

Stereochemistry of the Ethoxyethynyl Carbinol- $\alpha\beta$ -Unsaturated Ester Conversion

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Carbon dioxide in ethanol rearranges the ethoxyethynyl carbinol derivatives of ketones in the 1-tetralone, indan-1-one, and 2,3-dihydrophenanthren-4(1*H*)-one series to yield predominantly the *cis*- $\alpha\beta$ -unsaturated esters.

In earlier communications^{1,2} it was reported that whereas the vinyl alcohol (1) reacts readily with 2-methylcyclopentane-1,3-dione to yield compound (3), the halides prepared from it by the action of either phosphorus trichloride or tribromide and presumed to have structure (2; X = Cl or Br) reacted sluggishly, although compound (3) was obtained. Wendler *et al.*³ have shown that the tetralol (1) gives an isothiuronium salt [2; X = SC(NH₂)₂⁺OAc⁻], which reacts rapidly yielding the dione (3). The behaviour of the bromide (2; X = Br)

contrasts sharply with that of allyl bromide itself, which gives a 75% yield of the C-allyl compound² corresponding to (3). The structure of the halides (2) seemed to be confirmed, as the same two compounds were formed from the alcohol (2; X = OH), itself prepared by the action of ethoxyethynylmagnesium bromide on 6-methoxy-1-tetralone (4), rearrangement of the carbinol (5) to the ester (8; R = CO₂Et), and reduction with lithium aluminium hydride. The formation and structures of these compounds have now been reinvestigated.

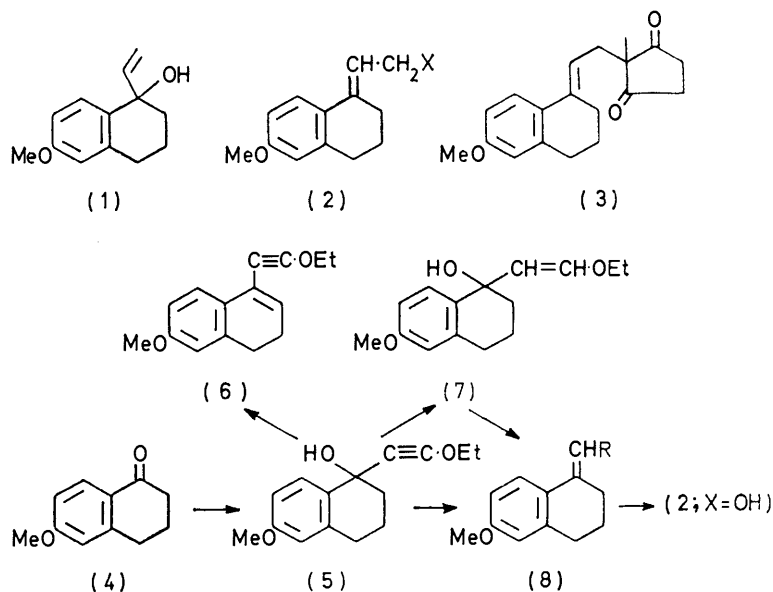
Improvements were made in the preparation of the

¹ D. J. Crispin and J. S. Whitehurst, *Proc. Chem. Soc.*, 1963, 22.

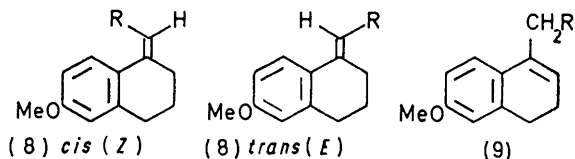
² D. J. Crispin, A. E. Vanstone, and J. S. Whitehurst, *J. Chem. Soc. (C)*, 1970, 10.

³ C. H. Kuo, D. Taub, and N. L. Wendler, *Angew. Chem. Internat. Edn.*, 1965, **4**, 1083; R. D. Hoffsommer, D. Taub, and N. L. Wendler, *J. Org. Chem.*, 1967, **32**, 3074.

alcohol (5). The latter is not stable and easily undergoes dehydration to the enyne (6) on heating or spontaneously. It was previously reported² that a solution of the alcohol (5) in ethanol on treatment with mineral acid gave the unwanted $\beta\gamma$ -unsaturated ester (9; R = CO₂Et), but that if its solution in ethanol was left for several days, rearrangement took place to give the unsaturated ester (8; R = CO₂Et), shown by g.l.c. to



contain 80% of one geometrical form of the compound. It has now been found that this reaction does not occur unless carbon dioxide (in the earlier work atmospheric CO₂) is admitted; the procedure adopted was to add a little solid carbon dioxide to the solution; after 12 h rearrangement to the ester (8) was complete. The product was separated cleanly by preparative layer chromatography into two isomers (72 : 28).



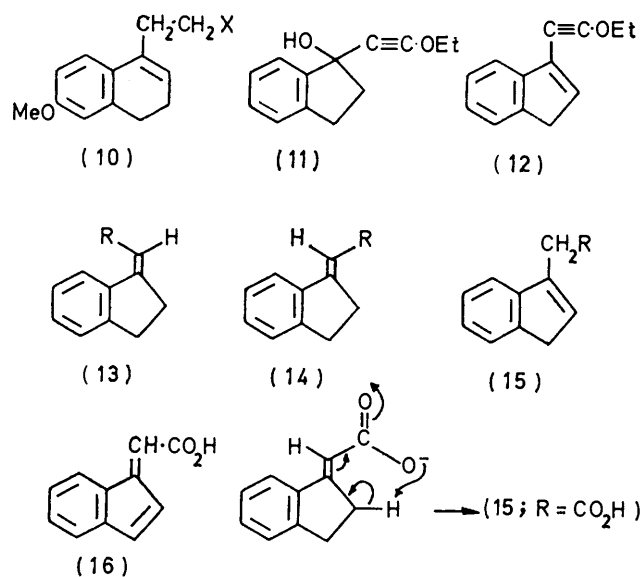
To our surprise the major component proved to have the *cis*-structure (*Z*)-(8; R = CO₂Et). In the n.m.r. spectrum of this compound the one proton singlet at τ 4.33 was obviously due to the olefinic proton; in the case of the other compound (*E*)-(8; R = CO₂Et) the corresponding signal was a broad singlet at τ 3.78, the proximity of the aromatic ring accounting for the downfield shift. The *cis*-compound was not stable to acid, alcoholic hydrogen chloride converting it into an equilibrium mixture of the *trans*-compound (*ca.* 30%) and the $\beta\gamma$ -unsaturated ester (9) (R = CO₂Et) (*ca.* 70%), the two

⁴ A. Görtz, Dissertation, Berlin, 1924.

