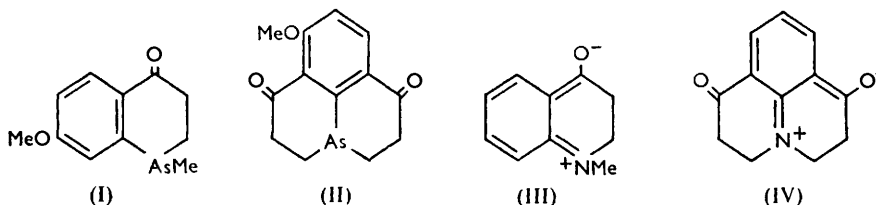


57. *The Synthesis and Structure of 10-Phenylarsacridone.*

By EMRYS R. H. JONES and FREDERICK G. MANN.

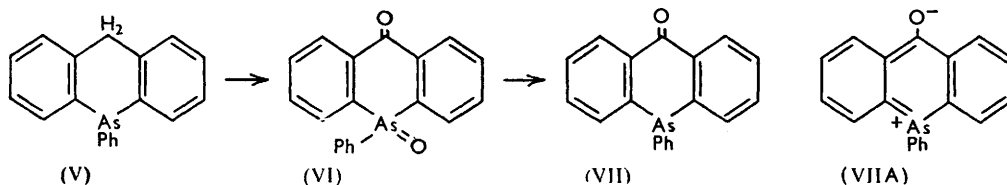
This arsacridone is the third example of a cyclic system having a keto- and a tertiary arsine group in one ring. The two previous examples, and their appropriate derivatives, showed very little evidence for charge separation within the molecule, whereby the arsenic atom would have become 4-covalent. In the arsacridone derivative, there is considerable chemical and physical evidence that this charge separation makes a substantial contribution to the structure.

ONLY two compounds having a tertiary arsine and a keto-group in one ring have hitherto been recorded, namely, (I) and (II), recently described by Mann and Wilkinson.¹ One characteristic property of these compounds, and of their appropriate derivatives, is that



internal charge separation, whereby the arsenic atom would become 4-covalent, is virtually non-existent, and they are thus in marked contrast to their nitrogen analogues which provide strong evidence for such separation. For example, the arsinoline (I) is a colourless solid, but 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline is a yellow liquid,² the colour being undoubtedly caused by a marked contribution by the polar form (III): this colour is associated in the ultraviolet spectrum with a broad band at 384 μ , which is absent in that of the arsinoline (I). Similarly, the arsulolidine (II) and 1 : 6-dioxojulolidine³ form colourless and bright yellow crystals respectively, the colour of the latter being caused by contributions of the two polar forms of type (IV). (Strict comparison of the two series is not possible because of the presence of the methoxyl group in the arsenic compounds but it is probable that this group has little effect in this respect.¹)

There is a similar contrast between the colourless 1 : 2-dihydro-1-methoxy-1-methylquinolino(3' : 2'-3 : 4)arsinoline, which gives a pale yellow hydrochloride, and the yellow 1 : 2-dihydro-1-methylquinolino(3' : 2'-3 : 4)quinoline, which forms a monohydrochloride⁵ whose purple colour is undoubtedly determined by a considerable contribution from the form in which the dihydroquinolino-nitrogen atom is positively charged.



We have therefore selected for study 10-phenylarsacridone (VII), for this ring system, by analogy with that of the markedly inert yellow 10-phenylacridone, appeared to offer a high chance of showing charge separation, as in (VIIA), with consequent considerable deactivation of both the arsine and the carbonyl group.

¹ Mann and Wilkinson, *J.*, 1957, 3336.

² Allison, Brauholtz, and Mann, *J.*, 1954, 403.

³ Mann and Smith, *J.*, 1951, 1898.

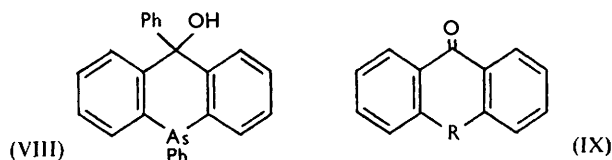
⁴ Mann and Wilkinson, *J.*, 1957, 3346.

⁵ Brauholtz and Mann, *J.*, 1955, 381.

