hr. After removal of the thionyl chloride, the residue was dissolved in nitrobenzene (30 ml.) and aluminum chloride (12 g.) was added gradually at 20–25°. The mass turned dark then violet. After overnight stirring at room temperature, the reaction product was drowned in ice and hydrochloric acid and the nitrobenzene was steam distilled. The residue was removed by filtration and slurried with an excess of dilute sodium hydroxide solution to separate unreacted starting material. The alkali insoluble product was purified by vatting to yield 1.1 g. of crude material, m.p. 325–328°, which on crystallization from toluene (Darco) gave 1.0 g. of VIII as orange crystals; m.p. 330–332°.

Anal. Calcd. for $C_{20}H_9BrO_3$: C, 63.6; H, 2.4. Found: C, 63.4; H, 2.4.

The alkaline filtrate upon acidification with concentrated hydrochloric acid gave 1.9 g. of unreacted 2-(*o*-bromobenzoyl)naphtho[2,1-*b*]furan-1-carboxylic acid (VII); m.p. 174–176°.

A mixture of VIII with the bromo compound obtained from V (m.p. 330–332°) melted at 330–332°. The identity of the two bromo derivatives was further substantiated by comparison of the infrared spectra.

9-(p-Tolylsulfonamido)dinaphtho[2,1-2′,3′]furan-8,13-dione. A mixture of VIII (0.2 g.), *p*-toluenesulfonamide (0.14 g.), sodium carbonate (0.08 g.), cuprous chloride (0.01 g.) and nitrobenzene (15 ml.) was heated at 200° for 6 hr. The crude product was removed by filtration, washed and crystallized from acetic acid to yield bright yellow crystals (90% yield) of m.p. 286–288°.

Anal. Calcd. for $C_{27}H_{17}NO_5S$: C, 69.0; H, 3.6. Found: C, 69.3; H, 3.8.

The identity of this derivative of VIII with the *p*-toluenesulfonamide obtained from V was established by mixed m.p. determinations and infrared spectra. On the other hand, the mixed m.p. of the *p*-toluenesulfonamides of VIII and VI (m.p. 282–284°) showed a significant depression (mixed m.p. 253–260°).

Condensation of 1-naphthol with 2,3-dichloro-5-nitro-1,4-naphthoquinone. 8- and 11-Nitrodinaphtho[1,2-2′,3′]furan-7,12-diones (X and IX). 2,3-Dichloro-5-nitro-1,4-naphthoquinone of m.p. 175° (13.5 g.), prepared by the method of Fries,[8] was reacted with 1-naphthol (8.0 g.) in the manner described for the nitro isomers III and IV. The precipitate, after filtration and repeated extraction with boiling water, gave 11.5 g. of an orange product of m.p. 306–308°, which was a mixture of X and IX. Microscopic examination showed the presence of orange-yellow and pale yellow crystals.

Anal. Calcd. for $C_{20}H_9NO_5$: C, 70.0; H, 2.6; N, 4.1. Found: C, 70.1; H, 2.7; N, 4.0.

The above mixture of nitro isomers X and IX (5 g.) was stirred with concentrated sulfuric acid in the manner described for the mixture of nitro isomers III and IV. The insoluble material crystallized from *o*-dichlorobenzene yielded 2.6 g. of IX as bright orange crystals; m.p. 344–346°.

Anal. Calcd. for $C_{20}H_9NO_5$: C, 70.0; H, 2.6; N, 4.1. Found: C, 70.0; H, 2.7; N, 4.0.

The sulfuric acid filtrate, drowned slowly on ice, gave 2.1 g. of X as a red-brown precipitate; m.p. 314–322°. Crystallization from *o*-dichlorobenzene yielded yellow crystals (m.p. 320–324°) with little loss.

Anal. Calcd. for $C_{20}H_9NO_5$: C, 70.0; H, 2.6; N, 4.1. Found: C, 70.2; H, 2.7; N, 4.0.

8-Aminodinaphtho[1,2-2′,3′]furan-7,12-dione (XII). The amine XII, obtained from the nitro isomer X as described for the amine V, crystallized from nitrobenzene as red-brown crystals of m.p. 362–364°.

