of 0.013 mole of aromatic bromide (XXX, XXXIII, or 9-bromoanthracene), 6 g. of magnesium, 25 ml. of ether, 75 ml. of benzene, and a small crystal of iodine was stirred for 20 hr. at reflux temperature in an atmosphere of nitrogen. After removal of excess magnesium, the ether was removed by distillation and a solution of 0.013 mole of the aliphatic nitrile (octadecanonitrile or propionitrile) in 25 ml. of benzene was added. The resulting mixture was heated to reflux, with stirring, for 24 hr. and was then hydrolyzed with 70 ml. of 10% acetic acid. The organic layer was washed successively with 36% hydrochloric acid, water, 10% aqueous sodium carbonate, and water. Evaporation of the solvents left a residue which was dissolved in a mixture of petroleum ether (b.p. 60–70°) and benzene (2:1) and the solution then was poured onto a column (40 × 4.5 cm.) of alumina. Development of the resulting chromatogram was effected with a mixture of petroleum ether and benzene (3:1) and its progress was followed by visible coloration and ultraviolet fluorescence of bands. Elution of the column with mixtures of benzene and petroleum ether of increasing benzene concentration allowed the separation of crystalline products. Aromatic nitriles XXXI[40] and XXXIV,[40] 9-cyanoanthracene,[41] and diheptadecyl ketone[42] were isolated in yields already mentioned and were identified by the method of mixed melting points with authentic samples of these known compounds. Considerable quantities (up to 36%) of the aromatic hydrocarbons (anthracene, benz[a]anthracene and 12-methylbenz[a]anthracene) also were isolated but none of the expected ketones (XXXII or XXXV, for example).

LOS ANGELES, CALIF.

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[41] W. E. Bachmann and M. C. Kloetzel, *J. Org. Chem.*, **3**, 55 (1938).

[42] F. S. Kipping, *J. Chem. Soc.*, **57**, 532 (1890).

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH
PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE]

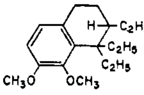
Studies in the Tetrahydronaphthalene Series: Synthesis of 1-Methyl-1-ethyl-2-*n*-propyl-7,8-dimethoxy-1,2,3,4-tetrahydronaphthalene

LEWIS J. SARGENT

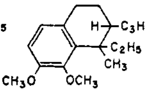
Received September 1, 1960

The synthesis of the above-titled naphthalene derivative is described.

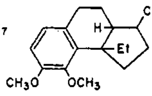
The degradation of dihydrothebaine to a novel nitrogen-free end product was reported from this laboratory, and four plausible structures (A–D)



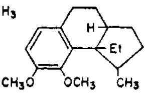
A



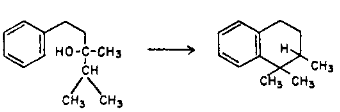
B



C



D



were proposed for the substance.[1] Because the analytical data, at the time, appeared to favor a tetralin system exemplified by structures A or B, attempts to synthesize these highly substituted species were initiated. It should be mentioned at the outset, however, that recent NMR studies[2] of the degradation product have necessitated altering our former views in favor of structures C or D. In the light of these new findings, we are prompted to report on the earlier synthetic approaches at this time. Experiments directed toward the synthesis of structures C and D, along with a detailed account of the NMR data, will form the body of a later communication.

Of the several possible routes to structures A or B that were considered, the first was patterned after the work of Bogert *et. al.*[3] who prepared 1,1,2-trimethyltetralin (II) through cyclodehydration of the pentanol (I). Regarding the present problem it is evident that, to arrive at structure A, for example, a logical intermediate would be 1-(3,4-dimethoxy-6-bromophenyl)-3,4-diethylpentanol-3, in which the halogen serves as a blocking group in order to direct the subsequent cyclization to the desired position on the aromatic ring. This involved synthesizing 1-(3,4-dimethoxy-6-bromophenyl)pentanone-3 and treating it with the Grignard reagent prepared from 3-bromopentane. The route to the pentanone originated with methyl homoveratrate[4] which was reduced to the corresponding phenethanol and the latter converted, in turn, *via* the chloride, iodide and nitrile to 3,4-dimethoxyhydrocinnamic acid. Bromination of the latter to the 6-bromo derivative (bromine position established) was followed by conversion to the acid chloride which, on treatment with diethylcadmium,[5] afforded the required pentanone in

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[1] L. J. Sargent and L. F. Small, *J. Org. Chem.*, **16**, 1031 (1951).

[2] We are indebted to Dr. E. D. Becker and Mr. R. B. Bradley, Laboratory of Physical Biology, NIAMD for these data.