Various unsuccessful attempts to synthesise the arsacridone system, as in (VII), were made by Aeschlimann and McClelland:⁶ these usually involved the very difficult cyclisation of an *o*-carboxydiphenylarsine unit (or its acid chloride). Failure was also recorded by Sakellarios.⁷

We find however that 5 : 10-dihydro-10-phenylarsacridine (V) is readily oxidised by hot aqueous potassium permanganate to the 10-phenylarsacridone oxide (VI), which is reduced in turn by sulphur dioxide–hydrochloric acid to the colourless, crystalline arsacridone (VII).

10-Phenylarsacridone (VII) showed the expected chemical inertness. The carbonyl group did not react with hydroxylamine, hydrazine, phenylhydrazine, 2 : 4-dinitrophenylhydrazine, or malononitrile under the normal conditions. It did react, however, with phenylmagnesium bromide to give the alcohol (VIII), a reaction comparable to that shown by analogous acridones. The tertiary arsine group in the arsacridone (VII) also showed marked deactivation, for although the arsacridine (V) was readily quaternised by boiling methyl iodide, the arsacridone (VII) was unaffected in these conditions, and did not apparently react with methyl toluene-*p*-sulphonate below 190–200°. Furthermore, whereas most tertiary arsines react exothermally with cold acetone–hydrogen peroxide, the arsacridone required this boiling reagent for reconversion into the arsine oxide (VI).



The arsacridone reacted with ethanolic potassium palladobromide, but the highly insoluble nature of the covalent derivative, $[(C_{19}H_{13}OAs)_2PdBr_2]$, would promote its formation.

If the low reactivity of the carbonyl group and the arsine group is in fact caused by the contribution of the polar form (VIIA), conversion of the 3-covalent arsenic atom into the 4-covalent condition by an external reagent should, by destroying this charge separation, restore the activity of the carbonyl group. Chemical evidence on this point is not readily available, for phenylhydrazine merely reduced the arsacridone oxide (VI) to the arsacridone (VII), and the product of the interaction of phenylhydrazine and the arsacridone metho-toluene-*p*-sulphonate could not be crystallised and identified.

The absorption spectra, however, provide strong evidence for the polar separation (VIIA). The infrared carbonyl frequencies of the arsacridone (VII) and related compounds (IX) are shown in the Table. It is noteworthy that the carbonyl frequency of the

| Compound | (IX); R = | $\begin{array}{c} >CO \\ \text{frequency} \\ (\text{cm.}^{-1}) \end{array}$ | Compound | (IX); R = | $\begin{array}{c} >CO \\ \text{frequency} \\ (\text{cm.}^{-1}) \end{array}$ |
|--------------------------------|--------------------|---|----------------------------------|-----------|---|
| 10-Phenylanthrone | :CHPh | 1662 | 10-Phenylacridone | :NPh | 1632 |
| 10 : 10-Diphenylanthrone | :CHPh ₂ | 1665 | The arsacridone (VII) | :AsPh | 1647 |
| Xanthone | :O | 1660 | The arsacridone oxide (VI) | :As(O)Ph | 1662 |
| Thioxanthone | :S | 1645 | | | |

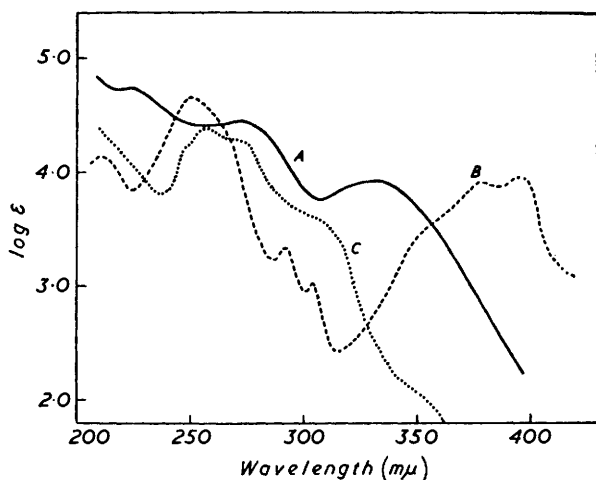
arsacridone (VII) is significantly lower (by *ca.* 15 cm.^{-1}) than the normal frequency in comparable anthrones, although the decrease in frequency is less than that shown by 10-phenylacridone, indicating a greater degree of lone-pair–carbonyl interaction in the last compound. Even more decisive is the restoration of the normal frequency in the arsacridone oxide (VI), in which this interaction is impossible. Further, the carbonyl frequency of xanthone is very slightly lower than that of the two anthrones, but the frequency of thioxanthone, in which greater charge separation would be expected, falls to almost that of the arsacridone (VII).