⁵ G. Schroeter, *Ber.*, 1925, **58**, 713; G. Haberland, *ibid.*, 1936, **69**, 1380; V. C. E. Burnop, G. H. Elliott, and R. P. Linstead, *J. Chem. Soc.*, 1940, 727.

being readily separated by preparative layer chromatography. The ester (9; R = CO₂Et) was easily identified by the presence in its n.m.r. spectrum of a one-proton triplet (*J* 4 Hz) at τ 4.16. The Reformatskii reaction^{4,5} between 6-methoxy-1-tetralone (4) and ethyl bromoacetate, followed by dehydration of the product with hot 98% formic acid, gave the same mixture of the compounds (*E*)-(8; R = CO₂Et) and (9; R = CO₂Et),

likewise treatment of compound (6) with hydrochloric acid-ethanol.



Each of the foregoing esters was reduced with lithium aluminium hydride in tetrahydrofuran. The products from the *trans*- and $\beta\gamma$ -unsaturated esters were the expected alcohols, but in the case of the *cis*-compound the product was an approximately 80 : 20 mixture of the *cis*- and *trans*-alcohols (*Z*)-(8) and (*E*)-(8) (R = CH₂OH).

Each of these alcohols on treatment at -80° with phosphorus tribromide in chloroform containing a little pyridine gave the same bromo-compound. Similar treatment with phosphorus trichloride gave the same chloro-compound, which was more stable than its bromine analogue. A detailed analysis of the n.m.r. spectra of these compounds showed their correct structures to be (10; X = Cl or Br). Thus for the chloro-compound double irradiation at the centre of the olefinic proton triplet [τ 4.27 (1H, J 4 Hz)] showed that this proton was coupled to the C-3 methylene protons (multiplet at τ 7.6–8.0). In either of the other two structures (8; R = CH₂Cl) coupling would be to a doublet which would be expected to occur at τ ca. 6. Furthermore the absorption in deuteriochloroform at τ 6.25–6.40 (5H) was evidently due to a methoxy-signal overlapping one arm of a triplet, and the remaining two arms of that triplet (J 8 Hz); in hexadeuteriobenzene this absorption was shifted to τ 6.47–6.75 and became a clear singlet (3H) and triplet (2H, J 8 Hz). Final proof was provided by comparison with the n.m.r. spectra of the compounds (8; R = CH₂·OH) and (9; R = CH₂·OH). The double-bond shift occurring in the formation of compounds (10; X = Cl or Br) from the compounds (8; R = CH₂·OH) even at -80° is noteworthy. The relative unreactivity of these halides with 2-methylcyclopentane-1,3-dione is now understandable,² as the compounds are substituted ethyl halides.

Torgov⁶ has reported the conversion of the acetylenic alcohol (5) into the vinyl ether (7) (not isolated) by catalytic reduction, and rearrangement of the latter in mineral acid to an aldehyde (8; R = CHO), reduction of which with lithium aluminium hydride gave an alcohol (8; R = CH₂·OH). The configuration about the double bonds in these compounds was not specified. This work has now been repeated and extended. Thus the semihydrogenation step (5) \longrightarrow (7) could be brought about with lithium aluminium hydride⁷ and the oxotropic rearrangement by carbon dioxide in ethanol. The alcohol finally obtained was identical with our *trans*-alcohol (*E*)-(8; R = CH₂·OH) and the aldehyde identical with that obtained from the latter by oxidation with chromium trioxide in aqueous pyridine.⁸

The formation, in the carbon dioxide-induced rearrangement, of the sterically more hindered ester as major product prompted an investigation of this reaction in other systems. Indan-1-one reacted normally with ethoxyethynylmagnesium bromide to yield the hydroxy-ethoxyethynyl derivative (11); this compound was even more prone to dehydration [to compound (12)] than the

tetralone analogue (5). It was, therefore, used immediately after its preparation. Two esters, (13; R = CO₂Et) and (14; R = CO₂Et) were formed in the ratio 83:17. In a separate experiment it was established that compound (12) was unaffected by the reagent. The i.r. carbonyl absorptions of the two esters appeared at 1713 and 1704 cm⁻¹, respectively thus making it unlikely for there to be $\beta\gamma$ -unsaturation. The major product showed in its n.m.r. spectrum a singlet at τ 4.06 (1H) in accord with the *cis*-structure (13; R = CO₂Et); the corresponding absorption for the minor product (14; R = CO₂Et), however, was a triplet (J 2.2 Hz) at τ 3.67. The meagre amount of this compound prompted us to obtain it from the more abundant *cis*-compound (13; R = CO₂Et). The latter, when refluxed for a short time with a solution of *N*-bromosuccinimide in carbon tetrachloride,⁹ was largely transformed into the *trans*-isomer (14; R = CO₂Et). This compound, when subjected to an osmium tetroxide catalysed sodium periodate oxidation¹⁰ gave indan-1-one. The assignment of the exocyclic position to the double bond in compound (14; R = CO₂Et) was therefore secure. The n.m.r. triplet at τ 3.67 for the ester (14; R = CO₂Et) must therefore be due to allylic coupling with the alicyclic protons at C-2.

When either the 83:17 mixture of the compounds (13; R = CO₂Et) and (14; R = CO₂Et) or the compound (12) was refluxed in ethanol containing a little hydrogen chloride the product was an approximately 50:50 mixture of the *trans*- (14; R = CO₂Et) and $\beta\gamma$ -unsaturated (15; R = CO₂Et) esters.¹¹ An exactly similar mixture resulted from the Reformatskii reaction¹² between indan-1-one and ethyl bromoacetate when the intermediary hydroxy-ester was dehydrated with hot 98% formic acid. This mixture of esters proved to be inseparable; on hydrolysis it was converted largely into the $\beta\gamma$ -unsaturated acid (15; R = CO₂H), from which the pure ester (15; R = CO₂Et) could be made only by treatment with dimethylformamide diethyl acetal.¹³ The best way of preparing this ester, however, was to esterify the benzofulvenecarboxylic acid (16)^{14,15} by the usual Fischer-Speier procedure and reduce the product in ether solution with aluminium amalgam (83% yield; g.l.c. pure). The olefinic protons in compounds (15; R = CO₂Et) and (15; R = CO₂H) were only slightly coupled (J ca. 1 Hz) to the adjacent methylene protons. The *cis*-acid (13; R = CO₂H) was prepared from its ester by the action of alcoholic barium hydroxide at room temperature for 3 days. However, all attempts to hydrolyse the *trans*-ester (14; R = CO₂Et) to its acid

⁶ T. I. Sorokina, I. I. Zaretskaya, and I. V. Torgov, *Doklady Akad. Nauk, S.S.S.R.*, 1959, **129**, 345.

⁷ E. B. Bates, E. R. H. Jones, and M. C. Whiting, *J. Chem. Soc.*, 1954, 1854; J. D. Chanley and H. Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140.

⁸ R. H. Cornforth, J. W. Cornforth, and C. Popjak, *Tetrahedron*, 1962, **18**, 1351.

