to whom the author is grateful for a fellowship award.

Experimental

Reaction of α-Bromo-4′-phenylchalcone with Methylamine.—A 5.1-g. (0.014 mole) sample of α-bromo-4′-phenylchalcone[4] in 50 ml. of benzene was mixed with a cold ether solution containing about 0.05 mole of methylamine. After standing at room temperature for 10 hours and at 5° for 12 hours the methylamine hydrobromide was removed by filtration and the ether–benzene filtrate concentrated to produce 4.1 g. (92% yield) of a pale-yellow colored mixture of the *cis* and *trans* forms of 1-methyl-2-phenyl-3-(p-phenylbenzoyl)-ethylenimine, m.p. 102–114°. An 0.8-g. sample of this mixed product was dissolved in benzene and placed on a 20 × 2 cm. column packed with 50 g. of activated alumina. The column was developed with 200 ml. of 1:100 abs. ethanol–dry benzene solution. The eluent was 2:100 abs. ethanol–dry benzene. The initial eluates contained the low-melting *trans* isomer (0.52 g., 68% of total material recovered, m.p. 120–121°). The final eluates contained the higher-melting, *cis* isomer (0.24 g., 31% of total recovered, m.p. 140°). The isolation of 0.76 g. of material represents a 95% recovery. These products were colorless in contrast with the lightly colored materials previously obtained from the corresponding dibromoketone.[14]

Reaction of α-Bromo-4′-methylchalcone with Methylamine.—A 4.25-g. (0.014 mole) sample of α-bromo-4′-methylchalcone was dissolved in 40 ml. of benzene and mixed with an ether solution containing about 0.05 mole of methylamine. After standing at room temperature for 24 hours the usual working up of the reaction mixture gave an oily product, 3.25 g., which was apparently a mixture of the *cis* and *trans* forms of 1-methyl-2-phenyl-3-(p-toluyl)-ethylenimine. Chromatographic separation on activated alumina gave in the first eluates the *trans* isomer (1.88 g., 60% of recovered material, m.p. 76–78°).[9] The final eluates, which probably contained mainly the *cis* isomer, produced 1.26 g. (40% of recovered material) which was an oil that was not crystallized. The total material recovered was 3.14 g.

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(14) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

LINCOLN, NEBRASKA

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

The Metalation of 1,7-Dimethoxynaphthalene[1]

BY RODERICK A. BARNES AND WALTER M. BUSH[2]

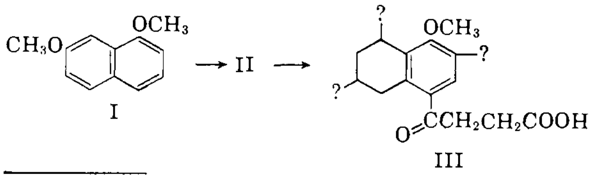
RECEIVED JANUARY 8, 1959

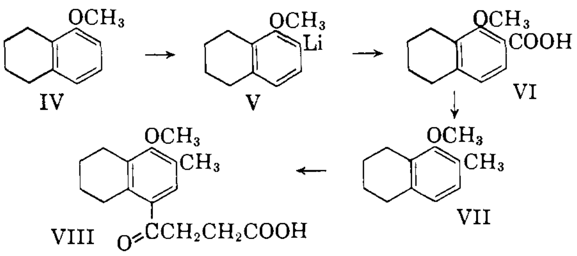
It has been demonstrated that 1,7-dimethoxynaphthalene is metalated in good yield at the 6-position. The bearing of this observation on the mechanism of the metalation reaction has been discussed.

The substitution reactions of 1,7-dimethoxynaphthalene (I) were of interest in connection with synthetic experiments directed toward 19-norsteroids[3]; the metalation of I was examined because it seemed likely that this reaction would introduce a substituent into a different position from the usual electrophilic aromatic substitutions.

When compound I was metalated by butyllithium in ether and the resulting lithium derivative treated with dimethyl sulfate, a crystalline methyl-1,7-dimethoxynaphthalene (II) could be isolated; the reaction of the lithium derivative with carbon dioxide and N-methylformanilide also produced crystalline substances. In all of the three experiments the yields were about 70% and there was no evidence for the presence of more than one isomer in the products. From this it was concluded that the lithium atom had entered almost exclusively at a single position of compound I.