⁶ Aeschlimann and McClelland, *J.*, 1924, 2025.

⁷ Sakellarios, *Ber.*, 1926, 59, 2552.

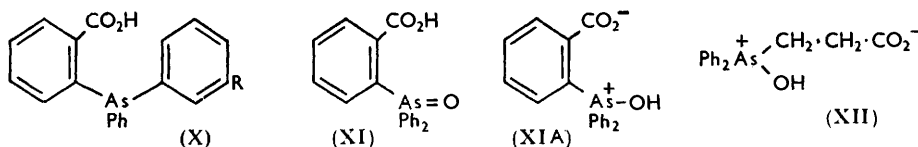
The ultraviolet absorption spectra of 10-phenylacridone and the arsacridone (VII) are not greatly dissimilar (see Fig.), but the region of large absorption which is, by comparison with the spectrum of anthrone,⁸ due to the electronic change introduced by the Group V element, has undergone a smaller shift to longer wavelength in the arsacridone than in the acridone, indicating a smaller degree of conjugation in the former compound and accounting for its colourless appearance in contrast to the yellow colour of the acridone.

There is thus considerable chemical and physical evidence that the polar form (VIIA) contributes substantially to the structure of 10-phenylarsacridone (VII), which becomes an addition to the small number of heterocyclic arsenic compounds in which the arsenic atom is apparently linked by a single and a double bond respectively to the two adjacent carbon atoms of the ring. It is noteworthy that these compounds also have the anthracene-type of ring system: there is considerable evidence for the above structure in the 5:10-disubstituted arsanthronium ions,^{9,10} but at present only weak evidence for its existence in the products claimed to be phenarsazine¹¹ and arsanthren.¹²



A, 10-Phenylarsacridone (VII).
B, 10-Phenylacridone.
C, Anthrone, copied from R. N. Jones.⁸
All in ethanol.

Our earlier attempts to prepare an arsacridone of type (VII) were based on the projected synthesis of *o*-carboxy-*m'*-methoxytriphenylarsine (X; R = OMe), in which it was hoped that the activation of the benzene ring by the methoxyl group would promote subsequent cyclisation. These attempts were discontinued when it was found that *o*-carboxytriphenylarsine (X; R = H) in organic solvents underwent exceptionally rapid



conversion into the arsine oxide (XI), the stability of which was so high that the methiodide of this arsine on attempted recrystallisation was also converted into the oxide, although the tertiary arsine was characterised as its palladium bromide complex, of composition $[(C_{19}H_{15}O_2As)_2PdBr_2]$.

⁸ R. N. Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2141.

⁹ Chatt and Mann, *J.*, 1940, 1184.

¹⁰ Emrys R. H. Jones and Mann, *J.*, 1955, 411.

¹¹ Wieland and Rheinheimer, *Annalen*, 1921, **423**, 1.

¹² Kalb, *ibid.*, p. 39.

Evidence that the arsine oxide exists as the zwitterion (XIA) is provided by the infrared spectrum, the salient features of which are closely similar to those shown by 2-carboxy-ethylidiphenylarsine oxide¹³ (XII). The evidence for the structure (XIA) is: (a) the spectrum shows bands at 1620 and 1382 cm^{-1} , characteristic of the $\cdot\text{CO}_2^-$ ion, but none in the 1680 cm^{-1} region where a carbonyl group would be manifest; (b) there are broad bands at 2900 and 2300 cm^{-1} ; (c) although there are small sharp bands at 905, 842, and 817 cm^{-1} , there is no dominant absorption in this region comparable to that shown in the spectra of the acids $\text{PhAs(O)}[(\text{CH}_2)_n\text{CO}_2\text{H}]_2$, where $n = 1$ or 3,¹³ and attributed to the $\text{As}\cdot\text{O}$ group. The zwitterion structure (XIA) apparently confers quite exceptional stability, for this compound, unlike normal tertiary arsine oxides, did not form a hydroxy-salt with picric acid or with the stronger inorganic acids.

