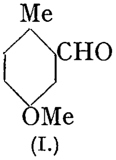
51. *Syntheses in the Phenanthrene Series. Part V.*
4-*Methoxy*-1-*methylphenanthrene.*

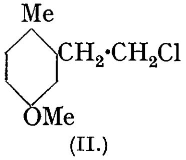
By ALICE HIGGINBOTTOM, PETER HILL, and W. F. SHORT.

IN attempting the synthesis of 4-*methoxy*-1-*methylphenanthrene* (IV) we first prepared 4-*methoxy*-o-*tolualdehyde* (I). For this purpose *p*-nitrotoluene was converted successively into 2-bromo-4-nitrotoluene, 2-bromo-*p*-toluidine and 2-bromo-*p*-cresol. This phenol was isolated in an unstable form, m. p. 16°, which subsequently changed into the stable form, m. p. 55°, described in the patent literature (D.R-P. 15,633). Methylation gave 2-bromo-*p*-tolyl methyl ether, the Grignard compound of which was converted into the required aldehyde on heating with ethyl orthoformate. Alternatively, the Grignard compound was carbonated and the chloride of the resulting 4-*methoxy*-o-*toluic acid* reduced to the aldehyde by Rosenmund's method. No condensation product could, however, be obtained from 4-methoxy-*o*-tolualdehyde and sodium *o*-nitrophenylacetate; the aldehyde was recovered and the sodium salt converted into *o*-nitrotoluene.

In the next attempt, β-(4-*methoxy*-o-*tolyl*)*ethyl chloride* (II) was prepared from the Grignard compound of 2-bromo-*p*-tolyl methyl ether and β-chloroethyl toluene-*p*-sulphonate (compare Ferns and Lapworth, J., 1912, **108**, 273; Gilman and Beaber, *J. Amer. Chem. Soc.*, 1923, **45**, 839). The Grignard compound of this chloride and *cyclo*hexanone afforded 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*cyclo*hexan*-1-*ol*, accompanied by a small amount of $\alpha\delta$-*di*-(4-*methoxy*-o-*tolyl*)*butane*. The yield of carbinol was low and we have observed that a methoxy-group, especially when present in the *o*-position, depresses the yield both of the carbinol and of the tricyclic compound produced from it at a later stage. The alcohol was dehydrated to 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*-Δ^1-cyclo*hexene* (III), which, on treatment with aluminium chloride, afforded a mixture of substances from which we were unable to isolate a homogeneous fraction by distillation. On the assumption that the mixture contained 5-methoxy-8-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene, it was dehydrogenated with sulphur. A sparingly soluble *picrate*, m. p. 182—183°, was isolated from the



(I.)



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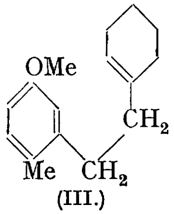

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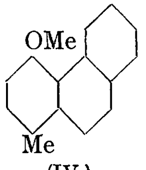


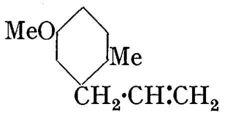
(IV.)

* We are grateful to Miss A. Higginbottom for this preparation.

distillate, and ammonia liberated a *compound*, m. p. 78·5—79°, giving the correct analytical figures for 4-methoxy-1-methylphenanthrene (IV).

Cook and his collaborators (J., 1933, 1101; 1934, 365) have shown that there is a tendency for compounds of type (III) to yield spirans in addition to or instead of phenanthrenes. In this instance the formation of a spiran appeared to be excluded by the analytical figures, but the synthesis could not be regarded as satisfactory since insufficient material was available for a detailed examination of the product. It was therefore decided to apply the simple and convenient method for the preparation of substituted phenylacetic acids described in Part IV (preceding paper) to the synthesis of 4-methoxy-1-methylphenanthrene by an unambiguous method.

The Grignard compound of 2-bromo-*p*-tolyl methyl ether (above) and allyl bromide furnished *2-allyl-*p*-tolyl methyl ether* (V), which was oxidised to *4-methoxy-*o*-tolylacetic acid* (VI).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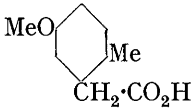
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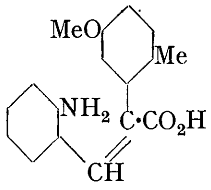
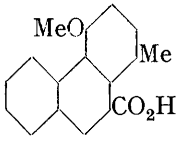

(VII.)


