52. *Addition Reactions of Heterocyclic Compounds. Part II.* Phenanthridine and Methyl Acetylenedicarboxylate in Methanol.*

By R. M. ACHESON and G. J. F. BOND.

Phenanthridine and methyl acetylenedicarboxylate, in methanol containing varying amounts of water, gave three *N*-substituted phenanthridinium derivatives. Interconversions, and degradations to phenanthridine, phenanthridone, and to *N*-(1 : 2-*trans*-dicarbomethoxyvinyl)phenanthridone, provide structural proofs. Conversion of the last compound into an anhydride followed by hydrolysis gave the isomeric acid, which can only be the *cis*-isomer.

DIELS and THIELE [1] reported that equimolecular proportions of phenanthridine and methyl acetylenedicarboxylate reacted in methanol to give a high yield of a yellow compound, $C_{20}H_{19}O_5N$, containing three methoxyl groups. They proposed the 9 : 10-dihydrophenanthridine structure (I) for this compound by analogy with their erroneous structure [2] for

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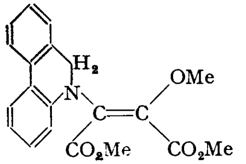
* The paper by Acheson and Burstall, *J.*, 1954, 3240, is considered as Part I.

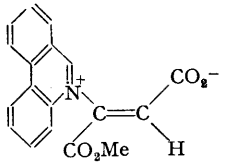
[1] Diels and Thiele, *J. prakt. Chem.*, 1940, **155—6**, 195.

[2] *Idem, Annalen*, 1939, **543**, 79.

one of the acridine–methyl acetylenedicarboxylate–methanol adducts. Melting this yellow compound followed by crystallising the product from acetonitrile was alleged to give the *trans*-isomer. A colourless compound, $C_{18}H_{13}O_4N$, containing one methyl group and reported to be formed in 10% yield in the original condensation, was given a phenanthridinium formulation (II) and stated to give a hydrate on crystallisation from water. No degradative evidence was offered in support of these claims.

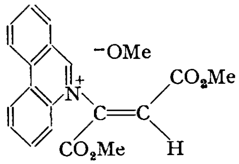
(I)



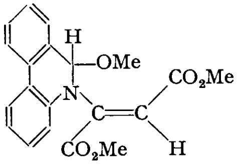


(II)

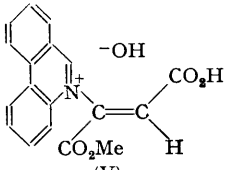
By analogy with the acridine–methyl acetylenedicarboxylate reaction which gives largely 10-(*trans*-1 : 2-dimethoxycarbonylvinyl)acridinium methoxide with a little of the *cis*-isomer,[3] the yellow compound from phenanthridine was thought to be probably 10-(*trans*-1 : 2-dimethoxycarbonylvinyl)phenanthridinium methoxide (III) or the conjugate 9 : 10-dihydrophenanthridine (IV). This formulation is not inconsistent with Diels and Thiele's data and has been verified.



(III)



(IV)



(V)

Phenanthridine and methyl acetylenedicarboxylate combined in anhydrous methanol to give a good yield of the yellow methoxide (III) alone. Crystallisation of this from methanol containing 5—15% of water gave exclusively and irreversibly the betaine (II or its isomer) whereas if the water content exceeded 15% the carboxyphenanthridinium hydroxide (V), Diels and Thiele's hydrate, was formed. The last two compounds were also obtained in excellent yield when the original condensation was carried out in the presence of the correct amounts of water, and were interconverted on crystallisation from the requisite aqueous methanol; it is clear that Diels and Thiele's methanol contained a few units per cent. of water.

Attempts to reconvert the betaine (II or its isomer) into the phenanthridinium methoxide (III) by boiling it with methanol left it unchanged; when the methanol contained some hydrogen chloride the ester group was hydrolysed. Attempts to esterify the betaine by diazomethane failed; both diazomethane and methyl diazoacetate gave cyclic compounds which may be dibenzopyrrocolines.

