Experimental[8]

Acylation of Cycloheptene.—Using 0.5 mole of cycloheptene,[9] 0.5 mole of acetyl chloride, 1.0 mole of granular aluminum chloride, and 100 ml. of cyclohexane as solvent, the acetylation was carried out essentially according to the procedure of Nenitzescu and Cioranescu.[1] In the final distillation of the product (A) there was obtained 28.3 g. (40%, based on olefin) of ketone, b.p. 65–66° at 7 mm., $n^{18}D$ 1.4518.

Product (A) readily formed a semicarbazone, white plates from diluted ethanol, m.p. 169–170°. *Anal.* Calcd. for $C_{10}H_{19}N_3O$: C, 60.89; H, 9.71. Found: C, 61.16; H, 9.53.

A crystalline 2,4-dinitrophenylhydrazone also was formed, m.p. 115–120°.

The oxidation of 5.5 g. of ketone (A) with a sodium hypobromite solution prepared from 24 g. of bromine and 15.2 g. of sodium hydroxide in 140 cc. of water gave a 92% yield of saturated acids, b.p. 121–123° (7 mm.). The acids readily formed an amide (or mixture of amides), white needles from water, m.p. 168–170° (lit. value[10] for the amide of cycloheptanecarboxylic acid, 194–195°).

Preparation of Methyl Cycloheptyl Ketone (I).—An authentic sample of this material was prepared from cycloheptyl bromide in 38% yield by the method of Newman and Booth,[4] and its structure proved by conversion to the acetate ester with perbenzoic acid and saponification to the known product, cycloheptanol.

The ketone was used to prepare a semicarbazone, white plates from 50% ethanol, m.p. 175–176°. *Anal.* Calcd. for $C_{10}H_{19}N_3O$: C, 60.89; H, 9.71. Found: C, 61.01; H, 9.65.

A 2,4-dinitrophenylhydrazone was also prepared, orange-yellow needles from ethanol, m.p. 117–118°. *Anal.* Calcd. for $C_{15}H_{20}N_4O_4$: C, 56.24; H, 6.29. Found: C, 56.50; H, 6.26.

These derivatives caused depression of the melting points when mixed with the corresponding derivatives of (A).

Reaction of (A) with Perbenzoic Acid.—Using known[5] procedures, a mixture of 7.4 g. (0.053 mole) of (A) and 150 ml. of a chloroform solution containing 0.057 mole of perbenzoic acid was allowed to react at room temperature for three days, and the ester product isolated.

The crude ester was saponified with 25% aqueous sodium hydroxide, the alcohol fraction separated by ether extraction, and the ether solution dried and evaporated. The crude alcohol was oxidized directly.

Oxidation of the Alcohol.—The alcohol obtained above was added in small portions with vigorous shaking to a solution of 8.4 g. of sodium dichromate and 7.0 g. of concentrated sulfuric acid in 42 ml. of water. The temperature rose to about 60°. After all the alcohol had been added, the flask was stoppered and shaken mechanically for two hours. The organic material was removed by ether extraction, and the ether solution washed with 5% sodium hydroxide until the washings were nearly colorless. The ether was evaporated, and the ketones converted directly to a 2,4-dinitrophenylhydrazone mixture, m.p. 110–126°.

Preliminary purification of this derivative was effected by passage through a column of alumina in 1:1 (by volume) benzene–hexane solvent, with a recovery of 95% of crystalline material. Fractional crystallization from 95% ethanol gave a small yield of pure (VI), m.p. and mixed m.p. with an authentic sample, 153–155°. The fractionation process failed to yield any other pure compound. Chromatography on alumina and on silicic acid—Super-Cel[6] also failed to yield any other pure isomer.

