow but could be realized without conversion of II into III. The mixture of acids could be separated into pure II and III by fractional crystallization or better by extraction of an ether solution of the mixture with sodium bicarbonate solution. II, the minor component, is a weaker acid and mostly remains behind in the ether (yield 15%); the bicarbonate-soluble fraction was completely isomerized to III (yield 80%) by one of the methods described in the experimental part.

A preliminary examination of the synthesis of the cyclohexane acids from 2,6-dibromoheptane and malonic ester by the general method used for the 2,5-dimethylcyclopentanecarboxylic acids[2] was not promising and was abandoned without isolation of any pure derivatives of 2,6-dimethylcyclohexane-1,1-dicarboxylic acid.

Pure methyl esters of II and III were prepared from the pure acids with diazomethane. Each was hydrolyzed in excellent yield in cold sulfuric acid as described in the experimental part. There was no evidence of inversion of II to III. It was found that conversion of this *meso cis* acid II or its derivatives to the *meso trans* series occurred less readily with the cyclohexane acids than with the cyclopentane acids. Hydrolysis of the *meso cis* ester to II without inversion was realized by refluxing with either aqueous sodium hydroxide or potassium hydroxide in 50% methanol. The methyl ester of II was not inverted by heating at 60° for 15 hours with methanolic sodium methoxide but at 95° inversion was complete in 20 hours, as indicated by hydrolysis of the recovered ester with cold sulfuric acid to pure III.

Inversion also occurred when the acid chloride was prepared from II with thionyl chloride in the usual way and hydrolyzed with alcoholic potassium hydroxide. This acid chloride gave the same amide, melting point 216–217.5°, by reaction with ammonium hydroxide as was obtained from the acid chloride prepared from III. The same anilide was also obtained from II and III. When the acid chloride of II was prepared with thionyl chloride in pyridine at 0° and treated with ammonium hydroxide at the same temperature, a new amide was obtained, melting point 184–185°.

Neither of the amides was hydrolyzed by the usual methods. More vigorous procedures gave low yields of III. The best results were obtained with 100% phosphoric acid,[2,7] which gave III from both amides, but in better yield and at lower temperatures from the *meso cis* derivative.

As was expected II and III gave different *p*-phenylphenacyl esters when the sodium salts were treated with *p*-phenylphenacyl bromide.

Noyes[3,4] prepared 2,6-dimethyl-1-cyclohexenecarboxylic acid from Iab by bromination of the acid chloride and elimination of hydrogen bromide from the bromoacid with alcoholic potassium hydroxide. We did not repeat the synthesis because so little Iab was available, but instead prepared the unsaturated acid from II or III. A 2,6-dimethyl-1-bromocyclohexanecarboxylic acid, melting point 141–142.3°, was obtained from either II or III; the preparations from the different acids gave no melting point depression when mixed. The bromoacid obtained from Iab melted at 150–151°.[3,4] The new bromoacid gave 2,6-dimethyl-1-cyclohexenecarboxylic acid, which had almost the same melting point as reported by Noyes. This unsaturated acid can exist in only two stereoisomeric forms which constitute a single racemic modification. The reduction of the acid to yield II thus completes an interconversion of the racemic series to the *meso*. The yield of II was only 30%, and the mixture of isomers that remained has not been successfully separated.

These qualitative experiments indicate that all of the stereoisomeric 2,6-dimethylcyclohexanecarboxylic acids are more hindered than even the most hindered 2,5-dimethylcyclopentanecarboxylic acid and are comparable in this respect to diisopropylacetic acid, the most similar acyclic compound.[8]

Experimental Part

All melting points are corrected.

2,6-Dimethylbenzoic acid was prepared from 2,6-dimethylaniline as reported by others.[6,9] 2,6-Dimethylaniline was obtained from Eastman Kodak Co. or from the Société Anonyme des Matières Colorantes et Produits Chimiques de Saint-Denis, Paris, and was fractionated carefully, b.p. 84° (8 mm.). It was converted to 2,6-dimethyliodobenzene, b.p. 58–59° (0.5 mm.), $n^{25}\text{D}$ 1.6003, d^{25}_4 1.6250, in 63% yield in the usual way[10] except that the diazonium solution was kept at 0° or below, a larger excess of potassium iodide was used, and the product was washed carefully with cold, concentrated sulfuric acid.