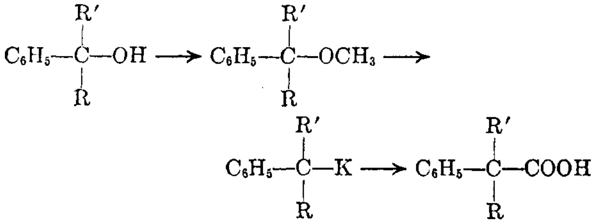
[3] D. Price, D. Davidson, and M. T. Bogert, *J. Org. Chem.*, **2**, 540 (1938).

[4] H. R. Snyder, J. S. Buck, and W. S. Ide, *Org. Syntheses*, Coll. Vol. II, 333 (1943).

[5](a) J. Cason, *Chem. Revs.* **40**, 15 (1947); (b) D. A. Shirley, *Org. Reactions*, **8**, 26 (1954).

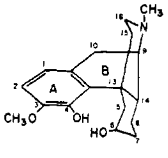
moderate yield. When this ketone was treated at 10–15° with 3-amylmagnesium bromide very little reaction occurred and 90% of the original ketone could be recovered. Repetition under forcing conditions (twenty-four hour reflux) gave an unpromising mixture consisting of ketone, carbinol, and olefin. Since Conant and Blatt[6] have shown that the reaction of secondary Grignard reagents with highly branched ketones frequently leads to reduction as well as to enolization of the ketone, this route became less attractive and was abandoned.

Two other approaches which likewise proved abortive are briefly: (a) the proposed Grignard reaction of 3,4-dimethoxy-6-chloro-phenethylmagnesium bromide with 4-ethylhexamone-3 to the desired 1-(3,4-dimethoxyy-chlorophenyl)-3,4-diethylpentanol-3. In view of the reported selective preparation of monohalomagnesium derivatives from certain dihalogen compounds,[7] it was thought feasible to convert selectively 3,4-dimethoxy-6-chlorophenethylbromide into 3,4-dimethoxy-6-chloro phenethylmagnesium bromide. Unfortunately, owing probably to the activating (electron donating) influence of the *p*-methoxyl group, the aryl chlorine appeared to react appreciably with magnesium (*i.e.*, one equivalent of magnesium turnings was consumed before all of the dihalogen derivative had been added). The resulting mixed Grignard reagent clearly was unsuited for further use. (b) Another method aimed at building up the requisite ring system (from a different direction) centered about the synthesis of α,α-diethylphenylacetic acid according to the methods developed by Conant[8] and Gilman[9] in their preparation of certain, less highly substituted congeners, *e.g.*,

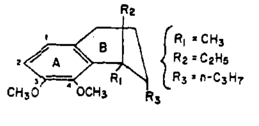


$$C_6H_5-\underset{R}{\overset{R'}{C}}-OH \longrightarrow C_6H_5-\underset{R}{\overset{R'}{C}}-OCH_3 \longrightarrow$$
$$C_6H_5-\underset{R}{\overset{R'}{C}}-K \longrightarrow C_6H_5-\underset{R}{\overset{R'}{C}}-COOH$$

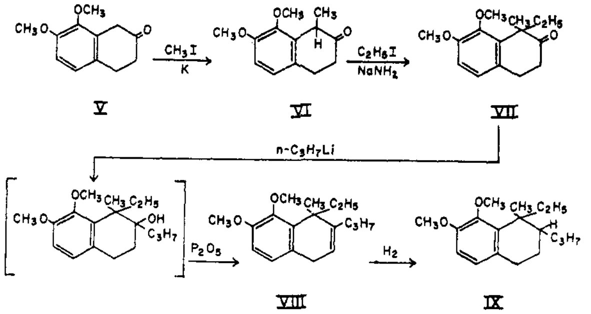
It was planned to build up the appropriate chain from the tertiary carboxylic acid by known techniques and cyclize the resulting aryl butyric acid to the dimethoxytrialkylated tetralone which could subsequently be reduced to the required tetralin by standard means. The required α,α-diethyl veratryl methyl ether was prepared without difficulty. However, when this substance was treated with sodium-potassium alloy[10] and the product carbonated with carbon dioxide, only a small amount (< 8%) of bicarbonate soluble (and partially demethylated) material was obtained. The bulk of the product consisted of neutral phenolics, probably arising through *O*-demethylation by the alloy. Cleavage of aryl ethers by alkali metals is not without precedent and has been observed by Gilman, *et al.*[11,12]



III



IV



The series of reactions that ultimately led to one of the desired isomers (B) was patterned after the work of Soffer[13] and Grob.[14]

Specifically, 7,8-dimethoxy-3,4-dihydro-2-(1 H)-naphthalenone (V) was initially C-methylated at position-1 using powdered potassium metal and methyl iodide in benzene according to Grob's[14] technique. It was also possible to obtain predominantly monoethylation of the tetralone by way of sodium ethoxide and ethyl iodide following a modification of Grob's[14] procedure which was based on earlier work of Cornforth and Robinson.[15] In the latter instance, however, in addition to some unchanged starting tetralone derivative, a small amount of higher boiling material was obtained which presumably was dialkylated product.

