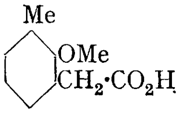
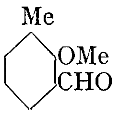
50. *Syntheses in the Phenanthrene Series. Part IV. 1-Methoxy-2-methylphenanthrene and the Preparation of Substituted Phenylacetic Acids.*

By Peter Hill and W. F. Short.

1-Methoxy-2-methylphenanthrene has been synthesised by Pschorr's method, 2-*methoxy*-m-*tolylacetic acid* (I) being used as one component. 2-Methoxy-*m*-tolualdehyde (II), the starting point for the preparation of this acid, was obtained from *o*-cresotic acid (2-hydroxy-*m*-toluic acid) by methylation and reduction of the carboxyl group by one of the following series of reactions: (1) 2-methoxy-*m*-toluic acid → 2-*methoxy*-m-*toluanilide* → 2-*methoxy*-m-*toluanilideiminochloride* → 2-*methoxy*-m-*tolylideneaniline* → 2-methoxy-*m*-tolualdehyde; (2) methyl 2-methoxy-*m*-toluate → 2-*methoxy*-m-*toluhydrazide* → 2-*methoxy*-m-*tolubenzenesulphonhydrazide* → 2-methoxy-*m*-tolualdehyde (compare McFadyen and Stevens, J., 1936, 584).



(I.)



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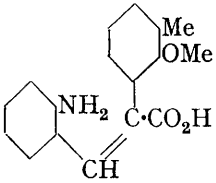

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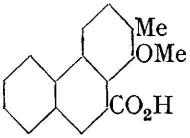
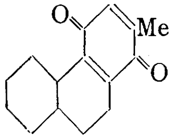


(IV.)

Condensation of the aldehyde with hippuric acid yielded 2-*phenyl*-4-(2'-*methoxy*-m-*tolylidene*)*oxazolone*, which was successively hydrolysed to 2-*methoxy*-m-*tolylpyruvic acid* and oxidised to 2-methoxy-*m*-tolylacetic acid. When the potassium salt of this acid was condensed with *o*-nitrobenzaldehyde, 2-*nitro*-α-(2'-*methoxy*-m-*tolyl*)*cinnamic acid* was formed, together with some *o*-nitrocinnamic acid. The nitro-acid, which was obtained in two forms, yielded 2-*amino*-α-(2'-*methoxy*-m-*tolyl*)*cinnamic acid* (III) on reduction with ferrous sulphate and ammonia. The corresponding diazonium salt was only slowly decomposed when shaken with copper powder, but when the solution was warmed with sodium carbonate 1-*methoxy*-2-*methylphenanthrene*-10-*carboxylic acid* (IV) was rapidly formed. Decarboxylation was smoothly effected by heating with quinoline and copper powder. Oxidation of the resulting 1-*methoxy*-2-*methylphenanthrene* produced an unexpected result. In place of the anticipated 9 : 10-quinone there was obtained a yellow compound, $C_{15}H_{10}O_2$, which we consider to be 2-*methylphenanthrene*-1 : 4-*quinone* (V), since it did not yield a quinoxaline. Reductive acetylation furnished 1 : 4-*diacetoxy*-2-*methylphenanthrene*.



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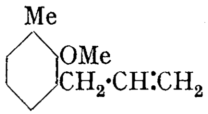
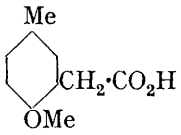


(VI.)



(VII.)

The preparation of substituted phenylacetic acids in quantity for use in the Pschorr synthesis is frequently attended with considerable difficulty and it occurred to us that they could be easily obtained from the corresponding allyl compounds, which are readily accessible. Reference to the literature showed, however, that oxidation of a large number of allyl compounds, even with ozone, invariably results in the production of a mixture of a phenylacetic acid and the corresponding benzoic acid. In order to explore the possibility of arresting the oxidation at the first stage, 3-*allyl*-o-*tolyl methyl ether* (VI), obtained in excellent yield from *o*-tolyl allyl ether by rearrangement (Claisen and Eisleb, *Annalen*, 1913, **401**, 56) and methylation, was subjected to oxidation under a variety of conditions. When potassium permanganate was employed as oxidising agent, moderate yields of 2-methoxy-*m*-tolylacetic acid (I) were obtained if the reaction was conducted in presence of alcohol (compare Higginbottom and Short, *Rec. trav. chim.*, **1934**, **53**, 1141). The influence of the alcohol was traced to the production of acetic acid, and 40% yields of the tolylacetic acid were obtained when the requisite quantity of acetic acid was introduced at the outset, a considerable quantity of the allyl compound being recovered unchanged. Other methods of acidification gave less favourable results. The method appears to be general and we now describe the transformation of 3-bromo-*p*-tolyl methyl ether into 3-*allyl*-p-*tolyl methyl ether* and 4-*methoxy*-m-*tolylacetic acid* (VII).