The structure proof for II was carried out using a two-stage reduction to remove the β-methoxy group; the resulting liquid tetralin derivative was characterized by converting it to the β-aroylpropionic acid (III) with the methyl group almost certainly in one of the three positions *ortho* to the methoxyl groups of I. One of the possible structures for III was synthesized from 5-methoxytetralin (IV). The metalation of IV has not been observed previously, but the structures of the products in this reaction sequence are correct because cleavage of the ether function of VI produced the previously known 5-hydroxy-1,2,3,4-tetrahydro-6-naphthalenecarboxylic acid.[4] The direct transformation of the aryllithium V to the methyl derivative VII was attempted, but the conversion of IV to V proceeds so poorly that the problem of separating pure VII from a much larger amount of unreacted IV was impractically difficult. However, acid VI was readily separated from the starting material and after reduction, first with lithium aluminum hydride and then with palladium and hydrogen, yielded pure VII. The aroylpropionic acid VIII from this series of reactions melted at 119–121.5°, while III melted at 158–160.5°; therefore compound I was not metalated at the 2-position.





The second possibility was synthesized starting from β-(2-bromo-5-methoxyphenyl)-ethyl tosylate

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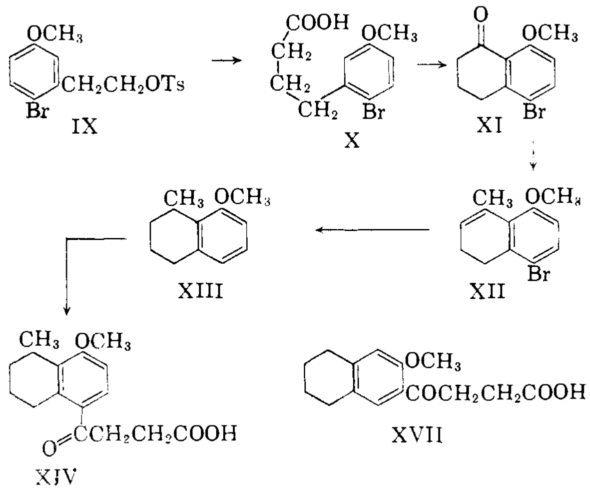
(1) Presented before the Division of Organic Chemistry, 128th Meeting of the A. C. S., Minneapolis, Minn., September 15, 1955.

(2) The major portion of this communication is abstracted from a thesis presented to the Graduate Faculty for the Ph.D. degree, May, 1955.

(3) R. A. Barnes and W. M. Bush, THIS JOURNAL, **80**, 4714 (1958).

(4) W. Hückel and E. Goth, *Ber.*, **57**, 1290 (1924).

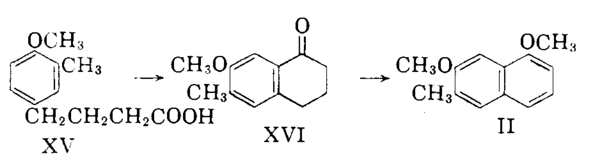
(IX) which had been prepared in connection with another synthesis. Alkylation of malonic ester



IX X XI XII XIII XIV XVII

by IX, followed by saponification and decarboxylation, produced acid X which was readily cyclized to XI. The methyl group was introduced by treating XI with methylmagnesium iodide to yield XII, after dehydration of the intermediate alcohol. Reductions to remove the bromine atom and to saturate the double bond produced the methylmethoxytetralin (XIII) necessary for the preparation of the β-aroylpropionic acid (XIV). This isomer had the same melting point as III, but the two were different as was demonstrated by the melting point of a mixture. The cyclization step in this synthesis might have taken place with displacement or migration of the bromine atom.[5] If this had occurred, the final acid would have differed from XIV by having the methoxyl group in a β-position and the succinoyl group *ortho* to it. The ultraviolet spectrum of an acid of this kind (XVII) was very different from that of acids III and XIV and provides good evidence that the assignment of structure XIV is correct.

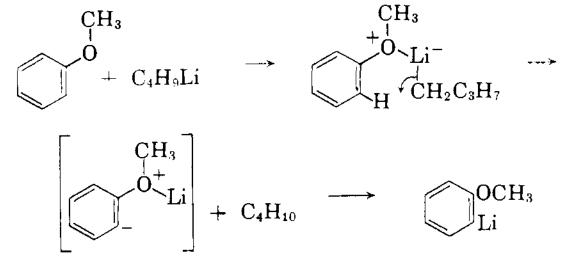
With the elimination of two possibilities, it was concluded that the original metalation must have been at position 6. This conclusion was valid only if the original assumption of only three possibilities was correct. To make certain, an alternate synthesis of II was carried out starting from γ-(4-methoxy-3-methylphenyl)-butyric acid (XV).