The introduction of the second alkyl (ethyl) group at C_1 (in VI) was achieved by means of ethyl iodide and sodamide in benzene solution. That the second alkyl group had, in fact, entered

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(6) J. B. Conant and A. H. Blatt, *J. Am. Chem. Soc.*, **51**, 1227 (1929).

(7)(a) R. C. Fuson, *Advanced Organic Chemistry*, John Wiley & Sons, Inc., New York, N. Y., 1951, p. 131. (b) J. von Braun, G. Irmisch, and J. Nelles, *Ber.*, 66B, 1471 (1933).

(8) J. B. Conant and G. H. Carlson, *J. Am. Chem. Soc.*, **54**, 4055 (1932).

(9) H. Gilman and R. V. Young, *J. Org. Chem.*, **1**, 315 (1936).

(10) We are indebted to the Inorganic and Physical Chemistry Section, Naval Research Laboratory, Washington, D. C., for samples of the alloy.

(11) H. Gilman, E. A. Zoellner, and W. M. Selby, *J. Am. Chem. Soc.*, **55**, 1252 (1933).

(12) D. F. Pollart, *Dissertation Abstracts*, **17**, 242 (1957).

(13) M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson, and E. A. Bowler, *J. Am. Chem. Soc.*, **72**, 3704 (1950); M. D. Soffer, U. S. Patent **2,644,836**, July 7, 1953.

(14) C. A. Grob and W. Jundt, *Helv. Chim. Acta*, **31**, 1691 (1948).

(15) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, **676** (1946).

position 1 was demonstrated by the preparation of a *benzal* derivative—evidence that position 3 was unsubstituted. Because subsequent reaction of VII with *n*-propyllithium was attended by partial *O*-demethylation,[11] it was necessary to remethylate the crude product (methyl sulfate) before proceeding further. This afforded a mixture of the expected carbinol and the corresponding olefin, doubtlessly formed through spontaneous dehydration during the reaction work-up. It may be noted that the introduction of the *n*-propyl group at position 2 (in VII) involves the creation of a new asymmetric center adjacent to an existing one. If one invokes Cram's rule of sterically controlled asymmetric induction[16] in this instance, it is plausible to assume that the *n*-propyl group enters *trans* to the bulkier ethyl group at C_1, concordant with the geometry suggested for this system (IV) by Ginsburg's conformational representation of the morphine congener dihydrothebainol (III).[17] Further treatment of the carbinol-olefin mixture with phosphorus pentoxide in benzene yielded essentially pure olefin (VIII) which was catalytically hydrogenated to *dl* B (IX).

EXPERIMENTAL[18]

3,4-Dimethoxyphenethyl alcohol. Methyl homoveratrate,[4] 75 g. (0.36 mole) in 300 ml. of anhydrous ether was added during 2 hr. (stirring) to 200 ml. of 1.8*M* ethereal lithium aluminum hydride diluted with 500 ml. of anhydrous ether. After being stirred 0.5 hr. longer, the system was cooled in ice, excess reagent decomposed with water and the mixture acidified (Congo) with 2*N* sulfuric acid. The crude sirup obtained from the concentrated ether solution was refluxed 1 hr. with 350 ml. of 2*N* ethanolic sodium hydroxide (to remove any unchanged ester). Water (200 ml.) was added, the ethanol removed (*in vacuo*) and the oily product was taken up in ether. The latter was washed with saturated sodium chloride solution, then dried. Fractional distillation of the resulting oil yielded 52 g. (80%) of carbinol, b.p. 131–136°/0.6 mm. A specimen, evaporatively distilled at 125°/0.5 mm., showed the m.p. 48.5–50°. Prepared by another method, this substance was reported to melt at 47–48°.[19]

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.9; H, 7.74. Found: C, 65.9; H, 7.81.

The *3,5-dinitrobenzoate*, bright yellow prisms (from acetone-methanol), m.p. 153–154.5°.

Anal. Calcd. for $C_{17}H_{16}N_2O_8$: C, 54.2; H, 4.29. Found: C, 54.3; H, 4.41.