⁹ A. Bruylants, *Bull. Soc. chim. belges*, 1950, **59**, 107; E. Ucciani, J. Chouteau, and M. Naudet, *Bull. Soc. chim. France*, 1960, 1511; B. P. McGrath and J. M. Tedder, *Proc. Chem. Soc.*, 1961, 80; A. Löffler, R. J. Pratt, H. P. Rüesch, and A. S. Dreiding, *Helv. Chim. Acta*, 1970, **53**, 383.

¹⁰ R. Pappo, D. S. Allen, R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, 1956, **21**, 478.

¹¹ Cf. tautomerism of $\alpha\beta$ - and $\beta\gamma$ -unsaturated acids discussed by G. A. Kon, R. P. Linstead, and G. W. G. MacLennan, *J. Chem. Soc.*, 1932, 2454.

¹² J. von Braun, E. Danziger, and Z. Koehler, *Ber.*, 1917, **50**, 56; D. A. H. Taylor, *J. Chem. Soc.*, 1960, 2805; H. Ahmed and N. Campbell, *ibid.*, p. 4115.

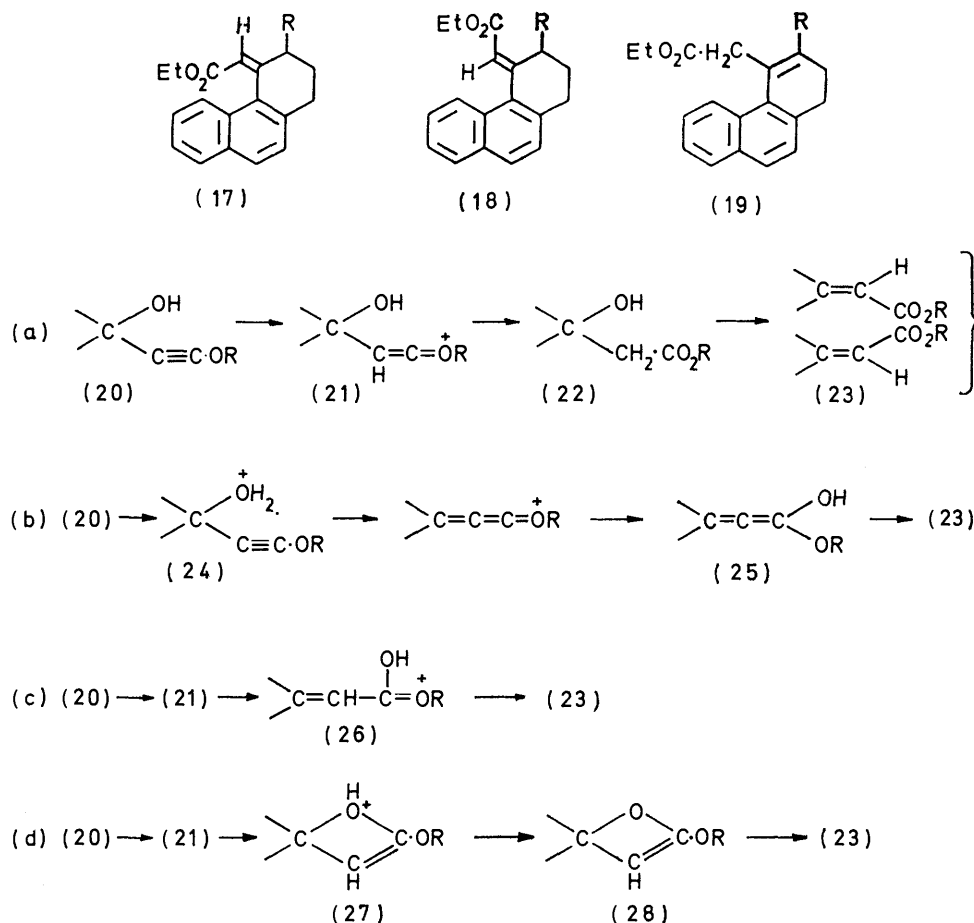
¹³ H. Brechbühler, H. Büchi, E. Hatz, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, 1965, **48**, 1746.

¹⁴ W. Wislicenus, *Ber.*, 1900, **33**, 771; J. Thiele, *ibid.*, p. 851.

¹⁵ J. Thiele and M. Rüdiger, *Annalen*, 1906, **347**, 275.

were frustrated by conversion into the foregoing $\beta\gamma$ -unsaturated acid (15; R = CO₂H), probably by the mechanism indicated. This acid has been prepared previously from the benzofulvenecarboxylic acid (16)¹⁵ as well as from indan-1-one,¹² although the assignment of the double bond position has relied to some extent on analogy and precedent. Previous workers do not seem have realised sufficiently the tautomeric mobility of the indene system.

nesium bromide followed by rearrangement of the product produced two esters in the ratio 60:40. The olefinic proton signals (n.m.r.) occurred at τ 3.85 and 3.78, respectively, the latter being the broader of the two. The methylene quartet and methyl triplet of the ethoxy-group were centred at τ 6.26 and 9.35 for the major compound and at τ 5.76 and 8.72 for the minor product. The former values are consistent with a strong shielding influence derived from the aromatic ring and



The compound (11) was treated with lithium aluminium hydride in ether. One portion of the ethoxyvinyl compound so formed was treated with carbon dioxide in ethanol and the other with dilute sulphuric acid. The crude products had similar n.m.r. spectra, τ 3.54 (intense) and 3.98. Purification gave an aldehyde which had only the τ 3.54 absorption (d, J 8 Hz). On this evidence the compound is assigned the *trans*-structure (14; R = CHO).

A somewhat severe test for the formation of a *cis*-ester is that leading to compound (17; R = H). Models show that steric crowding leads to eclipsing at C-1 and C-2 and that full rotation of the ethoxycarbonyl group demands the rotation in unison of bonds in the alicyclic ring. In one conformation the ethyl group lies directly over the naphthalene ring. The reaction between 2,3-dihydrophenanthren-4(1*H*)-one and ethoxyethynylmag-

consequently this ester is assigned structure (17; R = H). The other ester, therefore, should be the *trans*-compound (18; R = H). Further confirmation of these assignments was provided by the Reformatskii reaction. Thermal dehydration of the initially produced hydroxy-ester gave two unsaturated esters, one of which (30% of the product) was identical with the minor (40%) product from the ethoxyacetylene reaction. This further supports the *trans*-stereochemistry already assigned to this compound. The third unsaturated ester, the major product from the Reformatskii reaction, must, therefore, have structure (19; R = H). The olefinic proton signal is recognisable in the n.m.r. spectrum as a triplet (J 5 Hz) at τ 3.65. The double bond in the *cis*-compound (17; R = H) was too sterically hindered to be affected either by sodium ethoxide or by hydrochloric acid in ethanol. However, by briefly

