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10,10'-BI[4.5,6.7]DIBENZ[1.3]DIAZEPINO[2.1-*a*]-ISOINDOLINYLIDENES

NOVEL HETEROCYCLES RELATED TO β-ISOINDIGO

A. P. BINDRA and J. A. ELIX
Chemistry Department, Australian National University, Canberra 2600, Australia

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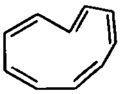
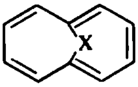
Abstract—The title compounds (V, VI), annelated analogues of diimino-β-isoindigo, have been prepared by the condensation of *o*-phthalaldehyde with 2,2'-diaminobiphenyl. The partially cyclized compounds VII and VIII were also obtained from this reaction.

CONSIDERABLE effort has been directed at the synthesis of monocyclic, conjugated compounds containing 10π-electrons and has recently led to the detection of the parent isomeric [10] annulenes (e.g. I),[1] the synthesis of the bridge-bonded derivatives (II)[2, 3] and the preparation of several annelated [10] annulenes.[4, 5]



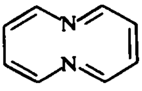
I



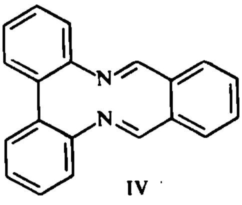
II

X = CH_2, O, NH, NMe, NCOMe

The effect of hetero atoms on the properties of such ring systems is still not known but would obviously be of considerable interest. For instance, molecular models of 1,6-diaza[10]annulene (III) appear to be reasonably strainless, and indicate that the deviation of the molecule from coplanarity should not be sufficient to compete with the predicted aromatic stabilization.



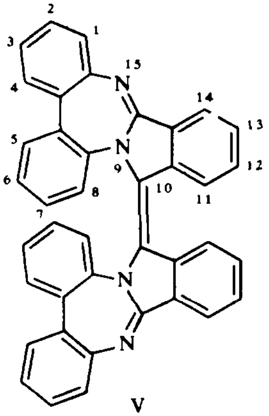
III



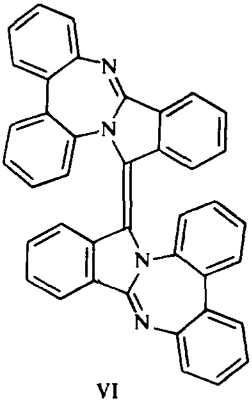
IV

An earlier attempt to prepare the annelated 1,6-diaza[10] annulene (IV) through the condensation of 2,2'-diaminobiphenyl and *o*-phthaladehyde failed to yield any identifiable products.[6] We have reinvestigated this reaction in an effort to isolate the annulene, IV.

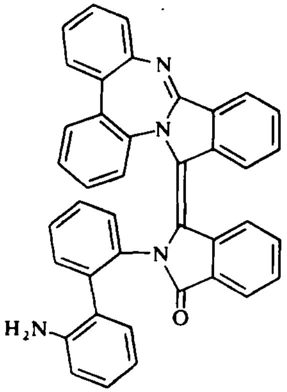
As was observed previously[6] the major product of the condensation was a "linear" polymer. In addition, four highly coloured products of relatively low molecular weight have been isolated and characterized, namely, *cis* and *trans* 10,10'-bi[4.5,6.7]dibenz-[1.3]diazepino[2.1-*a*]isoindolinylidene (V) and (VI) respectively, and *cis* and *trans* 10[N-(2''-amino-2'-biphenylyl)1-isoindol-3-onylidene]isoindolo[2.1-*a*]dibenzo[*d.f*]-1,3-diazepine, (VII) and (VIII). These compounds were separated and purified by repeated thick layer chromatography on alumina.



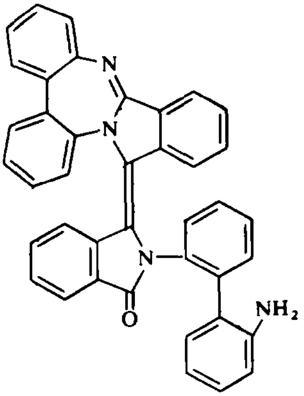
V



VI



VII



VIII

However no trace of the desired annulene (IV) was obtained.