Dehydrogenation of (A) with Sulfur.—A mixture of 2.80 g. (0.02 mole) of (A) and 1.92 g. (0.06 g. atom) of powdered sulfur was heated under reflux (190–200°) for 18 hours. Evolution of hydrogen sulfide was noted throughout the interval. The mixture was then steam distilled, and part of the resulting oil was used to prepare a 2,4-dinitrophenylhydrazone, which was recrystallized repeatedly from benzene to a constant melting point; red needles from benzene, m.p. and mixed m.p. with an authentic sample of VII, 253–255°.

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(8) Melting points are corrected; boiling points are uncorrected.

(9) Prepared from cycloheptanol according to the procedure of J. Böeseken and C. J. A. Hanegraaf, *Rec. trav. chim.*, **61**, 69 (1942).

(10) E. Buchner and A. Jacobi, *Ber.*, **31**, 2008 (1898).

Chromones. V. The Preparation of 2-Methyl-7-hydroxychromone and 2-Methyl-5,8-dimethoxy-7-hydroxychromone

BY T. A. GEISSMAN

The preparation of 2-methylchromones from polyhydroxyacetophenones by the reaction of *o*-hydroxyacetophenones with acetic anhydride and sodium acetate[1] is often unsatisfactory because of the formation of 4-methylcoumarin derivatives or of 3-acetyl-2-methyl-chromones which must be deacylated in a separate step. The C-acylation of *o*-hydroxyacetophenone with ethyl acetate and sodium[2] is a reaction which does not readily lend itself to extension to polyhydroxyacetophenones because of the formation of insoluble sodium salts; and the modification of this reaction in which a polyacetoxyacetophenone is used also leads in some cases to 3-acetyl-2-methylchromones.[3] Alternative methods of masking the hydroxyl groups during the condensation of the acetyl group with ethyl acetate include the benzylation and subsequent hydrogenolysis of the benzyloxy groups; but the multiplicity of steps and the over-all losses in yields accompanying such devices caused us to seek a superior method of performing syntheses of 2-methylchromones based upon the resorcinol and substituted resorcinol nucleus.

The successful preparation of 2,6-dihydroxybenzoic acid by a procedure involving the protection of the hydroxyl groups by tetrahydropyranyl ether formation[4] suggested the use of a similar procedure in the present work. The method proved to be an excellent one for the preparation of 2-methyl-7-hydroxychromone (from resacetophenone) and 2-methyl-5,8-dimethoxy-7-hydroxychromone (from 2,4-dihydroxy-3,6-dimethoxyacetophenone). In the case of the former synthesis, intermediates were isolated and characterized in the course of exploratory experiments; in the latter, the several steps were carried out without the isolation of intermediate compounds.

The extension of this reaction to the preparation of 2-methyl-5,7-dihydroxychromone from phloroacetophenone has so far proved to be unsatisfactory.

Experimental

Resacetophenone 4-Tetrahydropyranyl Ether.—To a mixture of 10.0 g. of purified resacetophenone and 25 ml. of redistilled dihydropyran was added 6 drops of concentrated hydrochloric acid. (In later runs *p*-toluenesulfonic acid was used.) The mixture was warmed gently to effect solution of the resacetophenone and allowed to stand overnight in a water-bath at room temperature. Ether and dilute aqueous potassium hydroxide were added and the aqueous layer separated. The ether layer was dried and evaporated and the oily residue converted to 2-methyl-7-hydroxychromone in the manner described below.

The aqueous layer was acidified and extracted with ether. The dried ether solution was allowed to evaporate slowly, and large colorless prisms separated (5.2 g.). Recrystallized from ether–petroleum ether, the compound formed glistening prisms, m.p. 76–78°. The compound gave a wine-red color with methanolic ferric chloride.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 66.10; H, 6.83. Found: C, 66.38; H, 7.23.

(1) S. v. Kostanecki and A. Rozycki, *Ber.*, **34**, 102 (1901).

(2) G. Wittig, *ibid.*, **57B**, 88 (1924).

(3) T. A. Geissman, unpublished observations; see also W. Baker, *J. Chem. Soc.*, 1381 (1933); 1953 (1934) for related work.