Anal. Calcd. for C_8H_9I: I, 54.69. Found: I, 54.64.

Carbonation of the Grignard reagent from this iodo compound gave a 73% yield of 2,6-dimethylbenzoic acid, m.p. 110–114°; two recrystallizations from cyclohexane raised the m.p. to 115.5–116°.

This acid was also prepared from mesitylene by the method of Noyes[3,4] with slight modification.[11] The over-all yield was 33%, but the procedure was very tedious.

Racemic 2,6-dimethylcyclohexanecarboxylic acid (Iab) was prepared as described by Noyes[3,4] except that the reduction was carried out under nitrogen. The yield of crystalline acid, m.p. 80.8–81.3° (from petroleum ether) was 30%. Mixed m.p.'s with *meso cis* II, *meso trans* III and 2,6-dimethylbenzoic acids gave depressions.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32; neut. equiv., 156.2. Found: C, 69.30; H, 10.21; neut. equiv., 156.7.

Resolution of Iab.—Attempts at resolution with strychnine were unsuccessful because the salts hydrolyzed too readily. Accordingly a strong base, cinchoninium methohydroxide, was employed.[12] The cinchoninium metho salt of Iab was fractionally recrystallized from acetone and the less soluble fraction gave an acid, m.p. 82.3–83.0°; *a*, −1.586° (1 dm. tube); *c*, 9.8 g./100 ml. in acetone; $\alpha^{23.7}\text{D}$ −16.18°. The more soluble fraction finally gave an acid, m.p. 82.1–83.1°; *a*, 0.810° (1 dm. tube); *c*, 9.8 g./100 ml. in acetone; $\alpha^{24}\text{D}$ +8.26°. Mixed m.p.'s of these fractions with Iab gave intermediate m.p.'s, but they gave depressions with II or III.

Ethyl 2,6-dimethyl-4-cyclohexanone-1-carboxylate (VI) was synthesized from acetaldehyde and ethyl acetoacetate by the Knoevenagel reaction which gave ethyl ethylidene-bis-acetoacetate (IV); this was cyclized, hydrolyzed and decarboxylated to ethyl 2,6-dimethyl-2-cyclohexen-4-one-1-carboxylate (V).[13] V was hydrogenated catalytically without purification over Adams platinum catalyst in alcohol to give VI which was distilled rapidly at 2 mm., b.p. 45–135°, and then fractionated through an 18-inch column packed with glass helices, b.p. 110–111° (5 mm.). There was a small forerun of 3,5-dimethylcyclohexanone, and a dark viscous polymeric residue accounted for most of the remaining starting material. The yield of IV, m.p. 77–79°, was 60–68% and the yield of VI based on IV was 57–61%.

Anal. of VI. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.51; H, 8.88.

The semicarbazone of VI was obtained in good yield, m.p. 180–181° after three recrystallizations from water.

Anal. Calcd. for $C_{12}H_{21}O_3N_3$: C, 56.45; H, 8.29. Found: C, 56.60; H, 8.23.

The conversion of IV to VI was also carried out by cyclizing IV with hydrochloric acid in benzene and ether[13a] to 4,6-dicarbethoxy-3,5-dimethyl-2-cyclohexen-1-one, hydrogenating this with Adams catalyst and hydrolyzing and decarboxylating the product with sulfuric acid in acetic acid. The yield of VI was approximately the same as by the alternative method but the procedure was more tedious.