A phenanthridinium ethoxide could not be obtained crystalline from the methoxide (III) and dry ethanol—only a gum was isolated. Attempts to convert the methoxide (III) into the *cis*-isomer by boiling it with acetonitrile as described by Diels and Thiele also gave a gum.

Preparation of phenanthridine methiodide from phenanthridine with methyl sulphate in boiling nitromethane, followed by conversion into the iodide, was much more convenient than heating the base with methyl iodide in a sealed tube.[4] The ultraviolet absorption spectra of phenanthridine[5] and its hydrogen sulphate and of 10-methylphenanthridinium iodide in neutral and alkaline methanol[6] are shown in Figs. 1 and 2 and confirm earlier work. The considerable spectral differences between the phenanthridinium ion and the 9 : 10-dihydro-9-methoxyphenanthridine obtained with excess of sodium methoxide enable these species to be easily differentiated.

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[3] Acheson and Burstall, *J.*, 1954, 3240.
[4] Pictet and Ankersmit, *Annalen*, 1891, **266**, 149.
[5] Cf. Badger and Pettit, *J.*, 1951, 3200.
[6] Cf. Tinkler, *J.*, 1906, 861.

The ultraviolet absorption spectra of the phenanthridinium methoxide (III) in alkaline or neutral anhydrous methanol were identical and show (Fig. 1) that the compound is better represented as the 9 : 10-dihydro-9-methoxyphenanthridine (IV) under these conditions. The addition of acid changed the spectrum to the phenanthridinium-ion type (Fig. 2). The betaine (II or its isomer) has a phenanthridinium-ion spectrum in neutral and acid solution changing to that of the 9 : 10-dihydro-form on basification. The structure of the ionised hydroxide (V) is also supported by its ultraviolet absorption spectrum and by an infrared band at 5·95 μ confirming the presence of an αβ-unsaturated carboxyl group.

Proof of the constitution of one of the three phenanthridines (II, III, and V) establishes that of the other two, so the betaine (II) was subjected to a number of degradations. Boiling hydrochloric acid only hydrolysed the ester group, but at 200° in a sealed tube almost quantitative fission to phenanthridine took place. Fission of other *N*-alkyldihydrophenanthridines to phenanthridine under acid conditions has also been reported.[7]

FIG. 1.

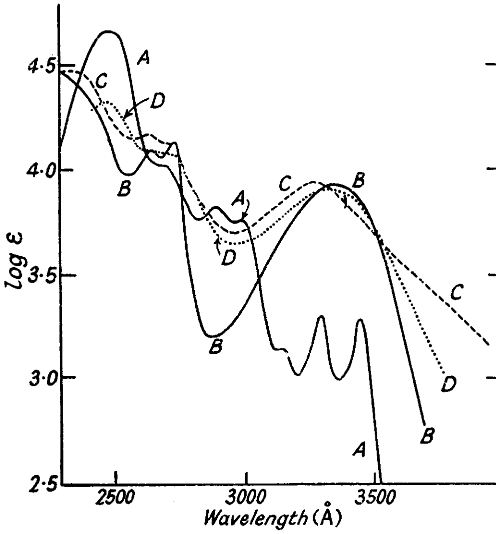

FIG. 2.