Structure determination of V, VI, VII *and* VIII

The determination of the structure of the novel, polycyclic heterocycles V, VI, VII and VIII presented considerable difficulties.

Probably the most informative evidence was provided by mass spectroscopy.

Accurate mass measurement of the respective molecular ions confirmed the empirical formulae, $C_{40}H_{24}N_4$ for V and VI, and $C_{40}H_{26}N_4O$ for VII and VIII. However the mass spectral fragmentation patterns were obscure and of no aid in the structure elucidation.

The empirical formulae provided an insight into the relation between V, VI and VII, VIII and this was further substantiated by the infrared and NMR spectra of the compound VII.

$C_{40}H_{24}N_4$	$C_{40}H_{26}N_4O$
V, VI	VII, VIII(?)
(di-anils)	(keto-amines)

More precisely, the NMR spectrum of VII showed that this compound contained two exchangeable protons (with D_2O). The IR spectrum confirmed that these were due to a primary amino group (ν 3450, 3360 cm^{-1}), and also exhibited CO absorption at 1710 and 1690 cm^{-1}, consistent with the cyclic imidimine structure assigned.

This interpretation of the spectral data for the compounds V, VI and VII was subsequently confirmed by their chemical interconversion. Both the anhydro-compounds V and VI rapidly hydrolysed when a chloroform solution was exposed to the atmosphere, to give a mixture of VII and VIII. This behaviour is typical of a Schiff's base or an enamine. Conversely, dehydration of either VII or VIII with phosphorus oxychloride and pyridine, regenerated a mixture of the anhydro compounds V and VI. However the latter two compounds have been shown to equilibrate in the presence of these reagents.

At this stage of the structural investigation of V, VI, VII and VIII, the major feature still to be determined was the nature of the overall polycyclic system. As expected,

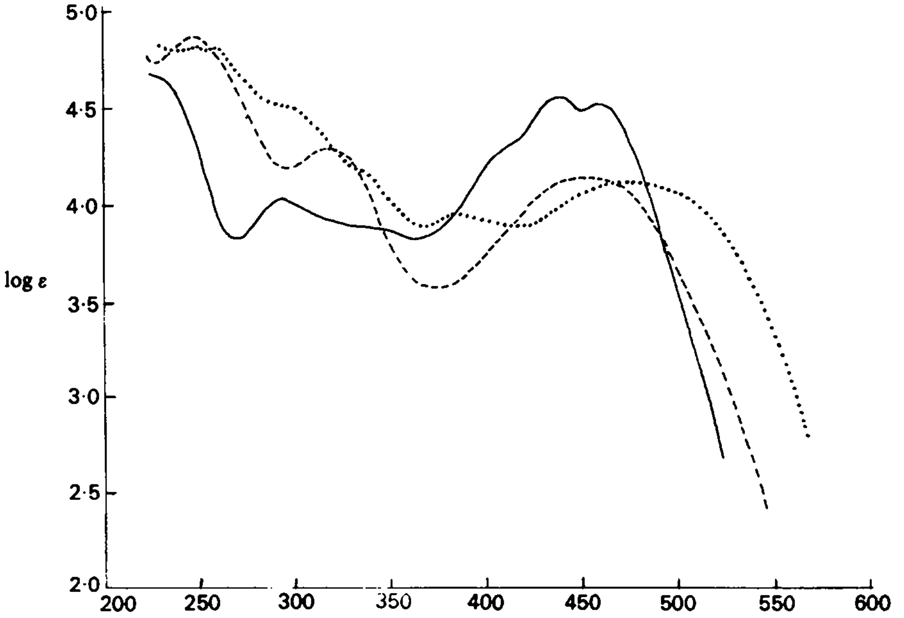
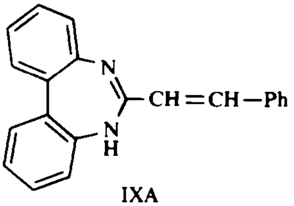
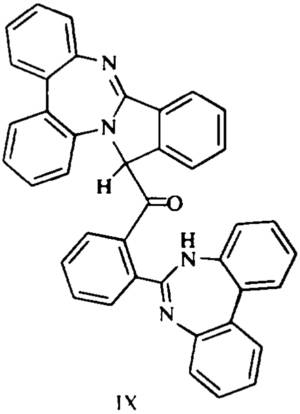