Anal. Calcd. for $C_{20}H_{11}NO_3$: C, 76.6; H, 3.5; N, 4.4. Found: C, 76.8; H, 3.3; N, 4.6.

The benzamide of XII crystallized from chlorobenzene as orange needles, m.p. 310–312°.

Anal. Calcd. for $C_{27}H_{15}NO_4$: C, 77.7; H, 3.6; N, 3.35. Found: C, 77.5; H, 3.3; N, 3.4.

11-Aminodinaphtho[1,2-2′,3′]furan-7,12-dione (XI). The amine XI, obtained from the nitro isomer IX, crystallized from nitrobenzene as violet-red crystals, m.p. 302–304°.

Anal. Calcd. for $C_{20}H_{11}NO_3$: C, 76.6; H, 3.5; N, 4.4. Found: C, 76.6; H, 3.3; N, 4.5.

The benzamide of XI crystallized from chlorobenzene as orange needles, m.p. 292–294°.

Anal. Calcd. for $C_{27}H_{15}NO_4$: N, 3.35. Found: N, 3.4.

Chromatographic separation of the 8- and 11-amino isomers (XII and XI). The mixture of the isomeric amines XII and XI (m.p. 294–298°), obtained from the mixture of the nitro isomers X and IX by reduction with alkaline sodium hydrosulfite, was chromatographed as described for the isomeric amines V and VI. The brownish-orange band gave XII (40% of the mixture) as dark red crystals, m.p. 362–364°, and the bright violet band gave XI (60%) as red crystals, m.p. 302–304°.

WILMINGTON, DEL.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, GEORGIA INSTITUTE OF TECHNOLOGY]

A New Synthetic Route to Methoxytetralones

J. W. HUFFMAN

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5-Methoxy-1-tetralone has been prepared from 8-chloro-5-methoxy-1-tetralone by preferential hydrogenolysis of the halogen atom. The chlorotetralone has also been converted to 5-chloro-8-methoxy-1-tetralone in low yield. The infrared and ultraviolet spectra of these compounds are discussed.

Although 5-methoxy-1-tetralone has been previously prepared, it, 8-methoxy-1-tetralone and their derivatives are relatively inaccessible, compared with the well known 6- and 7-methoxytetralones. 5-Methoxytetralone has been prepared from coumarin[1] in low yield by a six-step synthesis, and also by hydrogenation of substituted naphthalene derivatives,[2] followed by appropriate conversions. The preparation of 7-methoxytetralone from anisole *via* β-(4-methoxybenzoyl)propionic

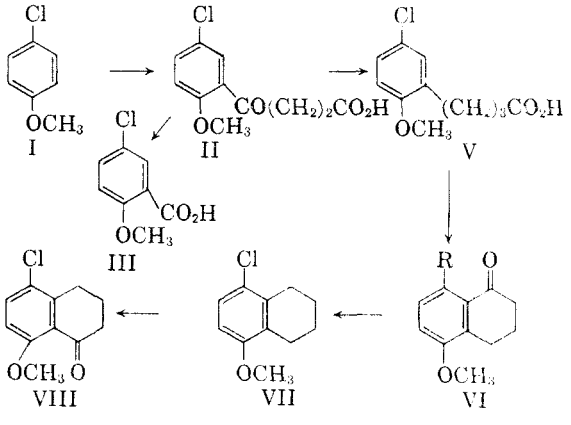
(1) J. Lockett and W. F. Short, *J. Chem. Soc.*, 787 (1939).