1-(2-Chloroethyl)-3,4-dimethoxybenzene. Thionyl chloride (31 ml., 0.44 mole) was gradually added during 40 min. (with stirring and ice-cooling) to a solution of 52 g. (0.286 mole) of the above carbinol and 55 ml. (0.44 mole) of dimethylaniline in 175 ml. of chloroform. After being stirred and cooled 0.75 hr. longer, the system was heated (steam) for 20 min., cooled, acidified with 2*N* hydrochloric acid, and extracted with ether which, after the usual treatment, yielded an oil that was fractionally distilled; yield 48 g. (84%), b.p. 106–109°/0.6 mm., m.p. 42–44°.

Anal. Calcd. for $C_{10}H_{13}ClO_2$: C, 59.8; H, 6.53. Found: C, 59.9; H, 6.45.

3,4-Dimethoxyhydrocinnamonitrile. A mixture of 57 g. (0.285 mole) of 1-(2-chloroethyl)-3,4-dimethoxybenzene with 107 g. (0.72 mole) of sodium iodide in 600 ml. of 95% ethanol was refluxed 24 hr. After collecting the sodium chloride and dilution of the filtrate with water (100 ml.), the ethanol was distilled (*in vacuo*). The product, in ether, was washed with dilute aqueous thiosulfate and dried. Fractionation gave 69 g. (82%) of the *2-iodoethyl* derivative, b.p. 138–142°/0.8 mm. A mixture of the latter with 36 g. of potassium cyanide, 75 ml. of water, and 750 ml. of ethanol was refluxed 17 hr. Removal of the ethanol (*in vacuo*) and the addition of 100 ml. of water yielded an oil which, in ether, was washed with water and dried. Fractional distillation afforded 39 g. (82%) of a colorless oil, b.p. 145–150°/0.8 mm.; slender prisms (from ether) m.p. 49–50.5°. Prepared by another method, the substance showed the m.p. 46.5°.[20]

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.1; H, 6.85. Found: C, 69.2; H, 6.75.

3,4-Dimethoxyhydrocinnamic acid. A mixture of 3,4-dimethoxyhydrocinnamonitrile (38 g.), 125 ml. of 25% methanolic potassium hydroxide, and 35 ml. of water was heated (reflux) 60 hr. Water (100 ml.) was added, methanol removed (*in vacuo*), and unchanged nitrile was extracted with ether. Acidification of the ice-cooled alkaline solution with concd. hydrochloric acid gave the colorless product which was collected, washed with water and air-dried—yield 35.8 g. (85%). A specimen was sublimed at 130°/0.5 mm., m.p. 99.5–101°.

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.71. Found: C, 63.0; H, 6.59.

3,4-Dimethoxy-6-bromohydrocinnamic acid. During 70 min., a cooled (15°) and stirred solution of 38 g. (0.18 mole) of 3,4-dimethoxyhydrocinnamic acid in 350 ml. of glacial acetic acid was treated with 9.5 ml. (0.186 mole) of bromine in the same solvent. After being stirred 20 min. longer, the system was poured into 3 l. of cold water and the product collected, washed with water and air-dried. Recrystallization from alcohol-free ether gave 46 g. (87%) of colorless bromo acid. A sample, sublimed at 135°/0.5 mm., showed m.p. 121–123°.

Anal. Calcd. for $C_{11}H_{13}BrO_4$: C, 45.7; H, 4.53; Br, 27.6. Found: C, 45.6; H, 4.69; Br, 27.3.

No depression was observed on mixture melting point with a sample prepared (*via* the carbinol, chloride, and nitrile as above) from 3,4-dimethoxy-6-bromophenylacetic acid.[21]

1-(3,4-Dimethoxy-6-bromophenyl)pentanone-3. Fifty grams (0.275 mole) of cadmium chloride (previously dried at 110°) was added during 30 min. to a stirred ice-cooled Grignard solution prepared from 13.9 g. (0.57 g.-atom) of magnesium and 57 g. (0.54 mole) of ethyl bromide in 500 ml. of ether. Most of the solvent was removed by distillation (steam bath). Dry benzene (150 ml.) was added and the distillation process repeated (stirring). Another 150-ml. portion of benzene was added and again distilled. The solid residue was covered with 200 ml. of dry benzene and treated during 1 hr. (stirring) with a solution of 40 g. (0.13 mole) of 5,4-dimethoxy-6-bromophenylacetyl chloride in 125 ml. of dry benzene, and heated (reflux) 1 hr. The product was poured onto cracked ice and acidified with 2*N* sulfuric acid. After washing the benzene layer with water, the solvent was removed and the oily residue was heated with 200 ml. of 7% ethanolic sodium hydroxide to saponify any ester formed. Ethanol was removed (*in vacuo*), the product taken up in ether and

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[16] D. J. Cram and F. D. Greene, *J. Am. Chem. Soc.*, **75**, 6005 (1953).