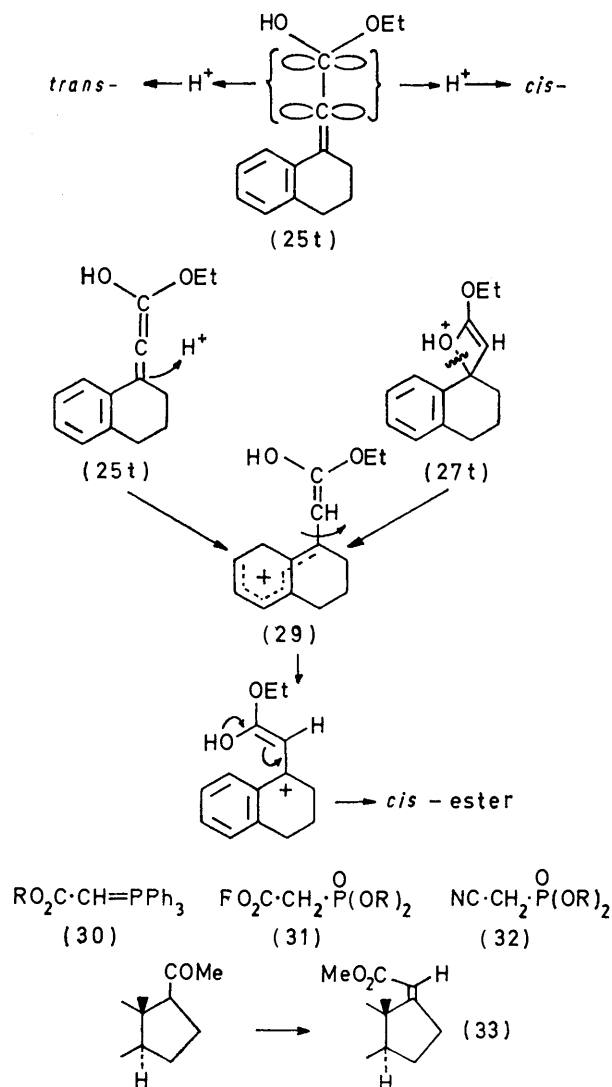
refluxing its solution in carbon tetrachloride with *N*-bromosuccinimide it was converted entirely into its *trans*-isomer (18; R = H).

Four mechanisms have been proposed for the conversion of α -hydroxyethynyl alkyl ethers (20) into $\alpha\beta$ -unsaturated esters. The first¹⁶ (a) involves hydration of the triple bond followed by loss of water. Such a mechanism does not account for the different products obtained in this and the Reformatskii reaction and was, indeed, discounted by Sarett,¹⁷ who showed that one compound of type (22) was unaffected by conditions which changed a congener (20) into an ester (23). Shchukina and Rubtsov¹⁸ proposed the sequence (b) leading to the allene (25) and thence by a tautomerisation to the final product (23). Sarett¹⁷ suggested (c) an initial protonation of the triple bond [to (21)] and thence a 1,3 shift of OH to yield (26) which then lost a proton to yield the final product. The most recent proposal (d) is that of Hekkert and Drenth¹⁹ and involves modification of Sarett's scheme (c) in that the intermediate (21) is considered to undergo cyclisation to (27) and thence to (28).

None of these schemes explains satisfactorily the formation of the higher energy *cis*-esters. For scheme (b) the allene intermediate (25t) (the tetralin ring system being used for illustration) can be protonated at the central *sp*-hybridised carbon atom²⁰ from either the aromatic or the alicyclic side of the terminal double bond. Alicyclic approach would lead to a *cis*-ester but for this it is necessary to postulate that the solvated proton is more sterically demanding than the C(OH)(OEt) group. This is unlikely. In scheme (c) the most probable conformation for the intermediate (21) would be that with the unsaturated side chain *trans*-oriented with respect to the aromatic nucleus and this would undoubtedly give rise to the *trans*-ester. For Hekkert and Drenth's scheme (d) the rearrangement of the oxetan (28), it is now realised,²¹ would be an electrocyclic reaction. The C-O σ -bond would thus undergo thermal fission in a conrotatory manner, but, unlike the cyclobutene-cyclobutadiene case,²¹ the ether oxygen is simply transformed into carbonyl oxygen for which, of course, *cis*- and *trans*-terms have no meaning. In effect both enantiomers of (28) would undergo conrotatory bond fission but in opposite senses and thus lead to the same product; on energetic grounds this should be the *trans*-ester.

The preferential formation of the *cis*-esters can be explained if electron participation of the aryl nuclei is invoked. Thus the protonation of the allene (25t) (electron abstraction from the penultimate double bond) can lead to (29); for maximum overlap of orbitals it now becomes necessary for the two-carbon system to undergo rotation by 90° about the carbon-carbon single bond.

Rotation in the direction illustrated brings together the electron-deficient (and positively charged) aromatic system and the electron-replete oxygen functions. Normal conjugative electron movements can then give rise to the *cis*-ester. The intermediate (29) may also conceivably arise by a carbon-oxygen fission in the ion (27t). If oxetan intermediates such as (27t) are involved in the ethoxyethynyl carbinol- $\alpha\beta$ -unsaturated ester conversion then transfer of oxygen will be expected to be intramolecular; it is hoped to be able to test this by oxygen-labelling experiments.



Other routes to $\alpha\beta$ -unsaturated esters involve the well-known Reformatskii, Wittig, and Favorskii reactions. The final result of the Reformatskii reaction is not predictable, as the intermediary β -hydroxy-esters can undergo dehydration to yield $\beta\gamma$ -unsaturated products. The reaction is also subject to steric hindrance. Thus

¹⁶ G. L. Hekkert and W. Drenth, *Rec. Trav. chim.*, 1961, **80** 1285.

¹⁷ C. U. Pittman, *Chem. Comm.*, 1969, 122.

¹⁸ M. N. Shchukina and I. A. Rubtsov, *J. Gen. Chem. (U.S.S.R.)*, 1948, **18**, 1645.

¹⁹ Sir Ian Heilbron, E. R. H. Jones, M. Julia, and B. C. L. Weedon, *J. Chem. Soc.*, 1949, 1823.

²⁰ C. E. Arth, G. I. Poos, R. M. Lukes, F. M. Robinson, W. F. Johns, M. Feurer, and L. H. Sarett, *J. Amer. Chem. Soc.*, 1954, **76**, 1715.

²¹ R. B. Woodward and R. Hoffmann, 'The Conservation of Orbital Symmetry,' Academic Press, New York, 1970.