EXPERIMENTAL

2-Aminodiphenylmethane was prepared by Mann and Stewart's method,¹⁴ and diphenylmethane-2-arsonic acid, 10-arsacridinic acid, and 10-chloro-5:10-dihydroarsacridine by the modifications introduced by Hewett *et al.*¹⁵ into Gump and Stoltzenberg's original method.¹⁶

5:10-Dihydro-10-phenylarsacridine (V).—A solution of 10-chloro-5:10-dihydroarsacridine (8.3 g.) in benzene (30 c.c.) was slowly added to a stirred solution of phenylmagnesium bromide prepared from bromobenzene (6.3 c.c., 2 mols.) and magnesium (1.44 g., 2 equivs.) in ether (30 c.c.). When the vigorous reaction had subsided, the mixture was boiled under reflux for 5 min., cooled, and hydrolysed with aqueous ammonium chloride. Removal of the solvents from the dried organic layer left an oil which solidified and on recrystallisation from ethanol afforded the *arsacridine* (V), m. p. 74—75° (9.4 g., 98%) (Found: C, 71.2; H, 4.8. $\text{C}_{19}\text{H}_{15}\text{As}$ requires C, 71.6; H, 4.7%). The methiodide was readily formed in boiling methyl iodide as a gum which when rubbed with acetone formed a solid, m. p. 151—152° (effervescence). This could not be recrystallised, but gave a *methopicrate*, yellow crystals (from ethanol-acetone), m. p. 260° (decomp.) (Found: C, 55.5; H, 3.8; N, 7.7. $\text{C}_{26}\text{H}_{20}\text{O}_7\text{N}_3\text{As}$ requires C, 55.6; H, 3.6; N, 7.5%).

10-Phenylarsacridone (VII).—A stirred suspension of the *arsacridine* (V) (4.59 g.) in water (100 c.c.) was kept at 70—80° whilst powdered potassium permanganate (4.56 g., 1.00 mol.) was added in *ca.* 0.5 g. portions. The mixture was boiled for 2 min., cooled, and extracted with chloroform (75 c.c.). Removal of the solvent gave the *arsacridine oxide* (VI) (4.90 g., almost 100%), m. p. 238° after crystallisation from acetone (Found: C, 65.6; H, 3.6. $\text{C}_{19}\text{H}_{13}\text{O}_2\text{As}$ requires C, 65.6; H, 3.7%). Sulphur dioxide was passed through a suspension of this oxide (4.5 g.) in concentrated hydrochloric acid (50 c.c.) and water (50 c.c.) containing potassium iodide (0.2 g.) for 30 min. The solid deposit, when recrystallised from ethanol, afforded the *arsacridone* (VII) (4.1 g., 95%), m. p. 138—139° (Found: C, 68.5; H, 3.8%; *M*, in boiling acetone, 321, 325. $\text{C}_{19}\text{H}_{13}\text{OAs}$ requires C, 68.7; H, 3.9%; *M*, 332).

A solution of the *arsacridone* in methyl iodide (with or without the addition of methanol) when boiled for 3 hr. afforded the unchanged *arsacridone*. A mixture of the *arsacridone* and methyl toluene-*p*-sulphonate (1.2 mols.), when heated at 120—125° for 2.5 hr., also afforded the *arsacridone*, but when heated at 200° for 1.5 hr. gave first a dark gum and then, when cold, a glass which, rubbed with acetone, formed a fine solid; recrystallisation of this from acetone afforded the *methotoluene-p-sulphonate*, m. p. 200°, in small yield (Found: C, 62.2; H, 4.8. $\text{C}_{27}\text{H}_{23}\text{O}_4\text{SAs}$ requires C, 62.5; H, 4.4%).

An acetone solution of the *arsacridone*, when boiled with dilute hydrogen peroxide for 5 min., and evaporated to dryness, gave the oxide (VI), m. p. and mixed m. p. 238° (from water).