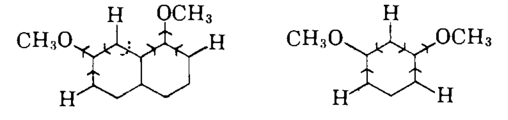
XV XVI II

The cyclization of acid XV to ketone XVI followed by dehydrogenation and methylation of the phenolic hydroxyl produced a substance identical with compound II from the metalation reaction. It might have been possible for acid XV to cyclize *ortho* to the methyl group with formation of an isomer of ketone XVI. However this ketone would have finally yielded, instead of II, an isomer with the methyl group at position 8 which has already been eliminated as the site of metalation. Thus the identity of the samples of II prepared in these two different ways serves to prove the structure of XVI as well as of the metalation product.

Previous work[6-8] has furnished considerable evidence bearing on the mechanism of the metalation of aryl ethers and related compounds. The fact that such metalations almost invariably take place at a position *ortho* to functional group is explained as resulting from a preliminary coördination of the lithium with an electron-donating atom.[9] This is followed by removal of an *ortho* hydrogen by the carbanion of the alkyllithium.

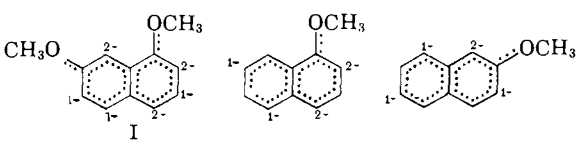


The results of Roberts and Curtin[9] together with previous observations seemed to indicate that the inductive effect was the most important factor in determining the position of metalation. When applied to compound I, this concept would predict that the methoxyl groups should make the hydrogen at position 8 slightly more acidic than at positions 2 and 6. A similar argument has been used



to explain the metalation of 1,3-dimethoxybenzene at the 2-position.

The actual metalation of I at the 6-position can be explained by taking into account the resonance effect of the methoxyl groups; the numbers (1-, 2-) refer to the number of important contributing resonance structures having a negative charge at the position in question. Thus it is clear that the



I

relative acidity of a hydrogen atom is determined by the total electron density on the nuclear carbon and the distribution of both π- and σ-electrons must be considered. For I the inductive removal of σ-electrons by the methoxyl groups is only slightly different at the three positions but the difference in distribution of the π-electrons is large and thus the hydrogen at position 6 is relatively more acidic. This concept also explains the fact that 2-meth-

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(5) H. T. Huang, D. S. Tarbell and H. R. V. Arnstein, THIS JOURNAL, **70**, 4181 (1948), and P. D. Gardner and W. J. Horton, *J. Org. Chem.*, **19**, 213 (1954). We wish to thank a referee for bringing these references to our attention.

(6) S. V. Sunthankar and H. Gilman, *ibid.*, **16**, 8 (1951).

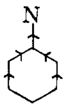
(7) G. Wittig and G. Fuhrman, *Ber.*, **73**, 1197 (1940), and previous papers.

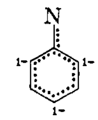
(8) A. A. Morton, *Chem. Revs.*, **35**, 1 (1944).

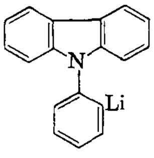
(9) J. D. Robert and D. Y. Curtin, THIS JOURNAL, **68**, 1658 (1946).

oxynaphthalene metalates at the 3-position more readily than 1-methoxynaphthalene at the 2-position.[5] It is interesting that for 1,3-dimethoxynaphthalene the resonance distribution of π-electrons is the same at the 2- and 4-positions and hence the inductive effect becomes the deciding factor. It is also important to recognize that in these metalation reactions it is the permanent resonance effect (mesomeric effect) of the substituent which must be considered, while in the usual electrophilic substitutions the substituent may participate strongly in distributing the positive charge (electromeric effect) in the transition state.