(2) (a) E. Hardegger, D. Redlich, and A. Gal, *Helv. Chim. Acta*, **27**, 628 (1944). (b) D. Papa and E. Schwenk, *J. Org. Chem.*, **14**, 366 (1949).

acid is well know,[3] and the preparation of 6-methoxy-1-tetralone in moderate yield has been reported.[4] Unfortunately all attempts at preparing 5- and 8-methoxytetralone by the direct succinoylation of an unsubstituted anisole ring afford as the final product, only 7-methoxy-1-tetralone. 5-Methoxy-8-methyl-1-tetralone has, however, been prepared from *p*-cresyl methyl ether,[5] and 5-methoxy-4,8-dimethyl-1-tetralone has been synthesized from the same starting material.[6]

The parent 5-methoxytetralone would appear to be readily available from some appropriately *para* substituted anisole derivative, containing an easily removable blocking group. Although the facile hydrogenolysis of halogen bound to an aromatic ring is well known,[7] and has been used in the preparation of tetracycline from aureomycin, without disturbing the sensitive ring system of these antibiotics,[8] this potentially useful blocking group has found little use in organic synthesis until this time. Haworth and Perkin attempted to use a bromine atom as a blocking group in order to accomplish the synthesis of a berberine alkaloid of the natural series rather than the *pseudo* alkaloid; however, this attempt led only to the extrusion of the bromine and cyclization to the *pseudo* berberine derivative.[9] An aromatic bromine has been reported to have been successfully employed in the Pschorr synthesis of a phenanthrene derivative,[10] while one failure of this blocking group in a similar synthesis has been observed.[11]

The present investigation is concerned with the use of chlorine as a blocking group in the synthesis of 5-methoxy-1-tetralone. Succinoylation of *p*-chloroanisole (I) with aluminum chloride in tetrachloroethane-nitrobenzene afforded β-(2-methoxy-5-chlorobenzoyl)propionic acid (II) in 51% yield.[12] In an effort to characterize this compound it was oxidized with alkaline permanganate to yield the known 2-methoxy-5-chlorobenzoic acid[13] (III); however, unexpected difficulties were encountered in identifying this material. Earlier workers had found the compound to melt at 79°; our substance had m.p. 97–98°, and the infrared spectrum in chloroform solution showed carbonyl absorption at 5.75 μ, and a sharp O—H stretching band at 3.00 μ. The expected spectrum for 2-methoxy-5-chlorobenzoic acid in chloroform solution would have a broad —OH band at 3.5 to 4.0 μ and a carbonyl band at 5.88 to 5.95 μ.[14] In spite of the anomalous spectrum, the compound was a strong acid, as evidenced by its solubility in aqueous bicarbonate solution, and analysis showed the correct empirical formula, $C_8H_7ClO_3$, for a chloromethoxybenzoic acid. Since 2-chloro-5-methoxybenzoic acid has m.p. 170°;[13] our oxidation product must be 2-methoxy-5-chlorobenzoic acid. It seems probable that the acid obtained by the Italian workers was a hydrate or polymorph, because recrystallization of the acid, m.p. 98°, from water gave material, m.p. 74–75°, which could in turn be recrystallized from cyclohexane to give the original melting point. Final confirmation of the structure of the



material came in the preparation of an authentic sample by the methylation of 2-hydroxy-5-chlorobenzoic acid.[15]

The anomalous infrared spectrum appears to be a general phenomenon of 2-methoxybenzoic acids. 2-Methoxybenzoic acid itself shows sharp O—H absorption at 2.96 μ, and carbonyl absorption at 5.76 μ, while *p*-anisic acid shows the usual broad band at 3.4–3.6 μ, and a strong carbonyl band at 5.93 μ. Yates has observed the same peculiarities in the infrared spectrum of a number of compounds of this type related to mangostin.[16] The sharp

(3) R. D. Haworth and G. Sheldrick, *J. Chem. Soc.*, 1951 (1934).

(4) (a) V. C. E. Burnop, G. H. Elliott, and R. P. Linstead, *J. Chem. Soc.*, 731 (1940). (b) G. Stork, *J. Am. Chem. Soc.*, 69, 576 (1947).

(5) R. B. Woodward and T. Singh, *J. Am. Chem. Soc.*, 72, 494 (1950).

(6) S. M. Bloom, *J. Am. Chem. Soc.*, 80, 6280 (1958).

(7) R. Baltzly and A. P. Phillips, *J. Am. Chem. Soc.*, 68, 261 (1946).