Ethyl 2,6-dimethylcyclohexanecarboxylates VII and VIII were prepared from VI by Clemmensen reduction. Four hundred grams of mossy zinc was amalgamated by stirring with 40 g. of mercuric chloride, 20 ml. of concentrated hydrochloric acid and 480 ml. of water. The aqueous layer was decanted, the zinc covered with 280 ml. of water and 400 ml. of concentrated hydrochloric acid, and 169 g. of VI added. The reaction mixture was refluxed for 35 to 40 hours until the zinc had dissolved, cooled, and the layers separated. Although the 2,4-dinitrophenylhydrazine test for the ketone was negative after about 30 hours of refluxing, some starting material remained and the yield was slightly better with the longer reflux time. The aqueous phase was saturated with salt and extracted once with ether which was then united with the oily layer. This ether solution was washed three times with water, dried over magnesium sulfate, and concentrated on the steam-bath in a current of air. The crude material, a yellow liquid of pleasant odor, 135–140 g. (87–93% yield), was used directly for the hydrolysis. It contained only traces of acid, which indicated the resistance to acid hydrolysis shown by these esters.

2,6-Dimethylcyclohexanecarboxylic Acids II and III.—To 400 ml. of 97.5% sulfuric acid at 0 to −2° was added dropwise with stirring 26.7 g. of the crude ester mixture slowly enough so the temperature remained below 0°. After standing at 0° for 15 hours the cloudy, tan solution was added slowly from a separatory funnel to a stirred mixture of ice and solid carbon dioxide. The acid mixture separated as a yellow oil which partially solidified. After the Dry Ice had evaported, the acids were taken up in carbon tetrachloride and the aqueous layer extracted several times with this solvent. The carbon tetrachloride solution was extracted several times with 5% potassium hydroxide; the extract was decolorized and the acids liberated with concd.

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[7] Berger and Olivier, *Rec. trav. chim.*, **46**, 600 (1927).

[8] Kinetic studies on the relative rates of esterification and hydrolysis of these acids and the corresponding esters are in progress and will be reported at a later time.

[9] Treffers and Hammett, THIS JOURNAL, **59**, 1708 (1937).

[10] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 351.

[11] The modifications are reported in a thesis submitted by Gustave B. Linden for the M.S. degree in Chemistry, University of California, Los Angeles, 1943. We wish to thank Dr. Linden and Mr. John Morrish for preparing the 2,6-dimethylbenzoic acid used in this work before 2,6-dimethylaniline was available.

[12] Major and Finkelstein, THIS JOURNAL, **63**, 1368 (1941).

[13] Horning, Denekas and Field, (a) *J. Org. Chem.*, **9**, 547 (1944); (b) *Org. Syntheses*, **27**, 24 (1947).

hydrochloric acid; yield 18 g., 77%. The carbon tetrachloride solution gave 6.3 g. of crude, recovered esters from which an additional 2.8 g. of acids was obtained by repeating the hydrolysis. The over-all yield was 89%, m.p. 55–90°.

If the hydrolysis was carried out without cooling, sulfur dioxide was produced, but an 80% yield of acids could be realized. If the sulfuric acid solution was left for shorter periods of time, the amount of recovered esters increased. The yields were lowered by using less sulfuric acid.

The acid mixture was fractionally crystallized from 60–70° petroleum ether to give the less soluble isomer III, m.p. 103–104° after three recrystallizations from the same solvent.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32; neut. equiv., 156.2. Found: C, 69.02; H, 10.20; neut. equiv., 156.1.

The petroleum ether was removed from the filtrate and the residue dissolved in a mixture of hot chloroform and ethyl acetate from which, on careful cooling, large hexagonal tablets, m.p. after drying 86–88°, were obtained. After these were removed the solution deposited small fern-like crystals of the isomer, m.p. 101–102.4°. The lower melting isomer was recrystallized from petroleum ether (b.p. 30–60°) to give the pure acid, m.p. 87.5–88°.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32; neut. equiv., 156.2. Found: C, 69.11; H, 10.11; neut. equiv., 156.0.

A more convenient separation of II and III was realized by extraction of an ether solution of the mixture with several portions of saturated sodium bicarbonate solution, the total amount being equivalent to the acids taken. Successive extracts gave melting points ranging from 99–101° (first) to 92–97°. The ether solution was finally extracted with 5% sodium hydroxide solution and the acid obtained by neutralization. The latter had a m.p. of 84–87°. One recrystallization gave a product, m.p. 86–87.5° in 15% yield. The various high-melting fractions were readily recrystallized to give pure III, m.p. 103–104°. The mother liquors were all combined and the residual acids isolated and isomerized to III as described below. The total yield of III based on starting acid mixture was 80%.