A solution of the *arsacridone* (VII) (0.70 g.) in benzene (5 c.c.) was added to a Grignard reagent prepared from bromobenzene (0.44 c.c., 2 mols.) and magnesium (0.10 g., 2 equivs.) in ether (5 c.c.). The mixture was boiled for 1 hr., cooled, and hydrolysed as before. The dried organic layer on evaporation gave 5:10-dihydro-5-hydroxy-5:10-diphenylarsacridine (VIII)

¹³ Braunholtz and Mann, *J.*, 1957, 3285.

¹⁴ Mann and Stewart, *J.*, 1954, 4127.

¹⁵ Hewett, Lermitt, Openshaw, Todd, Williams, and Woodward, *J.*, 1948, 292.

¹⁶ Gump and Stoltzenberg, *J. Amer. Chem. Soc.*, 1931, 53, 1428.

(0.65 g., 75%), m. p. 194° after crystallisation from ethanol (Found: C, 73.1; H, 4.9. $C_{23}H_{19}OAs$ requires C, 73.1; H, 4.7%).

A solution of the arsacidone (0.25 g.) in hot acetone, when treated with potassium palladobromide (0.19 g., 0.50 mol.) in a minimum of water, gave an immediate orange precipitate, which when washed with acetone and water, and recrystallised from dimethylformamide, afforded *dibromodi-(10-phenylarsacidone)palladium*, m. p. 298° (decomp.) (Found: C, 49.0; H, 3.2. $C_{38}H_{26}O_2Br_2As_2Pd$ requires C, 49.0; H, 2.8%).

The arsacidone oxide (VI) was treated with an excess of phenylhydrazine in ethanol containing acetic acid. The mixture, when boiled under reflux for 2 hr. and poured into water, deposited the arsacidone (VII), m. p. and mixed m. p. 137—138°. The methotoluene-*p*-sulphonate when similarly treated deposited a red gum which was soluble in all the usual solvents and could not be crystallised.

2-Methyltriphenylarsine.—A solution of chlorodiphenylarsine (10.0 g.) in ether (50 c.c.) was added to a Grignard reagent prepared from *o*-bromotoluene (9.7 g., 1.5 mols.) and magnesium (1.37 g., 1.5 equivs.) in ether (100 c.c.), which was then boiled for 30 min. The usual working-up gave a solid residue, which on crystallisation from ethanol afforded the *arsine* (9.8 g., 81%), m. p. 63—64° (Found: C, 70.9; H, 5.55. $C_{19}H_{17}As$ requires C, 71.2; H, 5.3%).

A mixture of the arsine (7.0 g.), potassium permanganate (10.2 g., 1.1 equivs.), and water was boiled under reflux for 1 hr., the pink colour disappearing. The mixture, when made alkaline with sodium carbonate, filtered through "Supercel," and acidified with hydrochloric acid, deposited the crude *o*-carboxytriphenylarsine oxide (XI) (4.4 g., 55%), m. p. 237—242°, increased to 246—247° after wasteful recrystallisation from ethanol (Found: C, 62.0; H, 4.2. $C_{19}H_{15}O_3As$ requires C, 62.3; H, 4.1%). The oxide was recovered unchanged after treatment in concentrated ethanolic solution with picric acid, sodium picrate, sodium iodide, or nitric acid.

When sulphur dioxide was passed through a suspension of the oxide (4.2 g.) in concentrated hydrochloric acid (40 c.c.) containing potassium iodide (0.1 g.) for 25 min., an oil separated and slowly became more viscous. A solution of this product in ethanol (7 c.c.), when set aside in a small closed flask at 0° for 4 days, deposited crystals (2.0 g.), m. p. 135—138°, presumably *o*-carboxytriphenylarsine (X; R = H), but a second recrystallisation gave solely the oxide, m. p. and mixed m. p. 245—246°. A solution of the crystals, m. p. 135—138°, in methyl iodide, when boiled for 10 min., deposited a methiodide, m. p. 102—104° (effervescence, rapid heating), but recrystallisation from ethanol again gave the oxide, m. p. and mixed m. p. 245—246°. A solution of the arsine in concentrated sulphuric acid, when heated at 100° for 45 min., cooled, and poured into water, again deposited the oxide.