The apparently anomalous metalation of triphenylamine at a *meta* position can also be explained if it assumed that in the "propeller" structure of this molecule the weakly basic nitrogen atom is effectively shielded and preliminary coördination by the metalating agent is prevented. For an aromatic nucleus in which coördination is impossible, all positions are possible sites for attack, however the resonance and inductive effects combine to make the hydrogen at the *meta* position the most acidic.[10] The closely related compound N-phenylcarbazole has a nitrogen of equal basicity but it is a more planar molecule and coördination is apparently possible here. The metalation on the phenyl ring rather than at the 1-position of the carbazole nucleus may be explained by the fact that resonance distribution of the π-electrons is most effective over the carbazole nucleus. The phenyl ring is somewhat twisted out of the plane of the rest of the molecule so that overlap with the p-orbital system of the more electron-rich carbazole nucleus is reduced, and since the inductive effect is not altered, the *ortho* hydrogens on the phenyl ring are the more acidic.







Experimental[11]

1,7-Dimethoxy-6-methylnaphthalene (II).—A solution of butyllithium was prepared[12] from finely cut lithium wire (8 g.), butyl chloride (40 g.) and dry ether (300 ml.). A solution of 1,7-dimethoxynaphthalene (52.8 g.) in ether (150 ml.) was added during one hour and the mixture was refluxed during an additional 9 hours. Dimethyl sulfate (52 ml.) in ether (100 ml.) was added cautiously and the solution refluxed for 5 hours. Water was added to the cold reaction mixture until all of the lithium hydroxide was in solution. The ether layer was separated, dried and concentrated. The residue was distilled and the fraction which boiled at 124–126° (0.43 mm.) was collected. When this fraction was seeded it crystallized almost completely. Recrystallization from petroleum ether (b.p. 30–60°) yielded 28 g. (52%) of colorless needles, m.p. 69–71.5°. The analytical sample melted at 72–73°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.97. Found: C, 77.14; H, 6.96.

The yields in the reaction are variable and probably depend on the amount of butyllithium actually formed. One run using 5 g. of I and a somewhat larger excess of butyllithium produced 75% of II.

A sample of II (1 g.) was refluxed with acetic acid (10 ml.) and 48% hydrobromic acid (12 ml.) for 6 hours. The solvents were distilled and the residue crystallized from aqueous ethanol to yield 1,7-dihydroxy-6-methylnaphthalene which melted at 150–151°.

Anal. Calcd. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.59; H, 5.86.

Methyl 1,7-Dimethoxy-6-naphthalenecarboxylate.—A solution of butyllithium prepared from lithium (0.5 g.) and butyl chloride (2.5 g.) in dry ether (25 ml.) was treated with 1,7-dimethoxynaphthalene (3.7 g.) as in the previous experiment. The aryllithium solution was poured into a suspension of Dry Ice and ether. Water was added to extract the lithium salt and on addition of hydrochloric acid to the aqueous solution there was obtained 3.3 g. (72%) of crude acid (m.p. 148–154°). Recrystallization raised the melting point to 165–166°. A portion (2 g.) of this acid was treated with an ether solution of diazomethane prepared from nitrosomethylurea (3 g.). A quantitative yield of the methyl ester, m.p. 91–92°, was obtained after evaporation of the ether. Recrystallization from ligroin–benzene did not change the melting point.

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.21; H, 5.80.

1,7-Dimethoxy-6-naphthaladehyde.—A solution of 1,7-dimethoxy-6-naphthyllithium was prepared exactly as in the previous experiment. A solution of N-methylformanilide (3.7 g.) was added dropwise and after 30 minutes the reaction mixture was poured into dilute sulfuric acid. The product was extracted with ether, the ether extract washed with dilute potassium hydroxide solution and the ether evaporated. There was obtained 3.6 g. (84%) of crude aldehyde, m.p. 121–122°. Recrystallization from methanol raised the melting point to 123–123.5°.

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.20; H, 5.60. Found: C, 72.25; H, 5.60.