FIG. 1 UV absorption spectra
X,R = Me (———————)
V (– – – – – – – – –)
VI (· · · · · · · · · · · · ·)

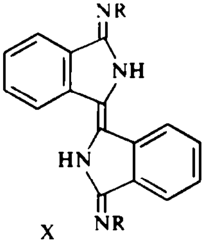
the UV spectra provided the most useful evidence in this respect. The striking similarity of the UV and visible spectra of the di(3-alkylimino-1-isoindolinylidenes) (X)[7] with the spectra of V, VI, VII and VIII identified the chromophoric groups present in these compounds (Figs, 1, 2). With this knowledge the overall structure of the products V, VI and VII could be deduced from the empirical formulae. The structure of VIII also followed. The isomers VII and VIII were obviously closely related structurally, because the chromatographic behaviour of these two compounds was extremely similar. Moreover, the electronic spectra confirmed that both compounds possessed substantially the same chromophoric group (Fig. 2) and showed no resemblance to that of IXA,[6] thus ruling out the alternative structure (IX).



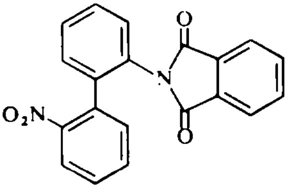
IXA



IX



X



XI

Since the inter-relation between the products V, VI and VII had already been established, it was only necessary to confirm the gross structure of one of these compounds by chemical means. This was achieved by oxidising VI with potassium permanganate in acetic acid. The major product was identified as N-(2'-nitro-2-biphenylyl)phthalimide (XI).

At this point, all that remained to be established was the structural differences between V and VI, and between VII and VIII. The equilibration studies mentioned previously, led to the surmise that these four compounds were, in fact, two pairs of geometrical isomers. This interpretation was also consistent with all the spectral data and, in particular, explained the close similarities between V and VI and between VII and VIII.

The assignment of configuration to the two pairs of geometrical isomers was based on a comparison of the NMR and electronic spectra, in conjunction with a study of molecular models. With each group of compounds, the isomer with higher R_f and

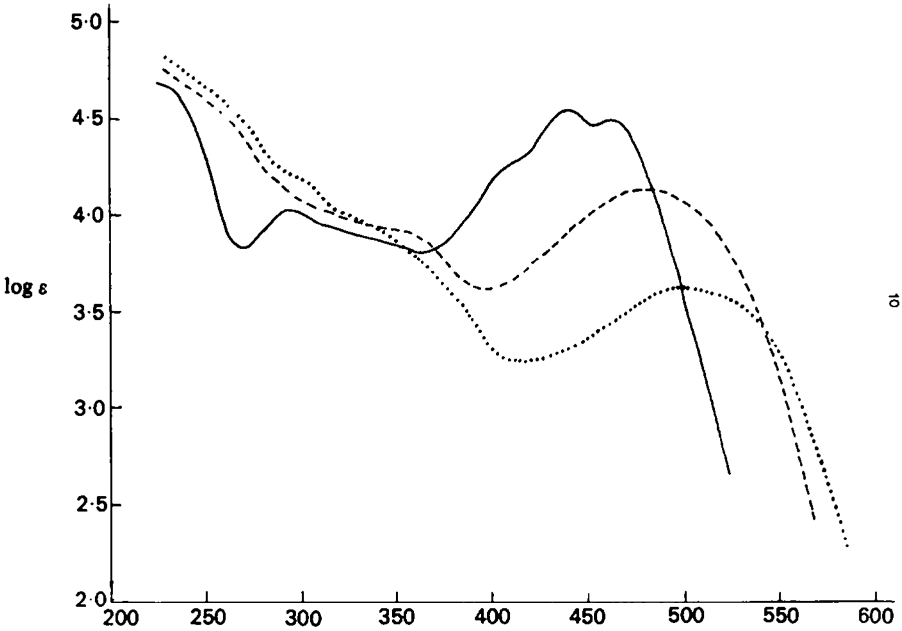


FIG. 2 UV absorption spectra

X,R = Me (————)
VII (- - - - - - - -)
VIII (·············)

shorter wavelength absorption (in the visible spectrum) was assigned the *cis* configuration. Molecular models confirmed that the *cis*-isomers were more compact, and that the component, conjugated systems show greater deviations from planarity.