[17] D. Ginsburg, *J. Am. Chem. Soc.*, **78**, 3691 (1956).

[18] The author thanks Mr. H. G. McCann and his associates of the Analytical Services Unit of the Laboratory of Chemistry for the elemental analyses and the various spectra recorded. Melting points and boiling points are uncorrected.

[19] J. D. Fulton and R. Robinson, *J. Chem. Soc.*, 1463 (1933).

[20] W. Baker and R. Robinson, *J. Chem. Soc.*, 1424 (1925).

[21] L. F. Small and S. G. Turnbull, *J. Am. Chem. Soc.*, **59**, 1541 (1937).

washed with dilute salt solution. Following the usual manipulation there resulted 22.7 g. of a colorless oil, b.p. 163–167°/0.5 mm. In order to separate ketone from concurrently formed tertiary carbinol, the oil was heated 6 hr. with 13 g. of semicarbazide hydrochloride and 9.6 g. of fused sodium acetate in 145 ml. of 70% ethanol. About half of the ethanol was distilled (*in vacuo*) and the solution was diluted with 500 ml. of water. After standing overnight the colorless precipitate was collected and recrystallized (methanol) to yield 14.7 g. of semicarbazone. A specimen, after another crystallization, showed the m.p. 183–185°.

Anal. Calcd. for $C_{14}H_{20}BrN_3O_3$: C, 46.9; H, 5.63. Found: C, 47.1; H, 5.77.

A mixture of the semicarbazone (15.6 g.) and 38.5 g. of oxalic acid in 75 ml. of water was heated on the steam bath 0.75 hr. The cooled system was extracted with ether and the latter solution washed successively with 0.5*N* sodium hydroxide and water. The dried solution gave an oil which was distilled to yield 12 g. of ketone, b.p. 159–160°/0.5 mm., n_D^{25} 1.5512.

Anal. Calcd. for $C_{13}H_{17}BrO_3$: C, 51.8; H, 5.69. Found: C, 51.9; H, 5.55.

Methyl 3,4-dimethoxy-6-nitrophenyl acetate. Methyl homoveratrate,[4] 61 g. (0.29 mole) was added during 2 hr. (with stirring and ice-salt cooling) to 300 ml. of concd. nitric acid (70–71%), the internal temperature being kept at 0° throughout. After stirring 0.5 hr. longer (at 0°), the system was gradually allowed to warm to 15° and maintained at this point 0.75 hr. following which the mixture was poured on cracked ice. The crude product was collected, washed with water, pulverized, resuspended in water, filtered and air-dried—66 g. This was recrystallized portionwise from a mixture of ether-methanol (10 g./750 ml. of ether and 15 ml. of methanol), concentrating to incipient crystallization and cooling in ice to yield 36.5 g. (50%) of product, m.p. 109–111°. The analytical sample was recrystallized again, m.p. 114–115.5°.

Anal. Calcd. for $C_{11}H_{13}NO_6$: C, 51.8; H, 5.13. Found: C, 51.5; H, 5.04.

Hydrolysis of a specimen with 10% methanolic sodium hydroxide followed by acidification gave the nitro acid, m.p. 205–206° (lit.[22] m.p. 207–208°).

Methyl 3,4-dimethoxy-6-aminophenyl acetate hydrochloride. A solution of 13 g. (0.51 mole) of the immediately above nitro ester in 250 ml. of ethanol was shaken in hydrogen with 300 mg. of platinum oxide; reduction was complete in 2.5 hr. Concentration of the filtered solution (*in vacuo*) gave a sirup which was taken up in ether (350 ml.), cooled to 0° and treated with gaseous hydrogen chloride. The colorless salt was collected, resuspended in 250 ml. of fresh ether, filtered, and dried in a vacuum desiccator. The salt was recrystallized by dissolving it in 120 ml. of warm methanol and gradually adding 375 ml. of dry ether with stirring—yield 8.4 g. (60%) colorless needles, m.p. 169–171° (foams and resolidifies).

Anal. Calcd. for $C_{11}H_{16}ClNO_4$: C, 50.5; H, 6.16. Found: C, 50.3; H, 6.18.

5,6-Dimethoxyoxindole. In an attempt to isolate a specimen of the free base, a quantity of the salt in water was basified with a slight excess of 2*N* sodium carbonate. Within a few minutes a magma of colorless needles separated which proved to be acid-insoluble. Recrystallization from ether afforded colorless needles that sublimed readily at 170°/0.4 mm., m.p. 201–202°. The ready cyclization of *O*-aminophenylacetic acid derivatives to oxindoles is well known (lit.[22] m.p. 204–205°).