β-8-(5-Methoxy-1,2-methyl-1,2,3,4-tetrahydronaphthoyl)-propionic Acid (III).—Sodium (7.8 g.) in small pieces was added to a refluxing solution of II (4.8 g.) in absolute ethanol (50 ml.) during three hours; small additions of absolute ethanol were necessary to keep the sodium ethoxide in solution. The reaction mixture was cooled and acidified with 6 *N* hydrochloric acid. The product was extracted with ether and after evaporation of the ether, the ketonic product was separated using Girard reagent T (8 g.).[13] This ketone (2.4 g., 60%) was characterized only by means of its infrared spectrum (carbonyl band at 5.83 μ).[14] Wolff–Kishner reduction of this product by the Huang-Minlon procedure[15] using diethylene glycol (15 ml.), potassium hydroxide (2. g.) and hydrazine hydrate (2 ml., 85%), yielded an oil which was evaporatively distilled. The colorless fraction (0.88 g.) which was collected at 60–70° (0.1 mm.) did not have any absorption bands in the carbonyl region of the infrared spectrum. This fraction was added to a solution of aluminum chloride (1.8 g.) and succinic anhydride (0.6 g.) in nitrobenzene (10 ml.). After standing for 6 hours at room temperature, the reaction mixture was steam distilled to remove nitrobenzene and the residue recrystallized from methanol to yield acid III as white crystals which melted at 158–160.5°; λ_{max}^{EtOH} 226 mμ (log ϵ 4.13), 274 mμ (log ϵ 4.09).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.74; H, 7.23.

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[10] For this to be true it is also necessary that the inductive withdrawal of σ-electrons from the 1-position is less than the donation of π-electrons of nitrogen or oxygen to this position. Although it is difficult to evaluate the resonance and inductive effects at *o*-positions because of steric complications, R. W. Taft in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 593, has concluded that for a series of *o*-substituted benzoic acids the resonance and inductive effects of the substituent are approximately the same as for the *p*-position.

[11] All melting points were determined either with the Kofler hot-stage or the Fisher–Johns melting point apparatus. Microanalyses were by W. Manser, Zurich, Switzerland, and G. Robertson, Summit, N. J.

[12] H. Gilman, W. Langham and F. Moore, THIS JOURNAL, **62**, 2327 (1940).

[13] A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

[14] M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson and E. A. Bowler, THIS JOURNAL, **72**, 3704 (1950).

[15] Huang-Minlon, *ibid.*, **68**, 2487 (1946).

5-Methoxy-1,2,3,4-tetrahydronaphthalene-6-carboxylic Acid (VI).—5-Methoxy-1,2,3,4-tetrahydronaphthalene (32.4 g.), prepared by hydrogenation of α-naphthylmethyl ether,[16] was dissolved in dry ether (60 ml.) and added dropwise to a refluxing solution of *n*-butyllithium prepared from lithium (5.4 g.) and butyl chloride (24.1 g.) in dry ether (120 ml.). After 10 hours at reflux temperature the reaction mixture was poured onto crushed Dry Ice which was covered with a layer of dry ether. Water was added to dissolve the lithium salts and upon acidification of the aqueous layer there was obtained 5.14 g. (6.3%) of crude acid, m.p. 105–120°. After two recrystallizations from acetone–hexane the purified acid (3.1 g., 3.8%) melted at 123–123.5°.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.71; H, 6.88.

A sample of this acid (120 mg.) was demethylated by refluxing a solution in acetic acid (2 ml.) and 48% hydrobromic acid (0.5 ml.) for 6 hours. The solid product which separated when most of the solvent was evaporated was recrystallized from aqueous ethanol, m.p. 165–167° (reported[4] m.p. 165–166°).

6-Hydroxymethyl-5-methoxy-1,2,3,4-tetrahydronaphthalene.—Acid VI (2.12 g.) was added to a solution of diazomethane prepared from nitrosomethylurea (10 g.). Acetic acid was added to decompose the excess diazomethane and the solvents were removed; the residue was evaporatively distilled at 85° (0.10 mm.) to yield 2.16 g. (95%) of the methyl ester of VI. A portion of this ester (1.52 g.) in dry ether (10 ml.) was added, during 40 minutes, to a suspension of lithium aluminum hydride (1.0 g.) in ether (15 ml.). When the exothermic reaction was complete, the mixture was refluxed for an additional three hours and then ethyl acetate added to decompose the excess hydride. Dilute hydrochloric acid was added to dissolve the inorganic hydroxides and the product extracted with ether. After processing the ether solution, the residue which remained was evaporatively distilled at 105° (0.01 mm.) to yield 1.78 g. (95%) of the alcohol which crystallized on standing, m.p. 60–61.5°. The analytical sample, prepared by recrystallization from petroleum ether, melted at 61–62°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.38.