EXPERIMENTAL.

Methyl 2-*Methoxy*-m-*toluate*.—A paste of *o*-cresotic acid (1 mol.) and 50% sodium hydroxide solution (2·4 mols.) was cautiously warmed with methyl sulphate (2·4 mols.). After the vigorous reaction, the product was washed with dilute sodium hydroxide solution to remove unchanged *o*-cresotic acid (8%), dried, and distilled. The resulting liquid, b. p. 116—125°/12 mm., which consisted of a mixture of methyl 2-methoxy-*m*-toluate with methyl 2-hydroxy-*m*-toluate (up to 30%), was remethylated with methyl sulphate (1·5 mols.) and sodium methoxide (from 1·5 atoms of sodium and 3 vols. of methyl alcohol) and afforded methyl 2-methoxy-*m*-toluate, b. p. 120°/12 mm., in an overall yield of 70%. Saponification now yielded pure 2-methoxy-*m*-toluic acid, m. p. 83—84°.

2-*Methoxy*-m-*toluanilide*.—The acid was warmed with thionyl chloride (3 mols.), the excess of the reagent removed under diminished pressure, and, after dilution with dry benzene, a dilute solution of aniline (2 mols.) in chloroform added at 0°. The *anilide*, b. p. *ca*. 210°/8 mm., separated from alcohol in long needles, m. p. 82·5—83° (Found: C, 74·6; H, 6·4; N, 5·9. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%). Yield, 65%.

2-*Methoxy*-m-*toluhydrazide*, obtained in almost quantitative yield from methyl 2-methoxy-*m*-toluate and 50% hydrazine hydrate (2·1 mols.) in alcohol, separated from benzene–light petroleum (b. p. 60—80°) in stout prisms, m. p. 79·5—80·5° (Found: C, 59·8; H, 6·8; N, 15·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7; N, 15·5%).

2-*Methoxy*-m-*tolubenzenesulphonhydrazide*.—The hydrazide was converted into the *benzenesulphonhydrazide* by the action of benzenesulphonyl chloride (1 mol.) and pyridine (10 mols.). The product, isolated in the usual way, crystallised from alcohol in rhombic prisms, m. p. 149—150° (Found: C, 56·4; H, 4·9. $C_{15}H_{16}O_4N_2S$ requires C, 56·3; H, 5·0%). The yield was 67%.

2-*Methoxy*-m-*tolualdehyde*.—(1) A solution of 2-methoxy-*m*-toluanilide in benzene (2 parts) was warmed at 50—110° for 1 hour with phosphorus pentachloride (1·1 mols.), the benzene and phosphorus oxychloride removed by distillation under diminished pressure, and the residue mixed with stannous chloride (3 mols.) dissolved in a saturated solution of hydrogen chloride in ether. After 3 days at room temperature, the yellow crystals were collected, acidified, and distilled with steam. The aldehyde, b. p. 118°/12 mm., was obtained in 62% yield and afforded a semicarbazone, m. p. 216—216·5°, which did not depress the m. p. of a specimen prepared by the Tiemann–Reimer method (Simonsen, J., 1918, **113**, 777). Substitution of thionyl chloride (3 mols.) for phosphorus pentachloride in the preparation of the iminochloride (compare v. Braun and Pinkernelle, *Ber*., 1934, **67**, 1218) lowered the yield of aldehyde to 36%. (2) Anhydrous sodium carbonate (8·3 g.) was added to a solution of 2-methoxy-*m*-tolubenzenesulphonhydrazide (10 g.) in ethylene glycol (50 c.c.) at 160°, the temperature maintained at 150—160° for 4—5 minutes, hot water then added, and the aldehyde extracted with ether. The yield of aldehyde (b. p. 115—120°/12 mm.; semicarbazone, m. p. 216—216·5°) was 66%.