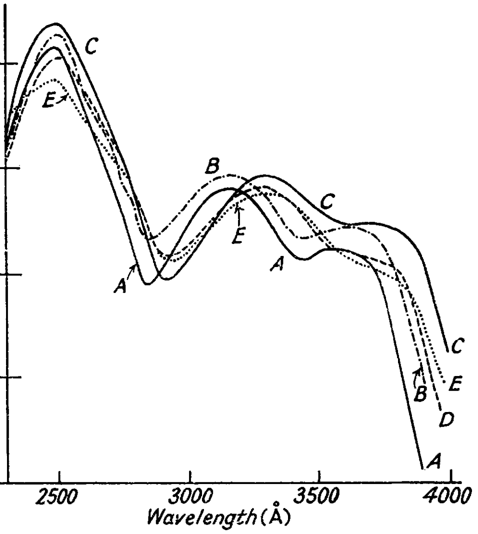

FIG. 1. *A, Phenanthridine in alkaline* MeOH. *B,* N-*Methylphenanthridinium iodide in alkaline* MeOH. *C, The methoxide in* MeOH. *D, The betaine in alkaline* MeOH.

FIG. 2. *A, Phenanthridine in acid* MeOH. *B,* N-*Methylphenanthridinium iodide in* MeOH. *C, The methoxide in acid* MeOH. *D, The betaine in* MeOH. *E, The hydroxide in* H_2O.

Refluxing the betaine with 20% aqueous potassium hydroxide also gave a good yield of phenanthridine, and oxidation with alkaline hydrogen peroxide gave phenanthridone. Hydrogenation over Raney nickel gave a dihydro-derivative, which contained 2 methoxy-groups but was not investigated fully, and then the side chain was split off with the formation of 9 : 10-dihydrophenanthridine; this was converted into the picrate which on crystallisation gave phenanthridine picrate, confirming other observations [7] on this easy oxidation. Several fruitless efforts were made to identify the other hydrogenation product. This type of reductive cleavage has also been reported in the acridine series [3] and these results leave no doubt that the side chain is attached only to the nitrogen atom.

Oxidation of the betaine (II) with alkaline ferricyanide to *N*-(*trans*-1 : 2-dicarboxyvinyl)phenanthridone proved this beyond all doubt. In refluxing acetic anhydride this acid was converted into the anhydride, which on hydrolysis gave the isomeric *N*-(*cis*-1 : 2-dicarboxyvinyl)phenanthridone, thus establishing the stereochemistry of these compounds and proving that the original condensation gave *trans*-products as is very largely the case also in the acridine series. It has not been possible to show if the carboxylate and the methoxycarbonyl group of the compound given structure (II) should be interchanged.

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[7] Bates and Cymerman-Craig, *J.*, 1954, 1153.

EXPERIMENTAL

Infrared data refer to paraffin pastes and the *ca.* 3—7 μ region only.

Phenanthridine and Methyl Acetylenedicarboxylate.—(*a*) Methyl acetylenedicarboxylate (3·40 ml.) was added to a solution of phenanthridine (5·0 g.) in anhydrous methanol (40 ml.). After 48 hr. at room temperature the yellow precipitate (7·5 g., 76%) was collected and, crystallisation from methanol, gave yellow prisms of 10-(trans-1 : *2-dimethoxycarbonylvinyl)phenanthridinium methoxide* (III), m. p. 108° (Found : C, 68·4; H, 5·4; N, 3·6; OMe, 26·5. $C_{20}H_{19}O_5N$ requires C, 68·0; H, 5·4; N, 4·0; 3OMe, 26·3%). Infrared maxima were at 5·78, 6·08, 6·21, 6·26, 6·46, 6·65, 6·71, 6·87, 6·96, and 7·12 μ.

(*b*) Repetition of experiment (*a*) but with methanol containing 5—15% of water gave an orange solid (7·2 g., 80%). Several recrystallisations from methanol gave colourless rhombs of the *betaine* (II), m. p. 180° (Found : C, 70·4; H, 4·1; N, 4·7; OMe, 11·0. $C_{18}H_{13}O_4N$ requires C, 70·4; H, 4·2; N, 4·6; 1OMe, 10·1%). Crystallisation from ethanol gave back the betaine (II), showing that the methoxy-group was non-ionic. With methanolic picric acid it gave a *semipicrate* which separated from methanol in yellow needles, m. p. 165° (Found : C, 59·4; H, 3·7; N, 8·7; OMe, 8·3. $C_{18}H_{13}O_4N,\frac{1}{2}C_6H_3O_7N_3$ requires C, 59·8; H, 3·4; N, 8·3; 1OMe, 7·4%). Infrared maxima of the betaine were at 5·79, 6·07, 6·18, 6·55, 6·70, 6·82, and 7·02 μ.