(VIII.)

The sodium salt of this acid and *o*-nitrobenzaldehyde yielded *2-nitro-α-(4′-methoxy-*o*-tolyl)-cinnamic acid*, which was reduced to the corresponding *amino-acid* (VII). When a solution of the diazonium salt of (VII) was heated, *4-methoxy-1-methylphenanthrene-10-carboxylic acid* (VIII) was obtained and decarboxylation furnished 4-methoxy-1-methylphenanthrene identical with that obtained by the first method. Demethylation of (IV) gave *4-hydroxy-1-methylphenanthrene.*

EXPERIMENTAL.

2-Bromo-4-nitrotoluene.—Scheufelen (*Annalen*, 1885, **231**, 171) brominated *p*-nitrotoluene in presence of ferrous bromide in a sealed tube at 70°; by substituting iron powder as catalyst, a 70% yield of 2-bromo-4-nitrotoluene was obtained in open vessels. Bromine (100 c.c.) was added during 3 hours to *p*-nitrotoluene (280 g.) and iron powder (10 g.) at 95—100°. The mixture was heated for ¾ hour and the oil, obtained by pouring into hot water, was washed with sodium bisulphite solution and hydrochloric acid. The oil, which solidified on cooling, melted at 76—77° after washing with water, and was sufficiently pure for reduction.

*2-Bromo-*p*-toluidine.*—Scheufelen (*loc. cit.*) reduced 2-bromo-4-nitrotoluene with tin and hydrochloric acid, but does not record the yield obtained. A 95% yield of 2-bromo-*p*-toluidine was obtained from 2-bromo-4-nitrotoluene (43 g.), concentrated hydrochloric acid (2 c.c.), alcohol (100 c.c.), and reduced iron powder (34 g.); West's technique (J., 1925, **127**, 494) was used, but the mixture was boiled for 9 hours after addition of the iron. The amine melted at 26—27° and afforded a *benzoyl* derivative, m. p. 132° (Found : N, 4·9. $C_{14}H_{12}ONBr$ requires N, 4·8%).

*2-Bromo-*p*-cresol.*—The conversion of 2-bromo-*p*-toluidine into 2-bromo-*p*-cresol, m. p. 55—56°, is recorded by the Badische Anilin- & Soda-Fabrik (Friedländer's " Fortschritte," 1905, **8**, 203), but no details are given. A 68% yield of the phenol was obtained when the diazonium solution, prepared from the base (10 g.), concentrated hydrochloric acid (6 c.c.), water (40 c.c.), and sodium nitrite (3·5 g.) at 0°, was slowly added to anhydrous sodium sulphate (420 g.), concentrated sulphuric acid (200 c.c.), and water (150 c.c.) at 120—130°. The phenol was removed in a current of superheated steam as it was formed. The first preparation melted sharply at 16°, but was transformed into the stable form, m. p. 54·5—55°, when inoculated with a crystal obtained in a subsequent experiment. Both forms afforded the same *benzoate*, m. p. 74·5—75·5° (Found : C, 57·7; H, 3·9; Br, 27·5. $C_{14}H_{11}O_2Br$ requires C, 57·7; H, 3·8; Br, 27·5%). Methylation with methyl sulphate (1·4 mols.) and 10% sodium hydroxide solution afforded 2-bromo-*p*-tolyl methyl ether, b. p. 103—105°/10 mm., in 72% yield and 8% of phenol was recovered.

*4-Methoxy-*o*-toluic Acid.*—Excess of solid carbon dioxide was added to a Grignard solution from the preceding bromo-ether (20 g.), magnesium (2·4 g.), and ether (50 c.c.) and, after standing for an hour, the complex was decomposed in the usual way. The *acid* (yield 31%) was recrystallised from hot water and melted at 142° (Found : C, 65·0; H, 6·2. $C_9H_{10}O_3$ requires C, 65·1; H, 6·0%). The chloride, b. p. 125—126°/10 mm., was obtained in 86% yield from the acid and excess of thionyl chloride.