2-*Phenyl*-4-(2′-*methoxy*-m-*tolylidene*)*oxazolone*.—This *azlactone* was obtained in almost theoretical yield by heating a mixture of 2-methoxy-*m*-tolualdehyde, hippuric acid (1 mol.), sodium acetate (1 mol.), and acetic anhydride (3 mols.) on a boiling water-bath for 2 hours. It separated from benzene in fine yellow needles, m. p. 160—161° (Found: C, 73·65; H, 5·0; N, 4·9. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1; N, 4·8%).

2-*Methoxy*-m-*tolylpyruvic Acid*.—When the azlactone was boiled for 5 hours with 10% sodium hydroxide solution (5 parts), and the product freed from benzoic acid by the sulphur dioxide method, the *pyruvic acid* was obtained in satisfactory yield. It separated from chloroform in colourless plates, m. p. 131—132° (Found: C, 63·7; H, 5·9. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

2-*Methoxy*-m-*tolylacetic Acid*.—An ice-cold solution of sodium 2-methoxy-*m*-tolylpyruvate in 10% aqueous sodium hydroxide was oxidised by a slight excess of 6% hydrogen peroxide. Next day the *tolylacetic acid* was precipitated by dilute sulphuric acid, dried, and recrystallised from light petroleum (b. p. 60—80°); it formed large rectangular plates, m. p. 98·6—99·6° (Found : C, 66·8; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

2-*Nitro*-α-(2'-*methoxy*-m-*tolyl*)*cinnamic Acid*.—A mixture of potassium 2-methoxy-*m*-tolylacetate (dried at 130°), *o*-nitrobenzaldehyde (1·2 mols.), and acetic anhydride (10 mols.) was heated under reflux at 100° for 26 hours. Water was then added to destroy the acetic anhydride, and the residual pasty mass was taken up in ether and repeatedly extracted with sodium hydroxide solution to separate a considerable quantity of the nitrostilbene. The solid precipitated by acidifying the alkaline solution consisted of a mixture of 2-*nitro*-α-(2'-*methoxy*-m-*tolyl*)*cinnamic acid* and 2-nitrocinnamic acid, which was separated by extraction with benzene, in which the second acid is relatively insoluble. 2-Nitro-α-(2'-methoxy-*m*-tolyl)cinnamic acid, obtained in 40—66% yield, crystallised from chloroform–light petroleum in rhombs elongated along one axis, m. p. 180—181° (Found : C, 65·1; H, 5·0; N, 4·6. $C_{17}H_{15}O_5N$ requires C, 65·2; H, 4·8; N, 4·4%). In one instance, the acid was obtained in stout hexagonal prisms, m. p. 198—199° (Found : C, 65·3; H, 4·8%). Both forms afforded the same amino-acid on reduction.

2-*Amino*-α-(2'-*methoxy*-m-*tolyl*)*cinnamic Acid*.—A hot ammoniacal solution of the nitro-acid was added to a reducing mixture prepared from crystalline ferrous sulphate (7·7 mols.) and excess of ammonia. After heating at 100° for 2 hours, the solution was filtered, and the *amino-acid* precipitated by dilute hydrochloric acid (yield, *ca.* 60%). This acid crystallised from absolute alcohol in long clustered rods, m. p. 188—188·5° (Found : N, 4·9. $C_{17}H_{17}O_3N$ requires N, 4·9%).

1-*Methoxy*-2-*methylphenanthrene*-10-*carboxylic Acid*.—A solution of the amino-acid in an equivalent of dilute aqueous sodium hydroxide was added to 2*N*-sulphuric acid (10 mols.) at 0° and the calculated quantity of *M*-sodium nitrite was then added slowly. As diazotisation was slow, the mixture was kept at 0° for 12 hours, and the small residue removed by filtration. The clear diazonium solution was only slowly decomposed on shaking with copper powder, but decomposition was complete in 10 minutes when the red solution, obtained by making alkaline with sodium carbonate, was heated on the water-bath. The solution was acidified with dilute sulphuric acid at 0°, and the *acid* recrystallised from acetic acid. It was obtained in almost colourless, stout prisms, m. p. 186·3—187·3° (Found : C, 77·0; H, 5·3. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·2%).