(8) (a) J. H. Boothe, J. Morton, J. P. Petisi, and R. G. Wilkinson, *J. Am. Chem. Soc.*, 75, 4621 (1953). (b) C. R. Stephens, L. H. Conover, R. Pasternak, F. A. Hochstein, P. P. Regna, F. J. Pilgrim, K. J. Brunings, and R. B. Woodward, *J. Am. Chem. Soc.*, 75, 4622 (1953).

(9) R. D. Haworth and W. H. Perkin, *J. Chem. Soc.*, 127, 1448 (1925).

(10) A. Girardet, *Helv. Chim. Acta*, 14, 573 (1931).

(11) E. E. Lewis and R. C. Elderfield, *J. Org. Chem.*, 5, 290 (1940).

(12) J. D. Reinheimer and J. C. Smith, *J. Org. Chem.*, 17, 1505 (1952) reported the preparation of this material; however, they failed to report analytical figures or to characterize the compound in any way. We were able to accomplish the acylation reaction using only nitrobenzene as a solvent; however, the yield and quality of the product were decidedly inferior.

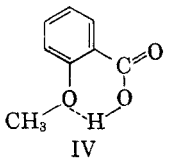
(13) A. Peratoner and G. B. Condorelli, *Gazz. chim. ital.*, 28 [I], 211 (1898).

(14) L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, Metheun, London (1954), pp. 140–150.

(15) The reaction of chlorosalicylic acid with dimethyl sulfate and base proceeded in low yield, and with some difficulty, as has been previously observed in the methylation of phenols bearing a carbonyl group *ortho* to the hydroxyl [ref. (5)].

(16) P. Yates, Private communication.

O—H band may be attributed to a tendency for the acid to internally hydrogen-bond (IV), rather than to exist as a dimer in dilute solution. The spectrum of *o*-methoxybenzoic acid in the solid state (nujol) indicates that under these conditions internal hydrogen bonding does not occur, for the infrared spectrum shows normal acid absorption peaks.



IV

Reduction of β-(2-methoxy-5-chlorobenzoyl)propionic acid under normal Clemmensen conditions gave a good yield of γ-(2-methoxy-5-chlorophenyl)-butyric acid (V). Cyclization of this acid to 5-methoxy-8-chloro-1-tetralone (VI. R = Cl) proceeded with some difficulty. Using polyphosphoric acid as the catalyst the tetralone could be obtained; however, 29% of the phenylbutryic acid was recovered, and the yield of cyclized product based on recovered acid never exceeded 42%. Classical aluminum chloride catalyzed cyclization of the acid chloride gave 21% recovery of (V), and 13% of tetralone of decidedly inferior quality to that obtained by the use of polyphosphoric acid.

The hydrogenolysis of the chlorotetralone proceeded extraordinarily smoothly, at atmospheric pressure, using 10% palladium-on-charcoal catalyst, with one equivalent of triethylamine added to neutralize the hydrogen chloride evolved. The dehalogenated tetralone (VI. R = H) was obtained in 56% yield after purification, and agreed well in its properties with those reported by earlier workers.[1]

An interesting comparison may be found in the ultraviolet spectra (Table I) of the chlorinated (VI. R = Cl), and dehalogenated tetralone (VI. R = H).

TABLE I

Compound	λ_{max}, mμ	log ε
5-Methoxy-8-chloro-1-tetralone	247	3.97
5-Methoxy-1-tetralone	257	4.10
1-Tetralone[a]	250	4.12
Benzophenone[b]	253	4.27
4-Chlorobenzophenone[c]	260	4.32
4,4′-Dichlorobenzophenone[c]	265	4.39

[a] G. D. Hedden and W. G. Brown, *J. Am. Chem. Soc.*, **75**, 3744 (1953). [b] R. N. Jones, *J. Am. Chem. Soc.*, **67**, 2141 (1945). [c] H. H. Szamant and C. McGinnis, *J. Am. Chem. Soc.*, **74**, 241 (1952).