II was also obtained in almost quantitative yield by hydrogenation of 2,6-dimethylbenzoic acid over Adams catalyst in gl. acetic acid. The hydrogenation went very slowly or not at all unless carefully purified solvent and compound were used.[6] As many as six recrystallizations from carefully purified acetic acid were sometimes necessary. The product melted at 85.5–87° as obtained from the hydrogenation. One recrystallization from formic acid raised the m.p. to 87–88°.

Hydrogenation of less pure 2,6-dimethylbenzoic acid over Raney nickel with ammonium chloroplatinate as a promoter at 3000 lb. and 200° for two days gave a mixture of isomers from which a low yield of II was isolated as the only pure product.

Isomerization of II to III was accomplished in almost quantitative yield by heating II in gl. acetic acid containing 2% hydrochloric acid at 130° for 24 hours. Longer heating or temperatures as high as 210° did not decrease the yield. No inversion occurred at 115–120° in 2.5 hours or in 98% formic acid containing 2% hydrochloric acid at 125–130° for 2.5 hours or at 100° for 30 hours. The crude product of the isomerization melted at 102–103°.

Methyl *meso cis* and *trans* 2,6-dimethylcyclohexanecarboxylates were prepared from the corresponding acids and diazomethane in ether solution. The *meso cis* ester had a strong camphor-like odor, b.p. 104–105° (58 mm.), $n^{25}D$ 1.4410.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.71; H, 10.45.

The *meso trans* ester had a slight camphor-like odor, b.p. 104–105° (59 mm.), $n^{25}D$ 1.4393.

Anal. Found: C, 70.67; H, 10.69.

Saponification of 1 g. of the *meso cis* ester by refluxing for 60 hours with 2 g. of potassium hydroxide in 10 ml. of methanol and 10 ml. of water gave 0.8 g. of crystalline II. Recrystallization from formic acid gave 0.7 g. of acid, m.p. 85.5–87°. After 48 hours of heating, considerable ester remained unsaponified. A similar experiment with *meso trans* ester gave 0.7 g. of once-recrystallized III, m.p. 100–102°.

***p*-Phenylphenacyl esters** were prepared from the acids as usual.[14] The *meso cis* acid gave needles, m.p. 79–80.5°, after recrystallization from methanol.

Anal. Calcd. for $C_{23}H_{26}O_3$: C, 78.82; H, 7.48. Found: C, 78.83; H, 7.48.

The *meso trans* acid gave an oily product which was recrystallized with difficulty from methanol–dioxane, m.p. 79–80°; a mixed m.p. with the *meso cis* derivative gave a depression.

Anal. Found: C, 78.80; H, 7.56.

The phenacyl ester of the *meso trans* acid was prepared, m.p. 95–96°, from methanol.

Anal. Calcd. for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.38; H, 8.14.

Attempts to prepare the phenacyl ester of the *meso cis* acid were unsuccessful.

***meso cis* and *trans* 2,6-Dimethylcyclohexanecarboxylic Acid Chlorides.**—Either the *meso cis* or *trans* acids dissolved in 10% excess of purified thionyl chloride with cooling. After heating at 80° for one hour, excess thionyl chloride was removed under reduced pressure and the product distilled, b.p. 64–65° (5 mm.).

Anal. Calcd. for $C_9H_{15}ClO$: Cl, 20.30. Found: Cl, 20.35.

The acid chloride was unchanged by contact with water for several weeks at room temperature, but gave an excellent yield of *meso trans* acid after refluxing for two hours with 6 *N* alcoholic potassium hydroxide. The product was the same no matter whether II or III was the starting material. This method of converting II to III is more rapid than that employing hydrochloric and acetic acids, but the product seems to be slightly less pure.