Anal. Calcd. for $C_{10}H_{11}NO_3$: C, 62.2; H, 5.74. Found: C, 61.9; H, 5.97.

Methyl 3,4-dimethoxy-6-chlorophenyl acetate. Using the technique described for the preparation of *o*-chlorotoluene,[23] 10 g. (0.383 mole) of the above 6-amino ester afforded a spontaneously crystallizing oil which was evaporatively distilled at 125–130°/0.35 mm., yield 7.4 g. (79%), colorless prisms m.p. 69–71°.

Anal. Calcd. for $C_{11}H_{13}ClO_4$: C, 54.0; H, 5.36. Found: C, 54.1; H, 5.38.

3,4-Dimethoxy-6-chlorophenethyl alcohol. A solution of 14 g. (0.057 mole) of the above 6-chloro ester in 200 ml. of dry ether was added during 1.5 hr. to 60 ml. of 1.5*M* lithium aluminum hydride diluted with 50 ml. of dry ether. After the usual processing the sirupy product (13.7 g.) was refluxed 1.5 hr. with 65 ml. of 5% ethanolic potassium hydroxide and the product isolated. Evaporative distillation at 115–120°/0.3 mm., yielded 10 g. (81%) of a thick oil which slowly crystallized, m.p. 63–65°.

Anal. Calcd. for $C_{10}H_{13}ClO_3$: C, 55.4; H, 6.05. Found: C, 55.6; H, 5.92.

The *3,5-dinitrobenzoate* crystallized in yellow needles (acetone), m.p. 173–175°.

Anal. Calcd. for $C_{17}H_{15}ClN_2O_8$: C, 49.7; H, 3.68. Found: C, 49.8; H, 3.78.

1-(2-Bromoethyl)-3,4-dimethoxy-6-chlorobenzene. Phosphorus tribromide, 2.7 ml. (0.028 mole) was added dropwise to a stirred and cooled (5°) solution of 7.3 g. (0.034 mole) of the above carbinol in 60 ml. of dry benzene containing 4 drops of pyridine. After being stirred at 5° 0.5 hr. and maintained at 25° 3 hr., the system was cooled in ice, diluted with 100 ml. of alcohol-free ether and treated with ice water. The organic layer was successively washed with water, 1.5*N* sodium hydroxide, saturated salt solution, dried, and concentrated (*in vacuo*). The product, which crystallized spontaneously, was triturated with 5 ml. of 60% methanol, dried, and sublimed at 100°/0.3 mm., yield 3.5 g. (37%), m.p. 77–78.5°.

Anal. Calcd. for $C_{10}H_{12}BrClO_2$: C, 42.9; H, 4.33. Found: C, 43.1; H, 4.19.

4-Ethylhexanone-3 semicarbazone. 4-Ethylhexanone-3 was prepared, in 45% yield, from diethylacetyl chloride and diethyl cadmium according to Cason's[5a] general procedure; colorless oil, b.p. 41–42°/10 mm. The *semicarbazone*, prepared in the usual way, crystallized in slender prisms (methanol-water), m.p. 160.5–162°.[24]

Anal. Calcd. for $C_9H_{19}N_3O$: C, 58.4; H, 10.3; N, 22.7. Found: C, 58.6; H, 10.3; N, 22.7.

3-(2,3-Dimethoxyphenyl)pentanol-3. Redistilled *o*-veratroyl chloride, 16 g. (0.08 mole), prepared from *o*-veratric acid and thionyl chloride, in 100 ml. of dry ether was added during 1 hr. to a stirred solution of 240 ml. of 0.93*M* ethylmagnesium bromide. After being stirred 1 hr. longer, the cooled system was poured into 500 ml. of ice-cold 2*N* acetic acid. The product, recovered from the washed (sodium bicarbonate) and dried ether solution, was distilled (*in vacuo*) to give 14 g. (80%) of a colorless oil, b.p. 100–102°/0.3 mm., n_D^{25} 1.5176.

Anal. Calcd. for $C_{13}H_{20}O_3$: C, 69.6; H, 8.99. Found: C, 69.7; H, 8.98.

3-(2,3-Dimethoxyphenyl) amyl methyl ether. A mixture of 31.2 g. (0.14 mole) of the above pentanol, 60 ml. of anhydrous methanol, and 1.9 ml. of concd. sulfuric acid was refluxed 8 hr. The cooled system was diluted with cold water (350 ml.) and the product extracted with ether. The latter, after the usual processing, gave an oil which was distilled, b.p. 97–101°/0.5 mm., 22.4 g. (68%). A sample was evaporatively distilled; n_D^{24} 1.5127.