Although the dehalogenated tetralone (VI. R = H) showed an ultraviolet spectrum very similar to that of 1-tetralone, there is a marked hypsochromic shift obtained by the addition of a halogen in the 8-position (−10 mμ). A study of the ultraviolet spectrum of benzophenone and substituted benzophenones (Table I) indicates that halogenation *para* to the carbonyl group results in a bathochromic shift of about 6 mμ for each halogen. On this basis one would predict from electronic considerations that the chlorotetralone (VI. R = Cl) would show ultraviolet absorption at about 263 mμ. Although a steric argument might be devised to explain these spectral anomalies, this does not seem too promising in the light of earlier work on the ultraviolet spectra of substituted benzaldehydes. It has been found that the only significant difference in the spectra of 2-methyl and 4-methyl benzaldehyde is in the intensity of the absorption.[17] This decrease in intensity may be attributed to a slight steric interaction between the carbonyl oxygen and the adjacent methyl group in 2-methylbenzaldehyde.[18] Since the chlorine atom in (VI) has a smaller Van der Waals' radius than a methyl group[19] (1.85 A as against 2.00 A); any steric effect must be smaller than that operative in the methyl benzaldehydes; however, the hypsochromic shift in the chlorotetralone is indicative of an effect of much greater magnitude. We would like to suggest that this hypsochromic shift of 10 mμ is caused by a dipole-dipole interaction between the halogen atom and the carbonyl group, resulting in either a slight out of plane twisting of the carbonyl group, or more probably, a simple electrical effect, which provides a greater ground to excited state energy barrier.[20]

It was felt that the smooth hydrogenolysis of the chlorine atom might provide an entry into the 8-methoxytetralone series *via* a three-step reaction sequence from VI (R = Cl). Reduction of VI under Clemmensen conditions afforded VII in mediocre yield as a yellow oil which decomposed slowly on standing. The oxidation of (VII) to (VIII) with chromic acid–acetic acid[21] gave erratic results, and generally low yields of impure product. The reaction product showed a maximum in the ultraviolet at 256 mμ and gave a 2,4-dinitrophenylhydrazone which had analytical data consistent

(17) E. A. Braude, F. Sondheimer, and W. F. Forbes, *Nature*, **173**, 117 (1954).

(18) The analogous methyl acetophenones have also been studied [ref. (17)] and although they give evidence of considerable steric hindrance between *ortho* methyl groups and the acetyl groups, this is explained by a methyl-methyl interaction. The only interaction possible on the chlorotetralone (VI, R = Cl) is, of course, a chlorine oxygen steric effect.

(19) W. Klyne, *Progress in Stereochemistry*, Butterworths, London, 1954, p. 365.

(20) J. H. Boothe, S. Kushner, J. Petisi, and J. H. Williams, *J. Am. Chem. Soc.*, **75**, 3261 (1953), have observed a similar, but previously unexplained effect in 2-carbomethoxy-6-chloro-3-methoxyacetophenone and the corresponding unhalogenated compound. This hypsochromic shift of 15 mμ is probably due to a dipole-dipole interaction, as is the 5 mμ hypsochromic shift in the ultraviolet spectra of equatorially substituted 2-bromocyclohexanones, R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

(21) J. C. Bardhan and D. N. Mukherjee, *J. Chem. Soc.*, 4629 (1956).

with the derivative of (VIII). It seems likely that the product is contaminated with unoxidized tetralin, (VII). In view of these difficulties this route to 8-methoxytetralone was abandoned; however, the use of aromatically bound chlorine atoms remains a potentially useful means of blocking a reactive position on the aromatic nucleus, in electrophilic aromatic substitution reactions.