(4) W. E. Parham and E. L. Anderson, THIS JOURNAL, **70**, 4187 (1948).

2-Hydroxy-4-tetrahydropyranyloxybenzoylacetone.—A solution of 5.0 g. of resacetophenone 4-tetrahydropyranyl ether in 35 ml. of dry ethyl acetate was added to 3.0 g. of powdered sodium. The reaction was lively but controlled; it was allowed to proceed at room temperature for 12 hours. Ice was added and the aqueous layer was separated, washed with ether, then poured onto a mixture of crushed ice and dilute sulfuric acid. The pasty precipitate soon became crystalline and after trituration with cold methanol formed a colorless crystalline solid (4.4 g.). Recrystallization from dilute methanol afforded colorless prisms, m.p. 97–98°.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.76; H, 6.51. Found: C, 64.91; H, 6.51.

Treatment of the diketone with methanolic hydrochloric acid resulted in ring closure and the simultaneous loss of the tetrahydropyranyl group with the formation in excellent yield of 2-methyl-7-hydroxychromone.

For preparative purposes, the three stages of the synthesis (tetrahydropyranylation, acylation and ring closure) are best carried out without isolation of the above-described intermediates.

2-Methyl-7-hydroxychromone.—A mixture of 15.2 g. (0.10 mole) of resacetophenone, 50 ml. of dihydropyran and 100 mg. of *p*-toluenesulfonic acid monohydrate was allowed to stand for 12 hours. Ether, 15 ml. of water and 2 ml. of 6 *N* sodium hydroxide were added, and the aqueous layer was separated and acidified. The monotetrahydropyranyl ether which separated was recrystallized from ether–petroleum ether (3.0 g.) and added to the alkali-washed ether solution containing the bulk of the material. The ether solution was dried over potassium carbonate and evaporated under reduced pressure to a semicrystalline residue. (Note: The weight of this residue, determined in another run, indicated that the main product was a bis-tetrahydropyranyl ether. This compound was not isolated.) The crude residue was dissolved in 75 ml. of dry ethyl acetate and 7.5 g. of powdered sodium was added. After two days, ice was added and the aqueous layer separated, washed with ether, and acidified. The gummy solid was stirred with cold methanol, leaving 17.0 g. of a nearly white, crystalline solid. This was dissolved in a mixture of 50 ml. of methanol and 5 ml. of concentrated hydrochloric acid, the solution was refluxed for several minutes, diluted with water, and cooled. The crystalline (pink-buff prisms) chromone weighed 10.0 g. Treatment of the methanol with which the gummy diketone had been triturated with hydrochloric acid afforded an additional 1.8 g. of chromone, m.p. 251–252°. The total yield was 11.8 g. (67% over-all) of chromone sufficiently pure for further use. This yield represents an average yield of 88% on each of the three chief steps in the over-all synthesis. When purified by recrystallization from methanol, the chromone forms colorless prisms, m.p. 253–254° (reported[1] 250°).

2-Methyl-5,8-dimethoxy-7-hydroxychromone.—A solution of 5.0 g. of 2,4-dihydroxy-3,6-dimethoxyacetophenone in 25 ml. of dihydropyran and a trace of *p*-toluenesulfonic acid was allowed to stand overnight. Ether and a few drops of dilute sodium hydroxide were added and the ether layer was separated, dried over anhydrous potassium carbonate and evaporated. The oily residue was dissolved in 50 ml. of dry ethyl acetate and added to 2 g. of powdered sodium. The next day crushed ice was added and the aqueous layer separated, washed with ether, acidified with iced dilute sulfuric acid and extracted with ether. The sirup remaining after removal of the ether was refluxed for an hour with 20 ml. of methanol and 5 ml. of concentrated hydrochloric acid. Water (75 ml.) was added and the solution cooled. The crystalline product which separated was washed with ether, the washings being used to extract the aqueous alcoholic mother liquors. The residual material from this ether extract was treated again with methanol–hydrochloric acid, yielding a second crop of crystalline chromone. The two crops (2.8 and 1.3 g.) were combined and recrystallized from methanol, yielding 2.8 g. (53%) of pure chromone, white needles, m.p. 247–248°.