***meso trans* 2,6-Dimethylcyclohexanecarboxanilide** was prepared from the undistilled acid chloride from either II or III in 95% yield, m.p. 201–202° from benzene.

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15. Found: C, 77.76; H, 9.10.

***meso trans* 2,6-Dimethylcyclohexanecarboxamide** was prepared similarly in 96% yield, m.p. 215–217° from methanol, 216.5–217.5° after sublimation at 2 mm. and 100°.

Anal. Calcd. for $C_9H_{17}ON$: C, 69.63; H, 11.04. Found: C, 69.66; H, 11.34.

With both the amide and anilide the products from II and III had the same m.p. and showed no depression on mixing.

***meso cis* 2,6-Dimethylcyclohexanecarboxamide** was obtained in 17% yield by dissolving 2 g. of II in 40 ml. of anh. pyridine and cautiously adding 5 ml. of pure thionyl chloride during 20 minutes to the solution at 0°. After 15 minutes longer at 0° the pyridine was removed at 5–10 mm. and the orange crystals which formed were treated with 50 ml. of cold, concd. ammonium hydroxide. The dark red oil that formed crystallized after five hours at 0° to long, yellow needles, m.p. 181–182.5°. Recrystallization from benzene gave colorless needles, m.p. 183–184°, and sublimation at 3 mm. (100°) raised the m.p. to 184–185°. A mixed m.p. with *meso trans* amide gave an intermediate melting range.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.04. Found: C, 69.48; H, 11.30.

Hydrolysis of the amides was difficult. Sodium nitrite with sulfuric acid or acetic acid had no effect. Concd. sulfuric acid was without action up to 90–100°, and above that range decomposition occurred and no acid was isolable. With isoamyl nitrite and concd. hydrochloric acid at 100° for three hours a 3% yield of III was realized. A 30 molar excess of nitrosyl chloride at 70° for 30 hours (sealed tube) gave a 30% yield of III and 10% recovered amide (on *meso trans* amide only). From 1 g. of *meso cis* amide in 5 g. of 100% phosphoric acid[2,9] at 150° for 30 minutes was obtained a 50% yield of III. The rest of the starting material was obtained as a neutral solid of wide melting range, presumably largely nitrile. The *meso trans* amide was unaffected by similar treatment at 150°, but at 190° a 25% yield of III was obtained, more decomposition was evident, and slightly more of the neutral solid was isolated. Above 200° decarboxylation occurred and no III was recovered.

1-Bromo-2,6-dimethylcyclohexanecarboxylic acid was prepared from III in 82% yield by the method used previously

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(14) Drake and Bronitsky, THIS JOURNAL, **52**, 3715 (1930).

with the racemic acid[3,4] and with the cyclopentane acid.[2] The bromo acid chloride was hydrolyzed by refluxing with 85% formic acid. The crude bromo acid, m.p. 115–125°, was recrystallized twice from petroleum ether to give the pure compound, m.p. 141–142.3°.

Anal. Calcd. for $C_9H_{15}O_2Br$: C, 45.97; H, 6.43; Br, 33.99. Found: C, 45.81; H, 6.56; Br, 34.10.

A bromo acid which had the same m.p. and mixed m.p. was obtained from II but the yield was only 47%. Presumably inversion occurred through the acid chloride of the unsubstituted acid.

2,6-Dimethyl-1-cyclohexenecarboxylic acid was obtained in 90% yield by dehydrohalogenation of the bromo acid by refluxing for four hours in saturated methanolic potassium hydroxide, m.p. 88.2–89.7° (from petroleum ether).

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15; neut. equiv., 154.2. Found: C, 70.33; H, 9.19; neut. equiv., 154.5.

This acid was not pure enough for reduction at low pressures over Adams catalyst, but at 120 atmospheres it gave a crude acid, m.p. 50–70°. Purification by the sodium bicarbonate technique gave 30% of II, m.p. 86–87.5°. The acids recovered from the sodium bicarbonate solution were low melting but had a neutral equivalent of 155.3 (calcd. 156.2). Isomerization with hydrochloric and acetic acids gave III, m.p. 99–101°, which indicates that the hydrogenation product was mainly II and III. Very little of the starting material was present because the crude product did not react with bromine or neutral permanganate.