4-*Methoxy*-o-*tolualdehyde*.—(1) Ethyl orthoformate (7·4 g.) was added to a Grignard solution prepared from 2-bromo-*p*-tolyl methyl ether (20 g.), magnesium (2·4 g.), and ether (50 c.c.), and the complex decomposed with ice-cold hydrochloric acid. The oil, obtained from the ethereal layer, was boiled with 5*N*-hydrochloric acid to hydrolyse the acetal, and the aldehyde, b. p. 120°/11 mm., isolated in the usual way (yield 34%). It afforded a *semicarbazone*, m. p. 212—213° (Found: C, 58·2; H, 6·3; N, 20·1. $C_{10}H_{13}O_2N_3$ requires C, 58·0; H, 6·3; N, 20·3%). (2) A poor yield (13%) of the aldehyde (semicarbazone, m. p. 212—213°) was obtained by reducing 4-methoxy-*o*-toluoyl chloride (6 g.), dissolved in xylene (50 c.c.), in presence of palladium–barium sulphate (4 g.) (Schmidt, *Ber.*, 1919, **52**, 409).

β-(4-*Methoxy*-o-*tolyl*)*ethyl Chloride*.—β-Chloroethyl toluene-*p*-sulphonate (47 g.) in benzene (100 c.c.) was added to a solution of the Grignard compound of 2-bromo-*p*-tolyl methyl ether (from 4·8 g. of metal and 30·2 g. of the bromo-ether in 45 c.c. of ether), and the mixture warmed to 55°. A white solid separated and the temperature was maintained for an hour by the heat of the reaction. After 12 hours, the mixture was refluxed for 1 hour and then hydrolysed in the usual manner. Careful fractionation gave a 43% yield of β-(4-*methoxy*-o-*tolyl*)*ethyl chloride*, b. p. 126—134°/10 mm. A middle fraction, b. p. 132—133°/10 mm., was analysed (Found : Cl, 19·0. $C_{10}H_{13}OCl$ requires Cl, 19·2%).

1-β-(4′-*Methoxy*-o-*tolyl*)*ethyl*cyclo*hexan*-1-*ol*.—A cold solution of *cyclo*hexanone (48 c.c.) in ether (100 c.c.) was slowly added with stirring to the Grignard compound of the preceding chloride (48 g.; metal 18·8 g.; ether 400 c.c.) cooled in a freezing mixture. After 12 hours, the mixture was decomposed with acidified ammonium chloride solution, and the ethereal layer washed, dried, and evaporated. Repeated fractionation of the residue afforded (1) 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*-cyclo*hexan*-1-*ol* as a viscous oil, b. p. 175—180°/4 mm. (Found: C, 77·8; H, 9·4. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%) (yield, 40%), and (2) a smaller fraction, b. p. 200—220°/5 mm., which solidified on cooling. Recrystallisation from methyl alcohol gave 3·2 g. of αδ-*di*-(4-*methoxy*-o-*tolyl*)*butane*, m. p. 105—106° (Found : C, 80·5; H, 8·5. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7%).

1-β-(4′-*Methoxy*-o-*tolyl*)*ethyl*-Δ^1-cyclo*hexene* (III).—Dehydration of the carbinol by heating for 1¼ hours at 160—170° with potassium hydrogen sulphate (1·5 parts) gave a 94% yield of the cyclo*hexene* derivative as a pale yellow liquid, b. p. 150—155°/4 mm. (Found : C, 83·2; H, 9·25. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%).

2-*Allyl*-p-*tolyl Methyl Ether*.—Allyl bromide (1·1 mols.) was added to a Grignard solution prepared from 2-bromo-*p*-tolyl methyl ether (1 mol.), magnesium (1 atom), and ether (5 mols.) so that the mixture boiled gently. After standing for 12 hours, the solution was boiled for 3 hours, and the product decomposed with ice-cold dilute sulphuric acid, washed, and fractionated. The portion, b. p. 100—105°/10 mm., was a pleasant-smelling liquid (yield, 60%) and a fraction, b. p. 102—104°/10 mm., was analysed (Found: C, 82·0; H, 8·7. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%).