The identity of the chromone was established by its independent synthesis in the following way:

2-Hydroxy-3,6-dimethoxy-4-benzyloxyacetophenone was prepared by (A) the monobenzylation of 2,4-dihydroxy-5,8-dimethoxyacetophenone (5.0 g.) in acetone (150 ml.) with benzyl chloride (3.5 g.) in the presence of potassium carbonate (15 g.). The product (5.1 g.) formed pale yellow needles, m.p. 109–110°; (B) the reaction of 2,5-dimethoxyresorcinol dibenzyl ether with acetyl chloride and aluminum chloride in benzene solution at 0°. The yield of the desired compound, m.p. 109.5–110°, was about 35%, a non-phenolic by-product being formed in about an equivalent amount.

Anal. Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.23; H, 5.95.

2-Methyl-7-benzyloxy-5,8-dimethoxychromone was prepared by the C-acylation of the above acetophenone in the usual way with ethyl acetate and sodium, followed by ring closure of the resulting diketone. The chromone formed rosettes of crisp needles, m.p. 164–165°, from benzene–ethyl acetate.

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 69.91; H, 5.56. Found: C, 69.57; H, 5.55.

2-Methyl-5,8-dimethoxy-7-hydroxychromone.—A solution of 6.2 g. of 2-methyl-5,8-dimethoxy-7-benzyloxychromone in 150 ml. of warm ethanol was hydrogenated in the presence of 3 g. of 10% palladium–charcoal at an initial pressure of about 1.7 atm. of hydrogen. The absorption of the calculated amount (1 mole) of hydrogen was completed in about 5 min. The catalyst was removed by filtration and washed with dilute alcoholic sodium hydroxide (to remove chromone which had crystallized during the hydrogenolysis). The acidified and diluted filtrate yielded 4.1 g. (92%) of the hydroxychromone, m.p. 247–248°, identical with that obtained by way of the tetrahydropyranylation route.

The chromone was characterized by the preparation of the following ethers by treatment with the corresponding halides and potassium carbonate in acetone:

7-Carboethoxymethoxy Ether.—M.p. 124–125° (from ether–petroleum ether).

Anal. Calcd. for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.31; H, 5.68.

7-*n*-Propyl Ether.—M.p. 103–105° (from dilute methanol).

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.51; H, 6.50.

7-*n*-Butyl Ether.—M.p. 110–112° (from dilute methanol).

Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.80; H, 6.92. Found: C, 66.02; H, 6.76.

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The Reversibility of the Friedel–Crafts Condensation. Carbomethoxystilbenes

BY REYNOLD C. FUSON AND H. G. COOKE, JR.

The transformation of various types of substituted styryl compounds into the corresponding unsubstituted 1,1-diphenylethyl derivatives takes place in the presence of benzene, hydrogen chloride and aluminum chloride. For example, nuclear halostilbenes yield 1,1,2-triphenylethane.[1] The process involves the replacement of a halophenyl radical by a phenyl radical.

$$XC_6H_4CH{=}CHC_6H_4X \xrightarrow[AlCl_3]{C_6H_6} (C_6H_5)_2CHCH_2C_6H_5 + 2C_6H_5X$$

Experiments have been carried out to determine whether phenyl groups bearing substituents other than halogen could also be expelled from the molecule in this manner. Experiments with *p*-tolyl radicals[2] indicated that the phenomenon might be general for aryl groups that carry only ortho, para-directing substituents. As expected, benzalquinaldines and benzallepidines failed to yield quino-

(1) L. L. Alexander and R. C. Fuson, THIS JOURNAL, **58**, 1745 (1936).

(2) J. T. Eaton, D. B. Black and R. C. Fuson, *ibid.*, **56**, 687 (1934).