Anal. Calcd. for $C_{14}H_{22}O_3$: C, 70.5; H, 9.31. Found: C, 70.6; H, 9.09.

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(22) G. Hahn and H. J. Schulz, *Ber.*, **72B**, 1308 (1939).

(23) C. S. Marvel and S. M. McElvain, *Org. Syntheses*, Coll. Vol. **I**, 170 (1941).

(24) The preparation of this ketone, in unspecified yield, has been reported [D. Bardon, *Bull. Soc. Chim.*, **49**, 1875 (1931)]. However, because of the paucity of experimental details given as well as the low melting point (50–51°) reported for the semicarbazone, one is inclined to the view that a pure sample of the ketone was not, in fact, obtained.

1-Methyl-3,4-dihydro-7,8-dimethoxy-2(1H)-naphthalenone VI. Potassium metal (0.46 g., 0.0118 g.-atom) was powdered under dry xylene (40 ml.) and the solvent replaced by 25 ml. of dry benzene. Operating in an atmosphere of dry nitrogen, 2.3 g. (0.011 mole) of V[13] was added and the magnetically stirred system refluxed 2 hr., then cooled. Methyl iodide (3.5 ml., 0.056 mole) was added dropwise and heating resumed for 5 hr. After keeping overnight the mixture was acidified with 2*N* sulfuric acid, extracted with ether, and the latter washed with saturated sodium bicarbonate solution. Concentration of the organic phase afforded a brown oil which was taken up in 20 ml. of ether and mechanically shaken with 30 ml. of saturated sodium bisulfite solution 20 hr. The aqueous layer was washed twice with 15-ml. portions of ether and the combined organic phases washed with water, dried, and concentrated. Evaporative distillation of the residue at 100–105°/0.35 mm. yielded 1.6 g. (64%) of a colorless oil, n_D^{20} 1.5466. Tetralone blue test-negative.[25]

The *semicarbazone,* crystallized as colorless prisms (methanol), m.p. 213–215°.

Anal. Calcd. for $C_{14}H_{19}N_3O_3$: C, 60.6; H, 6.91; N, 15.2. Found: C, 60.6; H, 6.94; N, 15.1.

1-Ethyl-3,4-dihydro-7,8-dimethoxy-2(1H)naphthalenone. The technique described by Grob,[14] for a related alkylation was modified as follows: To a magnetically stirred solution of 1 g. (0.0049 mole) of V in 15 ml. of absolute ethanol (under nitrogen), 1 ml. of sodium ethoxide solution [0.6 g. of sodium (0.27 g.-atom) in 15 ml. of absolute ethanol] was added followed by 1 ml. (0.0124 mole) of ethyl iodide. Five additional 1-ml. aliquots of sodium ethylate solution were subsequently added at 5 min. intervals. After the addition of another 0.3 ml. of ethyl iodide the system was stirred 1.5 hr. then refluxed 1 hr. longer. The cooled solution was treated successively with 1 ml. of glacial acetic acid, 3 drops of concd. hydrochloric acid, 30 ml. of water, and stirred 10 min. Ethanol was removed (*in vacuo*) and the product taken up in ether. The latter, after being washed with sodium bicarbonate solution, afforded 0.95 g. of a pale-orange oil a solution of which in 8 ml. of ether was mechanically shaken with 12 ml. of saturated sodium bisulfite solution 15 hr. The aqueous phase yielded 0.15 g. of unchanged tetralone. After washing the ether solution with water and drying, concentration (*in vacuo*) yielded a pale-yellow, air-sensitive oil which was evaporatively distilled twice at 95–100°/0.1 mm., 0.45 g. (41%), n_D^{20} 1.5416 (tetralone-blue test was negative).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.8; H, 7.74. Found: C, 72.0; H, 7.90.

A higher boiling fraction (0.19 g.) was collected at 105–110°/0.1 mm. The *semicarbazone* (of the main product) crystallized in short, thick prisms (methanol), m.p. 195–196°.

Anal. Calcd. for $C_{15}H_{21}N_3O_3$: C, 61.8; H, 7.27; N, 14.4. Found: C, 62.1; H, 7.39; H, 14.0.

The same *mono*ethyl derivative (n_D^{20} 1.5413) was obtained when V was alkylated according to Soffer's technique[13] using ethyl iodide and sodium hydride. The *semicarbazone* had the m.p. 194–195° and was not depressed when mixed with the corresponding derivative obtained immediately above.