2,6-Dibromoheptane was prepared by the von Braun reaction.[15] N-Benzoyl-2,6-dimethylpiperidine was obtained in 60–90% yield, and the dihalide was formed from this in 35% yield, b.p. 94–94.5° (10 mm.).

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[15] Leonard and Nommensen, THIS JOURNAL, **71**, 2808 (1949).

LOS ANGELES, CALIFORNIA RECEIVED MARCH 26, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

Unsymmetrical 1,3-Diarylpropenes[1]

BY CHRISTIAN S. RONDESTVEDT, JR.

A series of unsymmetrical 1,3-diarylpropenes was prepared by dehydrating 1,3-diaryl-1-propanols. The latter were conveniently prepared in high yields by lithium aluminum hydride reduction of the corresponding chalcones. The method is more convenient than those in the literature.

In connection with an investigation of the mechanism of the reaction of maleic anhydride with olefins,[2] a series of unsymmetrical 1,3-diarylpropenes was needed. An examination of the literature revealed a number of possible syntheses, but some of them are not experimentally attractive. 1,3-Diaryl-1-propanols can be prepared from an aromatic aldehyde and a β-arethylmagnesium halide, but the requisite β-arethyl halide must first be synthesized. An alternate route from an arylmagnesium halide and a β-arylpropionaldehyde again requires preparation of the latter. More simply, commercially available aromatic aldehydes and substituted acetophenones may be condensed to chalcones which can then be reduced to the desired hydrochalcols.[3] The hydrochalcol can be dehydrated to the olefin directly or through the derived chloride.[4a,b]

Other routes described in the literature include coupling of an arylmagnesium halide with a substituted cinnamyl bromide[5a] and a Perkin condensation of an aromatic aldehyde with a β-arylpropionic acid accompanied or followed by decarboxylation.[4b,5b] Both methods require synthesis of one of the reaction components, the other in general being commercially available.

Some of these methods have been explored as routes to the desired unsymmetrical 1,3-diarylpropenes. Boeseken and Elsen[5a] recorded a low yield of 1,3-diphenylpropene in the coupling of phenylmagnesium bromide with cinnamyl bromide. In our hands, the corresponding reaction of *p*-tolylmagnesium bromide with cinnamyl bromide gave a poor yield of unsaturated material which could not be readily purified. Since the method appeared unpromising, no further experiments were tried with related compounds.

Addition of commercially available hydrocinnamaldehyde to *p*-methoxyphenylmagnesium bromide formed the carbinol in excellent yield. Substitution of *p*-tolylmagnesium bromide gave only low yields of impure carbinol, accompanied by small amounts of 4,4′-bitolyl and considerable toluene and unreacted aldehyde. With prolonged refluxing in ether or in benzene, the yields were still poor, but the recovery of starting material was less. This procedure was also abandoned as unpromising.

The synthesis of chalcones has been thoroughly studied, and all members of the series desired are known compounds. Although their reduction to hydrochalcols has been accomplished with hydrogen and platinum and with sodium amalgam, they are reduced by lithium aluminum hydride[6] much more conveniently, in good yield, and with no danger of hydrogenolysis of sensitive benzyl-type hydroxyls or ring halogens. The initial addition is evidently 1,4- to the conjugated system,[7] since in the reduction of anisalacetophenone, a small quantity of β-anisylpropiophenone was isolated. The matter was not further investigated, but it appears that 1,2- and 1,4-reduction of α,β-unsaturated carbonyl compounds by lithium aluminum hydride follows the same pattern that Kohler observed in addition of Grignard reagents.[8] This evidence supports the

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[1] Presented at the Meeting of the American Chemical Society in Boston, April, 1951.

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[8] *Cf.* F. A. Hochstein and W. G. Brown, *ibid.*, **70**, 3484 (1948); R. F. Nystrom and W. G. Brown, *ibid.*, **70**, 3738 (1948).