β-8-(5-Methoxy-6-methyl-1,2,3,4-tetrahydronaphthoyl)-propionic Acid (VIII).—A solution of the carbinol from the preceding experiment (1 g.) was hydrogenolyzed with palladium-on-charcoal[17] and hydrogen (50 p.s.i.). Although the hydrogen absorption was about half the calculated amount after ten hours, the reaction was stopped. The crude product was evaporatively distilled at 65–70° (0.05 mm.), to yield 507 mg. of distillate and a viscous residue. The distillate was redistilled at 45° (0.03 mm.) and the first fraction (134 mg.) was treated with succinic anhydride and aluminum chloride as in the preparation of acid IV. Acid VII obtained in this way melted at 119–212.5° after recrystallization from acetone–hexane.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.44; H, 7.22.

γ-(2-Bromo-5-methoxyphenyl)-butyric Acid (X).—Potassium metal (2.44 g.) was dissolved in *t*-butyl alcohol (80 ml.) and to this cold solution, diethyl malonate (10.7 g.) in toluene (20 ml.) was added. This solution was warmed to 50°, β-(2-bromo-5-methoxyphenyl)-ethyl *p*-toluenesulfonate (IX) (24 g.) and potassium iodide (0.6 g.) were added and the mixture heated to reflux temperature. After 12 hours at this temperature, water and benzene were added to the mixture. The organic layer was separated, dried and concentrated. This crude alkylated malonic ester was saponified by refluxing for 19 hours with a solution of potassium hydroxide (20 g.) in ethanol (100 ml.) and water (200 ml.). The alkaline solution was extracted with ether to remove non-acidic impurities and the aqueous solution acidified. The crude acid, β-(2-bromo-5-methoxyphenyl)-ethylmalonic acid (9.5 g., 48%), melted at 143–153°.

A portion (300 mg.) of this acid was decarboxylated by heating at 165–170° at 0.1 mm. for 15 minutes. The residual solid was recrystallized from hexane to yield 237 mg. (88%) of acid X as colorless plates which melted to 91–95°. The analytical sample prepared by further recrystallization melted at 94–95°.

Anal. Calcd. for $C_{22}H_{13}O_3Br$: Br, 29.26. Found: Br, 29.04.

β-5-(8-Methoxy-1-methyl-1,2,3,4-tetrahydronaphthoyl)-propionic Acid (XIV).—Acid X (6.9 g.) was mixed with phosphorus pentachloride (5.5 g.) and the mixture allowed to stand for one hour. Three portions (25 ml.) of dry benzene were added and distilled *in vacuo* with gentle warming and finally the acid chloride was heated under vacuum (25 mm.) for 45 minutes. Ethylene chloride (30 ml.) and anhydrous stannic chloride (3.3 ml.) were added to the cold acid chloride. This mixture was allowed to stand in the ice-bath for 6 hours and finally at room temperature for two days. The solution was treated with water and the organic product extracted with ether. The ether solution was washed with dilute potassium hydroxide solution, dried and the solvents removed. The residual ketone was distilled to yield 4.6 g. (70%) of product which boiled at 128–131° (0.09 mm.).

This ketone (XI, 3.5 g.) was added to a cold solution of methylmagnesium iodide prepared from magnesium (0.36 g.), methyl iodide (2.3 g.) and dry ether (50 ml.). The reaction mixtures was refluxed for three hours and then decomposed with dilute acid. The crude product was dehydrated by refluxing with acetic anhydride (30 ml.) and acetyl chloride (15 ml.). The solvents were removed *in vacuo*, the residue taken up in ether and washed with sodium bicarbonate solution. The ether was removed and the product evaporatively distilled. The first fraction (2.01 g.) was collected at 125° (0.14 mm.); a portion (1.69 g.) of this material was reduced first by sodium (7 g.) and absolute ethanol (65 ml.) at reflux temperature and then with 10% palladium-on-charcoal and hydrogen (50 p.s.i.) to make sure that both the bromine atom and the double bond were completely removed. The reduction product was distilled to yield 495 mg. of a fraction which was collected at 70° (0.07 mm.). This material (XIII) was treated with succinic anhydride in nitrobenzene by the same procedure used for acid III. Acid XIV was obtained as a colorless product which melted at 158.5–160°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.61; H, 7.28.