(*c*) A similar experiment but with methanol containing more than 15% of water gave a deposit of yellow crystals (6·5 g., 70%) which on crystallisation from the same solvent gave 10-(trans-x-*methoxycarbonyl*-x′-*carboxyvinyl)phenanthridinium hydroxide* (V) as pale yellow prisms, m. p. 154—155° (decomp.) (Found, after drying at 110° *in vacuo* : C, 66·0; H, 4·6; N, 4·4; OMe, 9·5. $C_{18}H_{15}O_5N$ requires C, 66·3; H, 4·6; N, 4·3; 1OMe, 9·5%), infrared maxima at 2·89, 3·05, 5·81, 5·95, 6·05, 6·17, 6·55, 6·69, 6·88, and 6·98 μ.

Cleavage of the Betaine (II) *to Phenanthridine.*—(*a*) The betaine (1 g.) was refluxed with concentrated hydrochloric acid (20 ml.) for 10 min. The clear golden-yellow solution first formed soon deposited a colourless solid (0·85 g.) which when crystallised from methanol gave the *betaine* of 10-(1 : 2-dicarboxyvinyl)phenanthridinium hydroxide as a colourless microcrystalline powder, m. p. 205° (Found : C, 69·0; H, 3·8; OMe, 0·0. $C_{17}H_{11}O_4N$ requires C, 69·5; H, 3·8; OMe, 0·0%).

(*b*) Basification of the clear yellow solution obtained by heating the betaine (II) (1 g.) with concentrated hydrochloric acid (5 ml.) in a sealed tube to 200° for 3 hr. gave a white precipitate (0·5 g., 90%). Crystallisation from aqueous methanol gave colourless needles, m. p. and mixed m. p. 104°, of phenanthridine.

(*c*) The betaine (II) (2·0 g.) was refluxed for 2 hr. with 20% aqueous potassium hydroxide (20 ml.). Phenanthridine (0·9 g., 80%), which separated, had m. p. and mixed m. p. 104° (from aqueous methanol).

Hydrogenation of the Betaine (II).—The betaine (2·0 g.) in methanol (150 ml.) was shaken with Raney nickel under hydrogen at room temperature and pressure for 12 hr., 2 mols. being absorbed. Filtration gave a solution with a strong blue-violet fluorescence, and addition of hot picric acid (1·5 g.) in methanol (5 ml.) gave an orange precipitate of 9 : 10-dihydrophenanthridine picrate (2·3 g., 85%). Crystallisation from dioxan gave yellow needles, m. p. and mixed m. p. 240° with phenanthridine picrate; the infrared absorptions of the specimens were identical. Evaporation of the methanol solution, obtained by repeating the above hydrogenation but omitting the picric acid stage, gave only a gum.

Oxidation of the Betaine (II).—(*a*) The betaine (1 g.), methanol (40 ml.) and 30% aqueous hydrogen peroxide (1 ml.) were heated on a steam-bath for 30 min. and then left at room temperature for 48 hr. Evaporation to dryness, extraction of the residue with ether, and evaporation of the extract gave phenanthridone (0·35 g., 50%) which yielded colourless needles, m. p. and mixed m. p. 293°, from aqueous ethanol.