1-Ethyl-1-methyl-3,4-dihydro-7,8-dimethoxy-2(1H)naphthalenone (VII). A solution of 1.55 g. (0.007 mole) of freshly distilled VI in 40 ml. of dry ether was magnetically stirred 6 hr. at 25° (under nitrogen) with 0.37 g. (0.0095 mole) of powdered sodamide. After removing the solvent in a stream of nitrogen 30 ml. of dry benzene was added, the stirred system treated with 2 ml. (0.0248 mole) of freshly distilled ethyl iodide and refluxed for 24 hr. Cold water and a slight excess of 2*N* sulfuric acid were added and the product extracted with ether. The latter solution was washed with dilute thiosulfate, water, then dried and concentrated (*in vacuo*). Two fractional, evaporative distillations of the product at 104–108°/0.2 mm. gave 1.3 g. (72%) of a pale yellow oil, n_D^{20} 1.5394, λ_{max} 280 mm. (ϵ 900).

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.6; H, 8.12. Found: C, 72.7; H, 8.14.

The *semicarbazone* crystallized in clusters of needles (acetone) m.p. 179–181°.

Anal. Calcd. for $C_{16}H_{23}N_3O_3$: C, 62.9; H, 7.59; N, 13.8. Found: C, 63.2; H, 7.64; N, 13.6.

The *benzal* derivative. A mixture of VII (0.2 g.), 0.55 ml. of 15% sodium hydroxide and 1.3 ml. of ethanol was treated with 0.15 ml. of freshly distilled benzaldehyde and the system kept at room temperature 9 days. Dilution with water precipitated an oil which was taken up in ether and the solution washed with water, dried, and concentrated (*in vacuo*); yield 0.23 g. pale yellow oil which was evaporatively distilled at 140–145°/0.35 mm., λ_{max} 347 (ϵ 13,100).

Anal. Calcd. for $C_{22}H_{24}O_3$: C, 78.5; H, 7.19. Found: C, 78.3; H, 6.83.

1-Ethyl-1-methyl-2-n-propyl-7,8-dimethoxy-1,4-dihydronaphthalene (VIII). A solution of 1.03 g. (0.0042 mole) of VII in 10 ml. of dry petroleum ether (b.p. 28–38°) was added during 2 min. to 17 ml. of magnetically stirred 0.74*N* *n*-propyllithium solution and the system refluxed 24 hr. (under helium). After decomposing excess reagent with ice water and acidification with dilute sulfuric acid, the product was taken up in ether, washed with saturated sodium bicarbonate solution, and dried. Evaporation of solvent (*in vacuo*) afforded an oil (0.9 g.) which gave a dark purple color (in ethanol solution) with aqueous ferric chloride. The latter oil (0.9 g.) in a solution of 30 ml. of 70% ethanol (containing 1.8 g. potassium hydroxide) was treated with 3.7 ml. of redistilled methyl sulfate and the system refluxed 5 hr. Excess methyl sulfate was decomposed by the addition of 5 g. of potassium hydroxide in 8 ml. of water and heating 30 min. longer. Most of the methanol was removed (*in vacuo*) and the product taken up in ether. After thorough washing with 2*N* sodium hydroxide and water, the dried solution yielded an amber sirup (0.75 g.—ferric chloride test virtually negative). Evaporative distillation at 98–105°/0.15 mm. gave 0.45 g. of a pale yellow oil whose solution in 15 ml. of dry benzene was magnetically stirred for 2 hr. with 0.4 g. of phosphorus pentoxide. The filtered solution was washed with dilute aqueous sodium bicarbonate, water, and dried. Removal of the solvent and evaporative distillation of the residue at 92–97°/0.12 mm. resulted in 0.32 g. of a pale yellow oil.

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.8; H, 9.55. Found: C, 78.7; H, 9.84.

1-Ethyl-1-methyl-2-n-propyl-7,8-dimethoxy-1,2,3,4-tetrahydronaphthalene (IX). When a solution of 0.15 g. of VIII in 8 ml. of glacial acetic acid was shaken in hydrogen with 25 mg. of platinum oxide, 1 mole of hydrogen was absorbed in 3 hr. After filtration and dilution with 20 ml. of water, the ice-cooled system was neutralized with powdered sodium bicarbonate and the product taken up in ether. The latter yielded a practically colorless oil which was evaporatively distilled at 87–91°/0.17 mm.—wt. 90 mg.

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.2; H, 10.2. Found: C, 78.3; H, 9.94.

BETHESDA 14, MD.

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[25] J. W. Cornforth, R. H. Cornforth, and R. Robinson, *J. Chem. Soc.,* 689 (1942).