EXPERIMENTAL[22]

β-(2-Methoxy-5-chlorobenzoyl)propionic acid. To a chilled mixture of 20 g. of *p*-chloroanisole and 16 g. of succinic anhydride in 200 ml. of a one-to-one mixture of *sym*-tetrachloroethane and nitrobenzene was added in portions 42.4 g. of aluminum chloride. The reaction mixture was allowed to stand in the cold for 7 days, then poured onto a mixture of ice and concentrated hydrochloric acid. The solvents were removed by steam distillation, and the resulting aqueous suspension of the product was made alkaline with 10% sodium bicarbonate, treated with decolorizing carbon, and filtered through celite. Acidification and cooling gave cream-colored crystals, which on recrystallization from cyclohexane–ethyl acetate afforded 16.2 g. (51%) of pale cream crystals, m.p. 114–116°. Further recrystallization from the same solvent pair gave crystals m.p. 118–119°.[12]

Anal. Calcd. for $C_{11}H_{11}ClO_4$: C, 54.44; H, 4.57; Cl, 14.61. Found: C, 54.63; H, 4.50; Cl, 14.59.

2-Methoxy-5-chlorobenzoic acid. (a) To a solution of 1.0 g. of β-(2-methoxy-5-chlorobenzoyl)propionic acid in 80 ml. of 1% potassium hydroxide was added 4 g. of potassium permanganate. The solution was heated under reflux 2 hr., acidified with dilute sulfuric acid and heated on the steam bath 30 min. On cooling the product crystallized out. Recrystallization from ethyl acetate–cyclohexane gave 0.22 g. (29%) of white needles, m.p. 92–95°. Recrystallization of this material from water gave fluffy white needles m.p. 74–75°.[13] Recrystallization of the lower melting form of this compound from cyclohexane ethyl acetate afforded material m.p. 97–98°.

Anal. Calcd. for $C_8H_7ClO_3$: C, 51.42; H, 3.79; Cl, 19.00. Found: C, 51.08; H, 4.11; C, 18.88.

(b) 2-Hydroxy-5-chlorobenzoic acid[23] was treated with dimethyl sulfate in base to give a 31% yield of crystals, m.p. and mixed m.p. 97–98°.

γ-(2-Methoxy-5-chlorophenyl)-butyric acid. The chloromethoxybenzoyl propionic acid was reduced under the usual conditions of the Clemmensen reduction.[24] From 18.0 g. of starting material 14.6 g. (86%) of white crystals, m.p. 78–80° were obtained. This material was sufficiently pure for cyclization to the tetralone. A sample was purified for analysis by distillation at 155–165° (air bath) and 1 mm., and recrystallization from hexane to give material m.p. 80–81°.

Anal. Calcd. for $C_{11}H_{13}ClO_3$: C, 57.77; H, 5.73. Found: C, 57.62; H, 5.51.

5-Methoxy-8-chloro-1-tetralone (8-chloro-5-methoxy-3,4-dihydronaphthalene-1(2)-one). (a) A mixture of 10 g. of γ-(2-methoxy-5-chloro)butyric acid and 125 g. of polyphosphoric acid[25] were heated on the steam bath 1.5 hr. with occasional stirring. The reaction mixture was cooled, poured into ice water, and extracted twice with ether. The ethereal extracts were combined, washed with water, and extracted with 10% sodium carbonate solution. Acidification of the basic extract afforded 2.89 g. (29%) of a brown powder with an infrared spectrum identical to the chloromethoxyphenylbutyric acid. The ethereal phase of the extract was washed again with water, dried, and the solvent removed *in vacuo* to give 3.40 g. of brown oil which partially solidified. Recrystallization from hexane afforded 2.73 g. (42% based on recovered acid) of pale yellow solid, m.p. 42–45°. Distillation of 150–160° (air bath) and 1 mm., followed by recrystallization from hexane gave small white needles, m.p. 47–48°.

Anal. Calcd. for $C_{11}H_{11}ClO_2$: C, 62.71; H, 5.26. Found: C, 62.38; H, 5.44.

The 2,4-dinitrophenylhydrazone formed orange crystals from ethyl acetate m.p. 226–228°.

Anal. Calcd. for $C_{17}H_{15}ClN_4O_5$: C, 52.25; H, 3.87; N, 14.34. Found: C, 52.23; H, 3.80; N, 14.61.