The melting point of a mixture of this acid with acid III (m.p. 158.5–160°) was 140–153°. The ultraviolet spectrum of this acid was nearly identical with that of acid III; λ_{max}^{EtOH} 225 mμ (log ε, 4.16), 273 mμ (log ε 4.10).

Acid XIV (165 mg.) was further characterized by reducing the keto group by the Clemmensen procedure using amalgamated zinc (5. g.), toluene (4 ml.) and concentrated hydrochloric acid (7 ml.). The mixture was refluxed for 80 hours with addition of portions (1.5 ml.) of hydrochloric acid, at 15-hour intervals. The cold reaction mixture was extracted with benzene and the acidic product removed by washing the benzene extract with 10% potassium hydroxide solution. The alkaline solution was acidified and the product recrystallized from ethanol to yield 80 mg. of β-5-(8-methyl-1,2,3,4-tetrahydronaphthyl)-butyric acid melting at 86.5–89°.

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.46. Found: C, 73.28; H, 8.35.

γ-(4-Methoxy-3-methylphenyl)-butyric Acid (XV).—A mixture of amalgamated zinc (38 g.), water (23 ml.), concentrated hydrochloric acid (54 ml.), toluene (56 ml.), acetic acid (25 ml.) and β-(4-methoxy-3-methylbenzoyl)-propionic acid[18] (17 g.) was refluxed briskly for 48 hours, during which time four portions (10 ml.) of hydrochloric acid were added. The toluene layer was separated, and the aqueous layer extracted with ether. The combined organic layer was washed with water and the solvents removed. The residue was recrystallized from petroleum ether to yield 13.5 (85%) of acid XV which melted at 59.5–60.5°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.22; H, 7.75. Found: C, 69.11; H, 7.82.

3,4-Dihydro-7-methoxy-6-methyl-1(2H)-naphthalenone (XVI).—Acid XV (10 g.) was mixed with anhydrous hydrogen fluoride (100 ml.). After 24 hours most of the hydrogen fluoride had evaporated and the residue was treated with ice

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(16) D. M. Musser and H. Adkins, This Journal, **60**, 664 (1938).

(17) E. Alexander and A. C. Cope, *ibid.*, **66**, 886 (1944).

(18) K. W. Rosenmund and D. Shapiro, *Chem. Zentr.*, **105 I**, 3337 (1934).

and ether. The ether solution of the product was washed with sodium carbonate solution and concentrated. The crude residual product was evaporatively distilled at 125° (0.4 mm.) to yield 7.8 g. (85%) of crystalline ketone XVI which melted at 44–45°. The analytical sample, recrystallized from methanol–water, had the same melting point.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.50; H, 7.53.

Ketone XVI (1 g.) and sulfur (125 mg.) were heated for 75 minutes under nitrogen at 220°. The mixture was cooled and dissolved in benzene–ether and then this solution was washed with 15% potassium hydroxide solution. Acidification of the alkaline solution yielded the crude naphthol, 1-hydroxy-7-methoxy-6-methylnaphthalene, which was purified by chromatography on neutral alumina. Elution with 50:50 benzene–ethyl acetate removed a brownish oil (400 mg.) which gave a positive ferric chloride test (blue precipitate). This naphthol was methylated by heating with acetone (25 ml.), potassium carbonate (3 g.) and dimethyl sulfate (2 ml.) for 24 hours; during this time three additional portions (1 ml.) of dimethyl sulfate were added at equal intervals of time. The reaction mixture was poured into water and the product extracted with ether. The crude product remaining after evaporation of the ether was chromatographed on basic alumina using hexane as the solvent. The first fraction (63 mg.) crystallized and melted at 72.5–73.5°. The melting point of a mixture of this substance and II prepared by metalation of 1,7-dimethoxynaphthalene was 72–73°.

β-7-(6-Methoxy-1,2,3,4-tetrahydronaphthoyl)-propionic Acid (XVII).[19]—β-6-Methoxy-1,2,3,4-tetrahydronaphthalene (2 g.), prepared by the method of Stork,[20] was allowed to react with succinic anhydride (1.2 g.) and aluminum chloride (3.6 g.) in nitrobenzene (25 ml.) as in the preparation of acid III. The dark-brown product was recrystallized first from benzene–isopropyl alcohol and then from methanol to yield nearly colorless needles which melted at 178–179°.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.51; H, 7.06.