3-methyl-2,3-dihydrophenanthren-4(1H)-one, like certain 17-oxo-steroids, will not undergo the Reformatskii reaction.²² This compound reacts smoothly in the ethoxyacetylene reaction to yield, after rearrangement of the carbinol produced, the two esters (17; R = Me) and (18; R = Me).²³ The mildness of the ethoxyacetylene method is attested in its use in two syntheses of cardenolides,²⁴ as the carbonyl components in both cases possessed readily eliminable tertiary hydroxy-groups. The three Wittig reagents are the compounds (30)—(32). Methoxycarbonylmethylenetriphenylphosphorane (30; R = Me) reacts well with aldehydes²⁵ (particularly if $\alpha\beta$ -unsaturated) but not with ketones.²⁶ Triethyl phosphonoacetate (31) also reacts well with aldehydes²⁷ but with ketones it is sterically selective.²⁶ The compound does not react with 6-methoxy-1-tetralone² or with 2,3-dihydrophenanthren-4(1H)-one.²³ Diethyl cyanomethylphosphonate (32) is the most reactive of the three Wittig reagents; in steroids²⁸ only carbonyl functions at C-1 and C-11 do not react. However, the hydrolysis of the nitrile group can present serious difficulty.²⁹ In the conversion of 11 α -hydroxyprogesterone into cortisone Hogg and his associates³⁰ made the important observation that the 20-oxopregnane side chain could be transformed stereoselectively into a *cis*-17(20)-ene ester (33) by a Favorskii-type procedure.

EXPERIMENTAL

All evaporations were performed under reduced pressure. M.p.s refer to specimens in open capillary tubes. I.r. peaks are given in descending order of intensity. U.v. spectra were taken for solutions in 95% ethanol. N.m.r. spectra were taken with a Perkin-Elmer R10 60 MHz instrument, with tetramethylsilane as internal standard and deuteriochloroform as solvent. pK_a values were determined for solutions in ethanol-water (50.1% ethanol w/w)³¹ by titration with sodium hydroxide in 50.1% ethanol, the results being recorded on a Radiometer automatic titrator (type TTT.Lc) and Titragraph recorder (type SBR.2c). Kieselgel GF 254 was used for layer chromatography. The samples were applied in chloroform; the plates were dried at 80° for 5 min, and then developed first with benzene and then with a 9 : 1 (v/v) mixture of petroleum (b.p. 60—80°) and acetone. Petroleum refers to the fraction of b.p. 60—80°.

Spectroscopic data are given in the Table.

Ethoxyacetylene,³² 6-methoxytetralin,² and 6-methoxy-1-tetralone³³ were made by published methods.

Ethyl cis-1,2,3,4-Tetrahydro-6-methoxy-1-naphthylideneacetate (Z)-(8; R = CO₂Et), *Ethyl trans*-1,2,3,4-Tetrahydro-6-methoxy-1-naphthylideneacetate (E)-(8; R = CO₂Et), and *Ethyl 3,4-Dihydro-6-methoxy-1-naphthylacetate* (9).—Mag-

²² J. W. Cook and C. L. Hewitt, *J. Chem. Soc.*, 1934, 365.

²³ Present work.

²⁴ N. Danieli, Y. Mazur, and F. Sondheimer, *J. Amer. Chem. Soc.*, 1962, **84**, 875; R. Deghenghi, A. Philipp, and R. Gaudry, *Tetrahedron Letters*, 1963, 2045.

²⁵ O. Isler, L. H. Chopard-dit-Jean, M. Montavon, R. Rüegg, and P. Zeller, *Helv. Chim. Acta*, 1957, **40**, 1256.

²⁶ A. K. Bose and R. T. Dahill, *J. Org. Chem.*, 1965, **30**, 505.

²⁷ D. H. Wadsworth, O. E. Schupp, E. J. Sens, and J. A. Ford, *J. Org. Chem.*, 1965, **30**, 680; T. H. Kinstle and B. Y. Mandanas, *Chem. Comm.*, 1968, 1699.

²⁸ A. K. Bose and R. M. Ramer, *Steroids*, 1968, **11**, 27.

nesium (2.6 g; washed with dilute hydrochloric acid, water, and acetone, and oven-dried at 80° for 15 min) was placed in a dry three-necked flask with one crystal of iodine. The flask was flame-heated and the iodine vapours removed by suction pump. A magnetic follower was put in and the flask was then equipped with a gas inlet, a reflux condenser with guard tube, and a dropping funnel. The air was replaced by dry oxygen-free nitrogen and then one third of a solution of dry ethyl bromide (10.9 g) in dry ether (150 cm³) was run in, the remainder being added more cautiously. At the end of the reaction the solution was stirred for 1 h. Ethoxyacetylene (7 g) in dry ether (30 cm³) was added dropwise (effervescence). To the two-phase system 6-methoxy-1-tetralone (8.8 g) in sodium-dried benzene (200 cm³) was added. The mixture, now homogeneous, was stirred for 1 h before being poured into ice-ammonium chloride solution. Work-up by ether extraction gave a light brown oil (13 g) which was checked (i.r.) for OH absorption. The oil was dissolved in 95% ethanol (150 cm³) and solid carbon dioxide (0.05 g) was added. The flask was loosely stoppered and left overnight. The solvent was then evaporated off and the product again checked (i.r.) for OH, C≡C, and CO absorption. The mixture was separated by preparative layer chromatography (p.l.c.) into the *cis*-ester (Z)-(8; R = CO₂Et) (oil; 72%) (Found: C, 72.85; H, 7.05. C₁₅H₁₈O₃ requires C, 73.15; H, 7.35%) and the *trans*-ester (E)-(8; R = CO₂Et) (oil; 28%) (Found: C, 73.1; H, 7.3%).

Gently heating 1-ethoxyethynyl-1,2,3,4-tetrahydro-6-methoxy-1-naphthol (5) or keeping it under nitrogen for 2 days gave the unstable 1-ethoxyethynyl-6-methoxy-3,4-dihydronaphthalene (6), which was purified by p.l.c. and used immediately. Alcohol containing hydrochloric acid (3% conc. acid) gave a product identical with that obtained by the Reformatskii reaction⁵ between 6-methoxy-1-tetralone and ethyl bromoacetate using 98% formic acid for the dehydration step. This consisted of the *trans*-ester (E)-(8; R = CO₂Et) (30%) and *ethyl 3,4-dihydro-6-methoxy-1-naphthylacetate* (9) (oil; 70%) (Found: C, 73.10; H, 7.45. C₁₅H₁₈O₃ requires C, 73.14; H, 7.37%), which were separated by p.l.c.

The *cis*-ester was stable in air; the *trans*-compound slowly formed 6-methoxy-1-tetralone, and ethyl 3,4-dihydro-6-methoxy-1-naphthylacetate gave a mixture of products containing peroxides.

The esters (1 g) were separately hydrolysed by the action of potassium hydroxide (5 g) in methanol (80 cm³) and water (20 cm³) under nitrogen at 55° for 12 h to give *cis*-1,2,3,4-tetrahydro-6-methoxy-1-naphthylideneacetic acid, needles, m.p. 152° (from aqueous ethanol) (Found: C, 71.8; H, 6.5. C₁₃H₁₄O₃ requires C, 71.55; H, 6.45%), pK_a 6.85; *trans*-1,2,3,4-tetrahydro-6-methoxy-1-naphthylideneacetic acid, needles, m.p. 189° (from aqueous ethanol) (Found: C, 71.5; H, 6.5%), pK_a 6.94; and 3,4-dihydro-6-methoxy-1-

²⁹ B. Gadsby, M. R. G. Leeming, G. Greenspan, and H. Smith, *J. Chem. Soc. (C)*, 1968, 2647; D. K. Patel, V. Petrow, R. Royer, and I. A. Stuart-Webb, *J. Chem. Soc.*, 1952, 161.