(b) To a solution of 1.0 g. of the γ-phenylbutyric acid in 30 ml. of dry benzene was added 1.44 g. of phosphorus pentachloride. The mixture was heated under reflux 3 hr., cooled to 0°, and 1.0 g. of aluminum chloride added. The cyclization mixture was allowed to warm to room temperature, heated under reflux 45 min., cooled, and poured into iced concentrated hydrochloric acid. The acid layer was drawn off, and extracted with ether. The organic phases were combined and washed with 5% sodium hydroxide. Acidification of the basic washings gave 0.21 g. (21%) of the starting acid. After drying and removal of the ether, 0.13 g. of neutral brown oil with an infrared spectrum virtually identical to the material obtained with polyphosphoric acid was obtained. The 2,4-dinitrophenylhydrazone formed crystals from ethyl acetate, m.p. 222–225°, undepressed on mixing with a sample prepared by the alternate route.

5-Methoxy-1-tetralone (5-methoxy-3,4-dihydronaphthalene-1(2)-one). To a solution of 0.41 g. of chloromethoxytetralone in 15 ml. of 95% ethanol was added 0.05 g. of 10% palladized charcoal, and 0.28 ml. of triethylamine. The reaction mixture absorbed 1.06 moles of hydrogen at room temperature and atmospheric pressure in 15 min., whereupon the rate of hydrogen uptake virtually ceased. The reaction mixture was filtered through celite, concentrated to a small volume, taken up in ether, and washed with successive portions of water and 5% hydrochloric acid. After drying and removal of the solvent a colorless oil which readily crystallized was obtained. Recrystallization from hexane afforded 0.18 g. (53%) of white needles m.p. 81–84°. A second recrystallization gave material m.p. 85–87°. Lockett and Short[1] gave a m.p. of 89° for this compound. The 2,4-dinitrophenylhydrazone formed beautiful deep red crystals from ethyl acetate, m.p. 227–228°.

Anal. Calcd. for $C_{17}H_{16}N_4O_5$: C, 57.30; H, 4.53; N, 15.72. Found: C, 57.08; H, 4.76; N, 15.95.

4-Chloro-1-methoxy-5,6,7,8-tetrahydronaphthalene. To a suspension of 5 g. of zinc amalgam in a mixture of 24 ml. of concentrated hydrochloric acid and 12 ml. of water was added a solution of 2.0 g. of chloromethoxytetralone in 12 ml. of ethanol. The reaction was heated under reflux 13 hr. With 5-ml. portions of concentrated acid being added at three-hour intervals. The yellow solution was decanted from the undissolved metals, extracted with 2 portions of ether, and washed with water. After drying and removal of the solvent a yellow oil remained which was covered with 20 ml. and 10% sodium hydroxide and 2.0 ml. of dimethyl sulfate and heated 30 min. on the steam bath. The basic solution was cooled, extracted twice with ether, washed with 5% hydrochloric acid, 5% sodium carbonate, and water.

After drying and removal of the solvent a yellow-brown

(22) Melting points were determined on a Fisher-Johns block, and are uncorrected. Infrared spectra were carried out in chloroform solution, or as liquid films on a Perkin-Elmer model 137 spectrophotometer, and ultraviolet spectra were determined in 95% ethanol on a Beckman model DK-1 recording spectrophotometer. Analyses performed by Galbraith Laboratories, Knoxville, Tenn.

(23) A. Leulier and L. Pinet, *Bull. soc. chim.*, [4], **41**, 1363 (1927).

(24) E. L. Martin, *J. Am. Chem. Soc.*, **58**, 1438 (1936).

(25) We would like to thank the Victor Chemical Works, Chicago, Ill., for a generous sample of this material.

oil was obtained, which distilled to give 0.66 g. (35%) of unstable pale yellow liquid, b.p. 125–135° (air bath) at 1 mm.

Anal.[21] Calcd. for $C_{11}H_{13}ClO$: C, 67.17; H, 6.66. Found: C, 65.93; H, 6.72.