1-*Methoxy*-2-*methylphenanthrene*.—The acid was smoothly decarboxylated by heating at 230° for 2¾ hours with 1/10th of its weight of copper powder and 5 parts of quinoline. The neutral *product* crystallised from methyl alcohol in colourless flakes, m. p. 82·5—83° (Found : C, 86·1; H, 6·6. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* separated from alcohol in orange-yellow needles, m. p. 127·5—128° (Found : C, 58·7; H, 3·7; N, 9·4. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·6; H, 3·8; N, 9·3%). When 1-methoxy-2-methylphenanthrene (0·6 g.), dissolved in acetic acid (3 c.c.), was oxidised below 70° with a solution of chromic anhydride (1·2 g.) in water (0·8 c.c.) and acetic acid (7·2 c.c.), a light yellow solid was deposited on cooling. Recrystallisation from alcohol afforded long orange-yellow needles, m. p. 153—154° (Found : C, 81·0; H, 4·7; *M*, Rast, 236. $C_{15}H_{10}O_2$ requires C, 81·1; H, 4·5%; *M*, 222). When this 2-*methylphenanthrene*-1 : 4-*quinone* was warmed with zinc dust, acetic anhydride and pyridine, it was reduced to 1 : 4-*diacetoxy*-2-*methylphenanthrene*, which separated from benzene–light petroleum in long colourless rods, m. p. 165—165·5° (Found : C, 74·2; H, 5·15. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

3-*Allyl*-o-*tolyl Methyl Ether*.—In the conversion of *o*-cresol into *o*-tolyl allyl ether and 3-allyl-*o*-cresol (Claisen and Eisleb, *loc. cit.*), 90% and 81% yields were obtained. The phenol was methylated without isomerisation of the side chain when 10% sodium hydroxide solution (2·25 mols.) and methyl sulphate (2·0 mols.) were added alternately below 60°. The *methyl ether* (yield, 81%) was obtained as a colourless liquid, b. p. 94—96°/10 mm. (Found : C, 81·6; H, 8·5. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%).

Oxidation of 3-*Allyl*-o-*tolyl Methyl Ether*.—After numerous trials with hydrogen peroxide and potassium permanganate, the following process was devised for the preparation of the phenylacetic acid. A mixture of the methyl ether with ice-water (100 vols.) and acetic acid (7·2 mols.) was cooled in a freezing mixture and stirred into an emulsion. Potassium permanganate (5% : equivalent to 6 atoms of oxygen) was then added at such a rate that the temperature remained below 1°. Unchanged methyl ether (13—20%) was removed in steam, the mixture made alkaline with dilute sodium hydroxide solution, filtered, and evaporated to a small volume. Acidification of the red liquid to litmus with hydrochloric acid afforded a sticky red precipitate, which was removed by decantation, and further addition of acid (Congo-red) then precipitated the bulk of the 2-*methoxy*-m-*tolylacetic acid* in almost pure condition. The aqueous layer was extracted with ether, and the red precipitate (above) dissolved in the solution, which was then dried and evaporated. Distillation of the residue under diminished pressure afforded (1) acetic acid; (2) almost pure 2-methoxy-*m*-tolylacetic acid, b. p. 187—189°/10 mm., and (3) a small quantity of a red semi-solid mass containing some tolylacetic acid. Only traces of 2-methoxy-*m*-toluic acid were present, so the crude acid was easily purified by crystallisation from light petroleum. The average yield of 2-methoxy-*m*-tolylacetic acid, calculated on the 3-allyl-*o*-tolyl methyl ether employed, was 40% of the theoretical.

4-*Methoxy*-m-*tolylacetic Acid*.—Dropwise addition of allyl bromide (1·1 mols.) to the Grignard compound of 3-bromo-*p*-tolyl methyl ether (J., 1936, 323), followed by boiling for 3 hours, afforded 3-allyl-*p*-tolyl methyl ether, b. p. 100—125°/10 mm., in 50% yield.* Oxidation of this ether under the conditions specified above for 3-allyl-*o*-tolyl methyl ether furnished 4-*methoxy*-m-*tolylacetic acid*, m. p. 131—132° (Found: C, 66·9; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

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