(*b*) The betaine (1·0 g.) in hot 10% aqueous potassium hydroxide (10 ml.) was treated with potassium ferricyanide (2·5 g.) in hot water (5 ml.) and left on a steam-bath for 3 hr. After filtration from a trace of phenanthridone (0·01 g.), acidification precipitated 10-(trans-1 : 2-*dicarboxyvinyl)phenanthridone* (0·89 g.), which, after several recrystallisations from water (charcoal) separated in pale yellow prisms, m. p. 261—263° (decomp.) (Found : C, 66·5; H, 4·1. $C_{17}H_{11}O_5N,1\frac{1}{2}H_2O$ requires C, 60·6; H, 4·2. Found, after drying at 110° *in vacuo* : C, 60·5; H, 3·8; N, 4·7. $C_{17}H_{11}O_5N$ requires C, 66·0; H, 3·6; N, 4·5%). The infrared absorption spectrum of the *hydrate* had maxima at 2·90, 4·00, 5·8—5·9, 6·02, 6·25, 6·37, 6·90, and 6·99 μ.

This acid (0·9 g.) was refluxed with acetic anhydride (2 ml.) for 30 min. The product which was precipitated on cooling crystallised from acetic anhydride, giving the *anhydride* as yellow needles, m. p. 196—197° (Found : C, 70·1; H, 3·3; N, 4·7. $C_{17}H_9O_4N$ requires C, 70·1; H, 3·1; N, 4·8%), infrared maxima at 3·25, 5·46, 5·67, 5·95, 6·15, 6·24, 6·75, 6·90, and 6·98 μ.

The anhydride was dissolved in just sufficient warm aqueous sodium hydroxide. Acidification with hydrochloric acid precipitated 10-(cis-1 : 2-*dicarboxyvinyl*)*phenanthridone dihydrate* which crystallised from water in colourless rhombs, m. p. 179—180° (yellow at 110—130°) (Found : C, 59·1; H, 4·3; N, 4·1. $C_{17}H_{11}O_5N,2H_2O$ requires C, 59·0; H, 4·4; N, 4·65%). Drying at 110—120° over P_2O_5 *in vacuo* gave the acid anhydride, identical in m. p. and infrared absorption spectra with an authentic specimen. Infrared maxima of the acid dihydrate were at 2·96, 3·9, 5·8—5·85, 6·05, 6·23, 6·36, 6·90, and 6·98 μ (shoulder).

Reaction of the Betaine (II) *with Diazo-compounds.*—(*a*) The betaine (3·0 g.) in methanol (200 ml.) was treated with diazomethane (0·4 g.) in ether (20 ml.). Nitrogen was evolved and evaporation yielded a solid *substance* (2·5 g.) which crystallised from methanol in orange prisms, m. p. 222° (Found : C, 70·8; H, 4·9; N, 4·3; OMe, 9·9. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·3; 1OMe, 9·7%), which may be a dibenzo[*eg*]pyrrocolinium betaine.

(*b*) The betaine (2·0 g.) in methanol (150 ml.) was treated with methyl diazoacetate (1·3 g.). Evaporation and crystallisation of the residue yielded mainly the original betaine, but from its mother-liquor a red solid (0·2 g.) was obtained. Crystallisation from methanol yielded red prisms of a *substance* (analogous to the above pyrrocoline), m. p. 179° (Found : C, 66·4; H, 4·7; N, 3·5; OMe, 16·0. $C_{21}H_{17}O_6N$ requires C, 66·4; H, 4·5; N, 3·6; 2OMe, 16·3%).

10-*Methylphenanthridinium Iodide.*—Phenanthridine (2·0 g.) in nitromethane (10 ml.) and methyl sulphate (2·0 g.) were refluxed for 1 hr., cooled, and diluted with dry ether (50 ml.). The hygroscopic precipitate was treated in water (15 ml.) with potassium iodide (6·0 g.) in hot water (6 ml.), 10-methylphenanthridinium iodide (3·43 g., 96%) being precipitated. Crystallisation from methanol gave orange rhombs (3·1 g.), m. p. 202—203° (Pictet and Ankersmit[4] give m. p. 200°).

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