8-Methoxy-5-chloro-1-tetralone (5-chloro-8-methoxy-3,4-dihydronaphthalene-1(2)-one. To a cold solution of 0.20 g. of chloromethoxytetralin in 3.0 ml. of acetic acid was added slowly 0.15 g. of chromic acid in 1 ml. of water and 2 ml. of acetic acid. The mixture was allowed to warm to room temperature, and stand overnight. The green solution was poured into water, extracted twice with ether, washed well with water, and then 10% sodium carbonate. The ethereal solution was dried, and the solvent removed at reduced pressure to give 0.1 g. of yellow oil which showed infrared absorption at 5.94 μ gave on treatment with 2,4-dinitrophenylhydrazine a small amount of derivative, m.p. 245–250° (dec.). The dinitrophenylhydrazone was purified by recrystallization from a relatively large volume of ethyl acetate to give small, very dark red crystals, m.p. 250–252° (dec.).

Anal. Calcd. for $C_{17}H_{15}ClN_4O_5$: C, 52.25; H, 3.87; N, 14.34. Found: C, 52.06; H, 4.01; N, 14.54.

ATLANTA, GA.

[CONTRIBUTION FROM THE WARNER-LAMBERT RESEARCH INSTITUTE]

Substituted 1,4-Dioxanes

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A number of substituted 1,4-dioxanes were prepared as part of a search for central nervous system depressants. Hydroxylation of 2-allyl-1,4-dioxane gave 2-(2-hydroxypropyl)- and 2-(2,3-dihydroxypropyl)-1,4-dioxane. 2,2-Dialkyl-1,4-dioxanes were prepared by cyclization of 2-(2-chloroethoxy)-1,1-dialkylethanols. Cyclization of methallyloxyethanol gave 2,2-dimethyl-1,4-dioxane. Three bis(hydroxyalkyl) ethers were also prepared.

Central nervous system depressants have been found among the dioxolanes and among glyceryl ethers.[1] Both these groups of compounds have in common α,β-dioxygen functions. In unreported work which was carried out in these laboratories some years ago, it was found that 2-hydroxymethyl-1,4-benzodioxane also exerts a depressing effect on the central nervous system. We thought it would be in order to explore the pharmacological effect of some 1,4-dioxane compounds as possible central nervous system depressants.

2-Allyl-1,4-dioxane[2] was monohydroxylated to give 2-(2-hydroxypropyl)-1,4-dioxane. The hydroxylation was accomplished using 75% sulfuric acid after finding that 50% sulfuric acid had negligible effect and 100% sulfuric acid gave tars.

The 2-allyl-1,4-dioxane was dihydroxylated according to the hydroxylation procedure of Swern *et al.*,[3] using performic acid to give 2-(2,3-dihydroxypropyl)-1,4-dioxane.

The 2-allyl-1,4-dioxane has greater central nervous system depression activity than either of its hydroxylated derivatives or than dioxane itself.

We next turned to the preparation of some 2,2-disubstituted dioxanes. A survey of the literature showed that no compounds of this type had been reported, and we thought that a quaternary carbon in such structures might enhance central nervous system depression. To this end, methyl β-chloroethoxyacetate[4] was prepared from β-chloroethoxyacetonitrile which was obtained by the action of cuprous cyanide on β-chloroethyl chloromethyl ether. Reaction of this material with ethylmagnesium bromide gave 2-(2-chloroethoxy)-1,1-diethylethanol which was cyclized to 2,2-diethyl-1,4-dioxane (I). The cyclizing agent was sodium ethylate. In a similar manner 2-(2-chloroethoxy)-1,1-dibutylethanol was prepared and cyclized to 2,2-dibutyl-1,4-dioxane (II) using sodium amide. When phenylmagnesium bromide in large excess was allowed to react with methyl chloroethoxyacetate there was obtained 1,1-diphenylethylene glycol. This compound probably resulted from the action of the excess phenylmagnesium bromide as a base, on the expected 2-(2-chloroethoxy)-1,1-diphenylethanol to give the glycol directly or *via* the intermediate 2-(vinyloxy)-1,1-diphenylethanol. Hydrolysis of this vinyl ether would furnish the 1,1-diphenylethylene glycol. When a more nearly theoretical amount of phenylmagnesium bromide was used in the reaction, the desired product, 2-(2-chloroethoxy)-1,1-diphenylethanol, was obtained. There was also ob-

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