The ultraviolet spectrum of this acid was quite different, $\lambda_{\max}^{\mathrm{EtOH}}$ 258 mμ (log ε 4.23) and 318 mμ (log ε 3.86), from that of acids III and XIV.

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[19] This structure was assigned rather than the alternate possibility, β-5-(6-methoxy-1,2,3,4-tetrahydronaphthoyl)-propionic acid, because similar Friedel–Crafts reactions in nitrobenzene introduce the substituent into the least sterically hindered position even if there are some opposing electronic factors.

[20] G. Stork, THIS JOURNAL, **69**, 576 (1947).

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, THE FLORIDA STATE UNIVERSITY]

cis- and *trans-*Bicyclo[3.2.1]octanol-2[1]

BY A. A. YOUSSEF, M. E. BAUM AND H. M. WALBORSKY[2]

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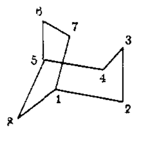
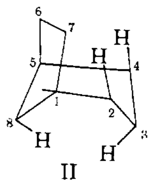
The synthesis and establishment of configuration of *cis-* and *trans-*bicyclo(3.2.1)octanol-2 is described. The rate of saponification of the acetates at 25° was found to be 1.05 × 10^{-3} l. mole^{-1} sec.$^{-1}$ for the *trans* isomer and 2.21 × 10^{-3} l. mole^{-1} sec.$^{-1}$ for the *cis* isomer. The saponification rate of the acetate of bicyclo(2.2.2)octanol-2 was found to be identical with that of *trans-*bicyclo(3.2.1)octyl-2 acetate. The reduction of bicyclo(3.2.1)octanone-2 by a variety of reducing agents to yield various ratios of *cis-* and *trans-*alcohols is described and the results are discussed.

Introduction

Previous syntheses[3] of bicyclo(3.2.1) octanol-2 have not been directed toward the procurement of the geometric isomers which were desired for further study. In contrast to bridged bicyclic systems such as bicyclo(2.2.1)heptane (norbornane) and bicyclo(2.2.2)octane where the six-membered ring is held rigidly in the boat conformation, the bicyclo(3.2.1)octane (I) system is unique in that it is composed of a six-membered ring which can exist in a chair conformation in which two *axial* carbon atoms (C-6 and C-7) are joined to form an ethylene bridge. Evidence which justifies looking upon this molecule as possessing a six-membered ring rather than a seven-membered (C-1 to C-7) can be found from the inspection of the carbonyl absorption in the infrared spectrum of bicyclo(3.2.1)octanone-2. The absorption occurs at 1715 cm.$^{-1}$ which is typical of a six-membered ring ketone.[4]



I



II

In substituted cyclohexanes a conversion of the ring can occur which transforms an *equatorial* bond into an *axial* bond and the molecule usually exists as an equilibrium mixture of these forms.[5] In the bicyclo(3.2.1)octane system this type of ring conversion is not possible because of the ethylene bridge at C-1 and C-5. The only ring conversion that is possible is a chair–boat interconversion by a flipping of the ring at C-2 and C-4. This type of conversion should be energetically unfavorable since in cyclohexane itself the boat conformation has been calculated to be less stable than the chair by 7–10 kcal.[6] In the bicyclo(3.2.1)octane system (I) the chair conformation should be more stable than the boat (II) by an amount greater than 7–10 kcal. since in the boat conformation there is also an eclipsing of the C-2 and C-4 hydrogen atoms with the C-6 and C-7 methylene groups. Therefore, one can describe this system as being essentially fixed in the chair conformation. On this basis it is possible to assign the *axial* (IIIa) conformation to the hydroxyl

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[1] *cis* and *trans* refers to the position of a substituent with respect to the *ethylene bridge*.

[2] To whom inquiries concerning this article should be sent.

[3] K. Alder and E. Windemuth, *Ber.*, **71**, 1939 (1938); M. S. Newman and Y. T. Yu, THIS JOURNAL, **74**, 507 (1952); K. Alder and Reubke, *Ber.*, **91**, 1526 (1958).

[4] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen Ltd., London, 1954.

[5] For excellent reviews on this subject see H. D. Orloff, *Chem. Revs.*, **54**, 347 (1954); W. Klyne, "Progress in Stereochemistry," Vol. I, Academic Press Inc., New York, N. Y., 1954.

[6] W. G. Dauben and K. S. Pitzer in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, 1956, p. 15.