4-*Methoxy*-o-*tolylacetic Acid*.—The aforesaid unsaturated compound was oxidised with 5% potassium permanganate solution and acetic acid exactly as in the preparation of the isomeric 4-methoxy-*m*-tolylacetic acid (preceding paper). The yield (21%) was considerably lower, but 33% of the unsaturated compound was recovered. 4-*Methoxy*-o-*tolylacetic acid* separated from light petroleum (b. p. 60—80°) in large rectangular plates, m. p. 103—104° (Found : C, 66·7; H, 6·7. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

2-*Nitro*-α-(4′-*methoxy*-o-*tolyl*)*cinnamic Acid*.—Potassium 4-methoxy-*o*-tolylacetate (1 mol., dried at 130°), *o*-nitrobenzaldehyde (1 mol.), and acetic anhydride (10 mols.) were maintained at 100° for 27 hours; water was then added, and the product isolated in the normal manner. The condensation *product* crystallised from benzene in almost colourless plates, m. p. 177—178° (Found : C, 65·1; H, 4·8; N, 4·55. $C_{17}H_{15}O_5N$ requires C, 65·2; H, 4·8; N, 4·4%). The yield was 51% and a small amount of *o*-nitrocinnamic acid was obtained as a by-product.

2-*Amino*-α-(4′-*methoxy*-o-*tolyl*)*cinnamic Acid*.—The nitro-compound was reduced at 100° with ferrous sulphate (7·7 mols.) and aqueous ammonia; the *amino-acid* (yield 79%) crystallised from alcohol in rhombic plates, m. p. 178—179° (Found : C, 72·1; H, 6·2; N, 4·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0; N, 4·9%).

4-*Methoxy*-1-*methylphenanthrene*-10-*carboxylic Acid*.—The above amino-acid (7·7 g.) was converted into the sulphate by adding 2*N*-sulphuric acid (98 c.c.) and methyl alcohol (123 c.c.), and the fine suspension diazotised at 0° by adding *M*-sodium nitrite (27 c.c.). Stirring was continued for 12 hours and the solution filtered (4·8 g. of amino-acid, crystallised once from benzene, m. p. 178—179°, were recovered). The filtrate was boiled, the precipitate collected, and the *acid* separated by extraction with sodium carbonate solution. It crystallised from acetic acid in small sandy rhombs, m. p. 213·5—214° (Found : C, 76·8; H, 5·3. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·2%).

4-*Methoxy*-1-*methylphenanthrene*.—(1) Powdered aluminium chloride (34 g.) was added to an ice-cold solution of 1-β-(4′-methoxy-*o*-tolyl)ethyl-Δ¹-*cyclo*hexene (22·5 g.) in carbon disulphide (380 g.). After being kept at 0° for 24 hours, the mixture was decomposed with hydrochloric acid and ice. Since no homogeneous fraction could be isolated from the product by distillation, the whole (20·7 g., b. p. 130—162°/5 mm.) was mixed with sulphur (6·7 g.) and heated to 235° during 5 hours. The mixture was then distilled under diminished pressure, and the distillate boiled with excess of alcoholic picric acid. The resulting *picrate* (1·0 g.) separated from alcohol in tawny orange needles, m. p. 182—183° (Found : C, 58·8; H, 4·0; N, 9·3. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8; N, 9·3%). 4-*Methoxy*-1-*methylphenanthrene*, regenerated from the pure picrate, separated from methyl alcohol in long rods, m. p. 78·5—79° (Found : C, 86·7; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). (2) Decarboxylation of 4-methoxy-1-methylphenanthrene-10-carboxylic acid (0·3 g.) was effected by heating with copper powder (0·15 g.) and quinoline (1·5 c.c.) for 2 hours at 230°. The product, purified by crystallisation from methyl alcohol, melted at 78·5—79° and afforded a picrate, m. p. 182—183°. There were no depressions of m. p.'s when the two substances last described were mixed with the corresponding compounds prepared by method (1).

4-*Hydroxy*-1-*methylphenanthrene*.—The methoxy-compound (0·2 g.), acetic acid (4 c.c.), and hydriodic acid (4 c.c., *d* 1·7) were boiled for 4½ hours, and the phenol (0·16 g.) isolated in the usual way. 4-*Hydroxy*-1-*methylphenanthrene* crystallised from chloroform–ligroin in colourless needles, m. p. 103—104° (Found : C, 86·4; H, 5·9. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%), and gave an olive-green coloration with aqueous ferric chloride. The *benzoate* separated from chloroform–methyl alcohol in prisms, m. p. 121—122° (Found : C, 84·2; H, 5·3. $C_{22}H_{16}O_2$ requires C, 84·6; H, 5·1%).

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