Aqueous-ethanolic potassium palladobromide was added with shaking to a cold sample of the freshly prepared viscous arsine, which had been washed with aqueous sulphur dioxide and then dissolved in ethanol. *Dibromodi-(o-carboxytriphenylarsine)palladium* separated as orange crystals, m. p. 255° (decomp.) after washing with water and ethanol and drying at 70°/0.1 mm. (Found: C, 47.1; H, 3.3. $C_{38}H_{30}O_4Br_2As_2Pd$ requires C, 47.2; H, 3.1%). The compound was insoluble in, and unaffected by, boiling methanol, ethanol, acetone, and benzene, but in boiling aqueous ethanol it rapidly decomposed with deposition of palladium.

Bart Reactions.—These reactions formed the basis of a preliminary study of compounds of type (X), and are briefly recorded.

(i) *Dichloro-m-methoxyphenylarsine*. *m*-Methoxyphenylarsonic acid,² when reduced with sulphur dioxide-hydrochloric acid in the usual way, afforded this *arsine* in 70% yield as a colourless liquid which soon became yellow, b. p. 157°/15 mm. (Found: C, 33.6; H, 3.1. $C_7H_7OCl_2As$ requires C, 33.2; H, 2.8%). An attempted Bart reaction, in which aqueous *o*-tolylidiazonium chloride and a solution of the dichloroarsine in aqueous sodium hydroxide-sodium carbonate were run concurrently into ice-water, yielded *m*-methoxyphenylarsonic acid,¹ m. p. and mixed m. p. 138—141° after crystallisation from water.

(ii) *m*-Nitrobenzenediazonium chloride, when brought into reaction with dichloro-*o*-tolylarsine in alkali, under the conditions used by Blicke and Webster¹⁷ for the preparation of *m*-nitrodiphenylarsinic acid, yielded solely *o*-tolylarsonic acid. The same result was obtained when *m*-nitroaniline was diazotised in 90% ethanol with concentrated sulphuric acid and sodium nitrite, and then treated directly with dichloro-*o*-tolylarsine.

(iii) A solution prepared by adding dichloro-*m*-nitrophenylarsine (5.0 g.), sodium hydroxide (3 g.), anhydrous sodium carbonate (1 g.), and copper sulphate crystals (0.2 g.) to water (100 c.c.)

¹⁷ Blicke and Webster, *J. Amer. Chem. Soc.*, 1937, 59, 534.

was added during 10 min. to a vigorously stirred solution prepared from *o*-toluidine (2.0 g., 1 mol.), concentrated hydrochloric acid (5 c.c.), and sodium nitrite (1.3 g., 1 mol.) in water (40 c.c.). The mixture was stirred for 30 min., then heated with charcoal and filtered. The filtrate, when made just acid (Congo-red), deposited a pink precipitate; this was purified by dissolution in aqueous sodium hydroxide, which was then boiled with charcoal, filtered, cooled, and again acidified. The fine colourless precipitated powder, which was almost certainly 3 : 3'-diarsonoazoxybenzene (2.0 g., 48%), did not melt below 400° (Found: C, 32.55; H, 3.2; N, 6.5. $C_{12}H_{12}O_7N_2As_2$ requires C, 32.3; H, 2.7; N, 6.3%).

This diarsonic acid (2.0 g.) was added during 1 hr. to a boiling, vigorously stirred mixture of iron "pin-dust" (4 g.) and 5% aqueous sodium chloride (20 c.c.). The mixture was boiled under reflux for 3 hr. and, after the addition of sodium hydroxide (0.5 g.), filtered through "Supercel." Evaporation of the filtrate to 30 c.c. and cooling gave orange crystals of 3 : 3'-diarsonoazobenzene (1.2 g., 62%), which after recrystallisation from water did not melt below 400° (Found: C, 33.8; H, 3.1; N, 6.6. Calc. for $C_{12}H_{12}O_6N_2As_2$: C, 33.5; H, 2.8; N, 6.5%). This product is apparently identical with the orange-yellow 3 : 3'-diarsonoazobenzene prepared by Lieb,¹⁸ who states that it effervesces feebly at 240° and then on further heating darkens without melting: he also describes it as extremely difficultly soluble in water.

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¹⁸ Lieb, *Ber.*, 1921, **54**, 1511.