³⁰ J. A. Hogg, P. F. Beal, A. H. Nathan, F. H. Lincoln, W. P. Schneider, B. J. Magerlein, A. R. Hanze, and R. W. Jackson, *J. Amer. Chem. Soc.*, 1955, **77**, 4436; R. E. Marker, H. M. Crooks, E. M. Jones, and A. C. Shabica, *ibid.*, 1942, **64**, 1276.

³¹ E. Grunwald and B. J. Berkowitz, *J. Amer. Chem. Soc.*, 1951, **73**, 4939.

³² G. Eglinton, E. R. H. Jones, B. L. Shaw, and M. C. Whiting, *J. Chem. Soc.*, 1954, 1860.

³³ S. N. Ananchenko, A. V. Platonova, V. N. Leonov, and I. V. Torgov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1961, 1074.

Spectroscopic data [τ values; $\nu(=\nu_{\max})$ in cm^{-1} ; $\lambda(=\lambda_{\max})$ in nm with ϵ in parentheses]

Compound	Compound	Compound
(Z)-(8); R = CO ₂ Et	τ 2.2—2.5 [1H, m, C(8)H], 4.33 (1H, s, C=CH), 7.18 [2H, t, <i>J</i> 6.3 Hz, C(2)H ₂], 7.53 [2H, split t, <i>J</i> 6.3 Hz, C(4)H ₂], 7.84—8.35 [2H, m, C(3)H ₂]; $\nu(\text{film})$ 1718; λ 304 (10,300).	(14; R = CHO)
(Z)-(8); R = CO ₂ H	τ -1.3br (1H, s, CO ₂ H), 4.31 (1H, s, C=CH); $\nu(\text{KBr})$ 1662; λ 296 (10,500).	(15; R = CO ₂ Et)
(Z)-(8); R = CH ₂ ·OH	τ 4.43 (1H, t, <i>J</i> 7 Hz, C=CH), 5.63 (2H, slightly split d, <i>J</i> 7 Hz, CH ₂ ·OH), 7.42 (1H, s, OH); $\nu(\text{film})$ 3390; λ 261 (10,950).	(15; R = CO ₂ H)
(E)-(8); R = CO ₂ Et	τ 2.2—2.49 [1H, m, C(8)H], 3.78 (1H, s, C=CH), 6.82 [2H, split t, <i>J</i> 6.25 Hz, C(2)H ₂], 7.26 [2H, t, <i>J</i> 6.25 Hz, C(4)H ₂], 7.95—8.43 [2H, m, C(3)H ₂]; $\nu(\text{film})$ 1705; λ 315 (18,450), 302sh (16,400).	(17; R = H)
(E)-(8); R = CO ₂ H	τ 1.0br (1H, s, CO ₂ H), 3.79 (1H, s, C=CH); $\nu(\text{KBr})$ 1680; λ 297 (16,300), 312 (17,000).	<i>cis</i> -1,2,3,4-Tetrahydro-4-phenanthrylideneacetic acid
(E)-(8); R = CH ₂ ·OH	τ 3.95 (1H, t, <i>J</i> 7 Hz, C=CH), 5.70 (2H, slightly split d, <i>J</i> 7 Hz, CH ₂ ·OH), 7.64 (1H, s, OH); $\nu(\text{film})$ 3373, λ 269 (11,275).	(17; R = Me)
(E)-(8); R = CHO	τ -0.2 (1H, d, <i>J</i> 8 Hz, CHO), 3.54 (1H, slightly split d, <i>J</i> 8 Hz, C=CH); $\nu(\text{KBr})$ 1651; λ 240 (19,500), 325 (15,010), 232—237sh (10,300).	<i>cis</i> -1,2,3,4-Tetrahydro-3-methyl-4-phenanthrylideneacetic acid
(9; R = CO ₂ Et)	τ 2.75—2.95 [1H, m, C(8)H], 4.16 (1H, t, <i>J</i> 4 Hz, C=CH), 6.63 (2H, s, CH ₂ ·CO ₂ Et); $\nu(\text{film})$ 1740; λ 274 (8850).	(18; R = H)
(9; R = CO ₂ H)	τ -1.25 (1H, s, CO ₂ H), 4.11 (1H, t, <i>J</i> 5 Hz, C=CH); $\nu(\text{KBr})$ 1698; λ 271 (13,000).	<i>trans</i> -1,2,3,4-Tetrahydro-4-phenanthrylideneacetic acid
(9; R = CH ₂ ·OH)	$\tau(\text{CDCl}_3)$ 4.23 (1H, t, <i>J</i> 5 Hz, C=CH), 8.0 (1H, s, OH); $\tau(\text{C}_6\text{D}_6)$ 6.26 (2H, t, <i>J</i> 7 Hz, CH ₂ ·CH ₂ ·OH); $\nu(\text{film})$ 3390; λ 270 (11,600).	(18; R = Me)
(9; R = CH ₂ Cl)	$\tau(\text{CDCl}_3)$ 2.8—3.02 [1H, m, C(8)H], 3.23—3.47 [2H, m, C(5)H and C(7)H], 4.27 (1H, t, <i>J</i> 4 Hz, C=CH), 6.28 (1H, s, OCH ₃), 6.42 (2H, t, <i>J</i> 8 Hz, CH ₂ Cl), 7.0—7.52 (4H, m, (CH ₂ ·CH ₂ ·Cl and 2 alicyclic H's), 7.6—8.0 [2H, m, C(3)H ₂]; $\tau(\text{C}_6\text{D}_6)$ 6.6 (3H, s, OCH ₃), 6.55 (2H, t, <i>J</i> 8 Hz, CH ₂ ·CH ₂ Cl); $\nu(\text{film})$ 1608, 826; λ 271 (10,220).	(19; R = H)
(9; R = CH ₂ Br)	τ 4.22 (1H, t, <i>J</i> 4 Hz, C=CH), 6.52 (2H, t, <i>J</i> 7 Hz, CH ₂ Br), 7.55—8.05 [2H, m, C(3)H ₂] (double irradiation at τ 7.73 caused the triplet at τ 4.22 to collapse to a singlet); $\nu(\text{film})$ 1608, 872, 850; λ 271 (11,200).	naphthylacetic acid, plates, m.p. 80° (from petroleum) (Found: C, 71.5; H, 6.9%), pK_a 5.97 Gortz ⁴ (quoted by Schroeter ⁵) has obtained acids of m.p. 75—76 and 182—183° from a Reformatskii reaction.
(13; R = CO ₂ Et)	τ 1—1.3 [1H, m, C(7)H], 4.06 (1H, s, 7.1 (4H, s, alicyclic H's); $\nu(\text{film})$ 1713; λ 288 (11,900), 304 (11,300).	2-(3,4-Dihydro-6-methoxy-1-naphthyl)ethanol (9; R = CH ₂ ·OH).—The ester (9; R = CO ₂ Et) (0.75 g) in tetrahydrofuran (6 cm ³) was added to lithium aluminium hydride (0.23 g) in tetrahydrofuran (6 cm ³). Work-up followed by p.l.c. gave the alcohol (9; R = CH ₂ ·OH) as a pale yellow oil (0.49 g, 83%) (Found: C, 76.35; H, 8.05. C ₁₃ H ₁₆ O ₂ requires C, 76.45; H, 7.9%). Reduction in the same way of the <i>cis</i> - and <i>trans</i> -esters (8; R = CO ₂ Et) gave the corresponding alcohols as oils.
(13; R = CO ₂ H)	τ -1.52br (1H, s, CO ₂ H), 1—1.3 [1H, m, C(7)H], 3.97 (1H, s, C=CH), 7.05 (4H, s, alicyclic H's); $\nu(\text{KBr})$ 1681; λ 274 (12,200), 283 (12,000), 306 (11,200).	<i>trans</i> -1,2,3,4-Tetrahydro-6-methoxy-1-naphthylideneacetaldehyde (E)-(8; R = CHO).—(a) The <i>trans</i> -alcohol (E)-(8; R = CH ₂ ·OH) (0.6 g) in AnalaR pyridine (2 cm ³) was added to a cold (0°) solution of chromium trioxide (1 g) in water
(14; R = CO ₂ Et)	τ 3.67 (1H, t, <i>J</i> 2.2 Hz, C=CH); $\nu(\text{film})$ 1704; λ 224 (14,750), 235 (14,700), 256 (14,100), 264sh (12,250).	

(0.6 cm³) and pyridine (10 cm³); the mixture was left for 2 h then poured into water and filtered through Celite. The pad and the filtrate were thoroughly extracted with ether. Work up gave the aldehyde (*E*)-(8; R = CHO) (0.44 g) (70%), pale yellow prisms, m.p. 94–95° (from ethyl acetate), identical with a specimen prepared by a published route⁶ and by the following method.

(b) 1-Ethoxyethynyl-1,2,3,4-tetrahydro-6-methoxy-1-naphthol (5), prepared from 6-methoxy-1-tetralone (2.5 g), was added dropwise, in ether (20 cm³) to lithium aluminium hydride (1.19 g) in ether (120 cm³) at 0°. The mixture was allowed to warm to 15° over 2 h (with stirring) and worked up by the addition of acetone and then Rochelle salt in water. Ether extraction followed by p.l.c. of the product gave 1-(2-ethoxyvinyl)-1,2,3,4-tetrahydro-6-methoxy-1-naphthol (7), which crystallised from petroleum at –80° [ν_{\max} (KBr) 1585, 1648, 1230, 1610, 1500, and 840 cm⁻¹]. Its solution in ethanol saturated with carbon dioxide gave the aldehyde, m.p. 94–95°, reported in (a).

Ethyl cis-Indan-1-ylideneacetate (13; R = CO₂Et) and *Ethyl trans-Indan-1-ylideneacetate* (14; R = CO₂Et).—When the Grignard reaction was performed as in the preceding case the product was mainly 1-ethoxyethynylindene (12). Making the solutions more concentrated and reducing the molar ratio of Grignard reagent to ketone from 2 : 1 to 3 : 2 proved satisfactory. The quantities employed were magnesium (2.6 g), ether (90 cm³), ethyl bromide (10.9 g), ethoxyacetylene (7.2 g), indan-1-one (10 g), and benzene (70 cm³). The pale brown crude carbinol (11) was dissolved in 95% ethanol saturated with carbon dioxide and the mixture worked up after 12 h. The product, obtained in almost quantitative yield, was a 83 : 17 mixture (n.m.r. evidence) of *cis*- (13; R = CO₂Et) (Found: C, 77.65; H, 7.0. C₁₃H₁₄O₂ requires C, 77.2; H, 7.0%) and *trans*- (14; R = CO₂Et) esters, which were separated by p.l.c. Both compounds were oils.

Ethyl cis-indan-1-ylideneacetate (13; R = CO₂Et) (1 g) was refluxed in carbon tetrachloride (12 cm³) with freshly recrystallised *N*-bromosuccinimide (0.385 g) for 10 min. The mixture was cooled, the solid removed, and the solution evaporated. Chromatography gave the *cis*-ester (0.25 g) and ethyl *trans*-indan-1-ylideneacetate (0.51 g). The latter (0.20 g) in a stirred mixture of dioxan (9 cm³) and water (1 cm³) was treated with osmium tetroxide (0.02 g) and after 30 min sodium periodate (0.43 g) was added in portions during 5 h. After a further 16 h, work-up gave a liquid which by p.l.c. was separated into unchanged ethyl *trans*-indan-1-ylidene acetate and indan-1-one, the latter being identical with an authentic specimen.

cis-Indan-1-ylideneacetic acid (13; R = CO₂H), formed by hydrolysis of the ethyl ester, formed microprisms, m.p. ca. 130° (sintering at ca. 120°) [from petroleum (b.p. 40–60°)] (Found: C, 76.25; H, 5.95. C₁₁H₁₀O₂ requires C, 75.85; H, 5.8%), p*K*_a 6.70. Both the melt and the mother liquors from the crystallisation furnished specimens of the isomeric $\beta\gamma$ -unsaturated acid (see later).

Inden-3-ylacetic Acid (15; R = CO₂H).—The Grignard reaction between ethoxyethynylmagnesium bromide and indan-1-one (6.6 g) carried out as for 6-methoxy-1-tetralone gave a pale brown oil (8.2 g) [OH deficient (i.r.)], which could be purified by p.l.c. to yield the unstable 3-ethoxyethynylindene (12). The crude material (8.0 g) was refluxed for 2 h in ethanol (60 cm³) containing concentrated hydrochloric acid (0.2 cm³). Work-up gave a liquid which on n.m.r. evidence was a mixture of ethyl inden-3-ylacetate

(50%) and ethyl *trans*-indan-1-ylideneacetate (50%). An identical product was formed from the Reformatskii reaction¹² between indan-1-one and ethyl bromoacetate followed by dehydration of the initially formed hydroxy-ester with hot 98% formic acid.

Hydrolysis [mixed esters (3 g), potassium hydroxide (1 g), water (5 cm³), methanol (45 cm³)] followed by crystallisation of the product from petroleum gave inden-3-ylacetic acid (15; R = CO₂H), m.p. 95–96° (Found: C, 76.05; H, 5.9; Calc. for C₁₁H₁₀O₂: C, 75.85; H, 5.8%) (lit.,¹² m.p. 93–95°; lit.,¹⁵ 95–96°), p*K*_a 5.79.

The acid (0.25 g) in dry benzene (6 cm³) was treated with dimethylformamide diethyl acetal (0.34 g) and the mixture refluxed for 90 min. Work-up gave an oil, *ethyl inden-3-ylacetate* (15; R = CO₂Et) (0.20 g) purified by p.l.c. (Found: C, 77.25; H, 6.9. C₁₃H₁₄O₂ requires C, 77.2; H, 7.0%). The same compound was prepared from benzofulvene-8-carboxylic acid¹⁵ (16) as follows. The acid (1 g) was refluxed for 3 h with absolute ethanol (30 cm³) and concentrated hydrochloric acid (1 cm³). Removal of solvent gave the ethyl ester (1.15 g). The latter (1 g) in ether (50 cm³) was treated with freshly prepared aluminium amalgam (6 g) and the mixture vigorously stirred with periodic additions of small amounts of water. After 3 h, the solids were removed and washed with ether. The combined liquid phase was dried (MgSO₄) and evaporated. The product (0.84 g) was pure ethyl inden-3-ylacetate (15; R = CO₂Et).

trans-Indan-1-ylideneacetaldehyde.—Indan-1-one (2 g) was treated with ethoxyethynylmagnesium bromide as previously described. The crude 1-ethoxyethynylindan-1-ol in dry ether (25 cm³) was added to a stirred mixture of lithium aluminium hydride (0.84 g) and ether (75 cm³). After 3 h the excess of reagent was destroyed with acetone, the mixture quenched with aqueous Rochelle salt, and the product extracted into ether. The solution was washed with water, then dried (MgSO₄) and evaporated. The product was dissolved in 95% ethanol (50 cm³) and divided into two equal parts. One was saturated with carbon dioxide, left overnight, and then evaporated. The other was treated with 5% sulphuric acid (0.1 cm³), then stirred for 45 min before being diluted with water and extracted with ether. The ether solution after being washed with water and dried (MgSO₄) was evaporated. The products in both cases gave identical n.m.r. spectra. P.l.c. furnished *trans-indan-1-ylideneacetaldehyde* (14; R = CHO) as pale yellow prisms, m.p. 69° (Found: C, 82.95; H, 6.4. C₁₁H₁₀O requires C, 83.5; H, 6.35%).

Ethyl cis-1,2,3,4-Tetrahydro-4-phenanthrylideneacetate (17; R = H) and *Ethyl trans-1,2,3,4-Tetrahydro-4-phenanthrylideneacetate* (18; R = H).—The reaction between 2,3-tetrahydrophenanthren-4(1*H*)-one (5.57 g) and ethoxyethynylmagnesium bromide was conducted as for indan-1-one. The crude carbinol (6.4 g), a brown oil, was dissolved in 95% ethanol (150 cm³); the solution was saturated with carbon dioxide and left overnight. Work-up in the usual way gave the *cis*-ester (17; R = H) (60%) (Found: C, 80.9; H, 7.0. C₁₅H₁₈O₂ requires C, 81.15; H, 6.8%) as prisms, m.p. 44–45°, and the *trans*-ester (18; R = H) (40%) as an oil. Hydrolysis of these esters gave respectively *cis*-1,2,3,4-tetrahydro-4-phenanthrylideneacetic acid, needles (from ether-petroleum) m.p. 183° (Found: C, 80.6; H, 5.95. C₁₆H₁₄O₂ requires C, 80.65; H, 5.9%), p*K*_a 6.65, and *trans*-1,2,3,4-tetrahydro-4-phenanthrylidene acetic acid, needles (from benzene-petroleum), m.p. 179° (Found: C, 80.6; H, 6.0%), p*K*_a 6.55.

The *cis*-ester (17; R = H) (0.22 g), treated with *N*-bromosuccinimide (0.15 g) in boiling carbon tetrachloride (5 cm³) for 5 min, gave the *trans*-isomer, isolated in pure form by p.l.c.

1,2-Dihydro-4-phenanthrylacetic Acid.—Ethyl bromoacetate (purified) (4.9 g), benzene (15 cm³), and 2,3-dihydrophenanthren-4(1*H*)-one (5.0 g) were refluxed with zinc wool (2.5 g) for 3 h. Work-up gave the crude hydroxyester (*ca.* 6.7 g), which was dehydrated by distillation (b.p. *ca.* 166° at 0.27 mmHg). The product was separated by p.l.c. into ethyl *trans*-1,2,3,4-tetrahydro-4-phenanthrylidene acetate (18; R = H) (τ 3.78, singlet) (30%) and ethyl 1,2-dihydro-4-phenanthrylacetic acid (19; R = H) (τ 3.65, triplet) (70%) containing some unchanged ketone. Hydrolysis of the last fraction with barium hydroxide (1 g) in 50% aqueous ethanol for 3 days at 15° under nitrogen gave, on work-up, 1,2-dihydro-4-phenanthrylacetic acid, plates (from petroleum) (orange yellow tinge), m.p. 124° (Found: C, 80.7; H, 5.85. C₁₆H₁₄O₂ requires C, 80.65; H, 5.9%), p*K*_a 6.63. Cook and Hewett²² have reported an acid of m.p. 173–174° from a Reformatskii reaction. If this acid

is the *trans*-acid (see before) then the cyclisation to 1,2,3,4-tetrahydrophenanthren-5-one reported by these authors must involve a double-bond shift.

2,3-Dihydro-3-methylphenanthren-4(1*H*)-one was prepared by cyclisation with polyphosphoric acid of α -methyl- γ -2-naphthylbutyric acid.³⁴ Obtained from it by methods similar to those recorded here were ethyl *cis*-1,2,3,4-tetrahydro-3-methyl-4-phenanthrylideneacetate (17; R = Me) (*ca.* 45% of the product), an oil (Found: C, 81.5; H, 7.25. C₁₉H₂₀O₂ requires C, 81.4; H, 7.2%) and ethyl *trans*-1,2,3,4-tetrahydro-3-methyl-4-phenanthrylideneacetate, (18; R = Me) (35%, the remaining 20% being unchanged ketone) (Found: C, 81.3; H, 7.2%). *cis*-1,2,3,4-Tetrahydro-3-methyl-4-phenanthrylideneacetic acid formed prisms (from petroleum-benzene), m.p. 187° (Found: C, 81.35; H, 6.6. C₁₇H₁₆O₂ requires C, 80.9; H, 6.4%); *trans*-1,2,3,4-tetrahydro-3-methyl-4-phenanthrylideneacetic acid also formed prisms (from petroleum-benzene), m.p. 189° (Found: C, 80.85; H, 6.35%).

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³⁴ R. D. Haworth, *J. Chem. Soc.*, 1932, 1125.