Furthermore, a model of the *cis* isomer (V) showed that a number of aromatic protons were held above the π-cloud of the adjacent benzene rings. Hence supporting evidence for the above assignation of configuration is provided by the NMR spectrum, since V shows a distinct upfield shift of the aromatic protons in comparison with VI ($\Delta\tau = 0{\cdot}95$).

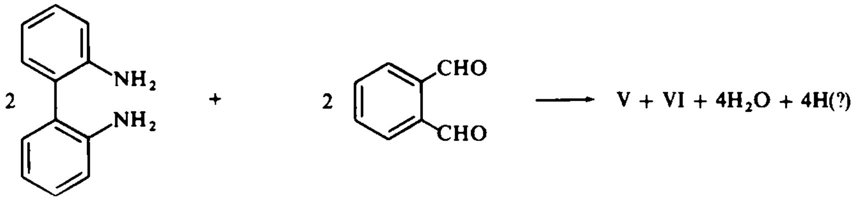
On closer inspection of a model of VIII, it became apparent that although the conjugated, β-isoindigoid system (see XV) was more nearly planar than that of VII the overall molecule suffered more serious steric interference than did the latter. This would explain why VII appears to be the thermodynamically stable isomer, and the proponderant hydrolysis product.

Reaction mechanism

Any speculations concerning the mechanism of this condensation are by necessity only tentative, since the large bulk of the product was composed of "linear" polymers and V, VI, VII and VIII are really only minor byproducts.

However, one of the most interesting questions which arose once the structures of V and VI had been established, was how to forward a convincing mechanism to account for the dehydrogenation which must have accompanied the normal amine-aldehyde condensation (Scheme I).

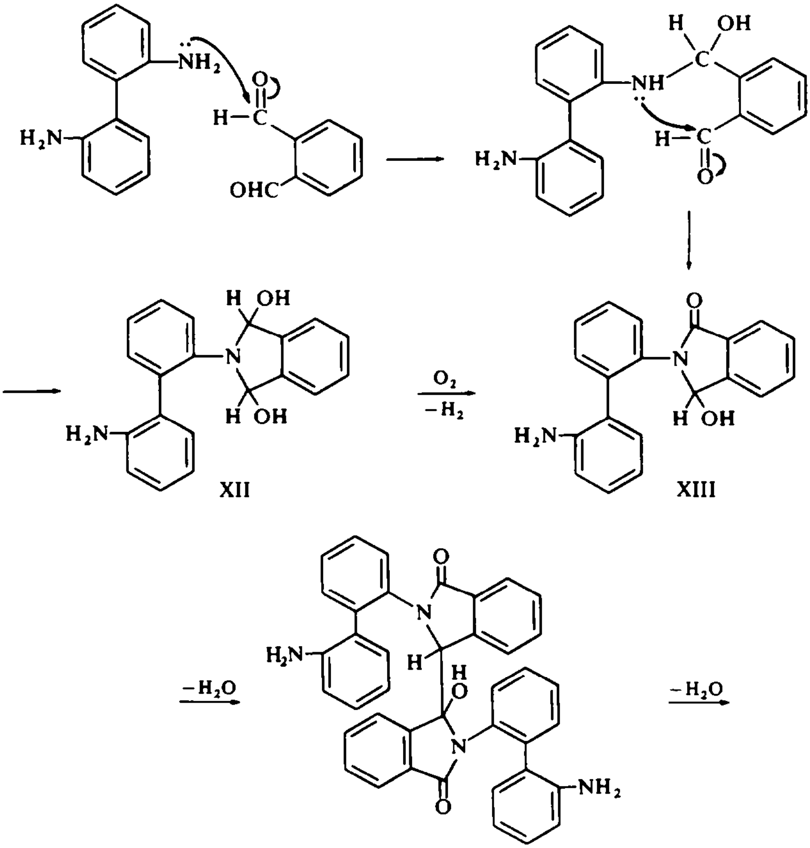
SCHEME I



A feasible mechanism for this reaction is outlined in Scheme II.

The key intermediate involved is the dicarbinolamine (XII), the formation of which can readily be accounted for by a normal amine-dialdehyde condensation.

SCHEME II

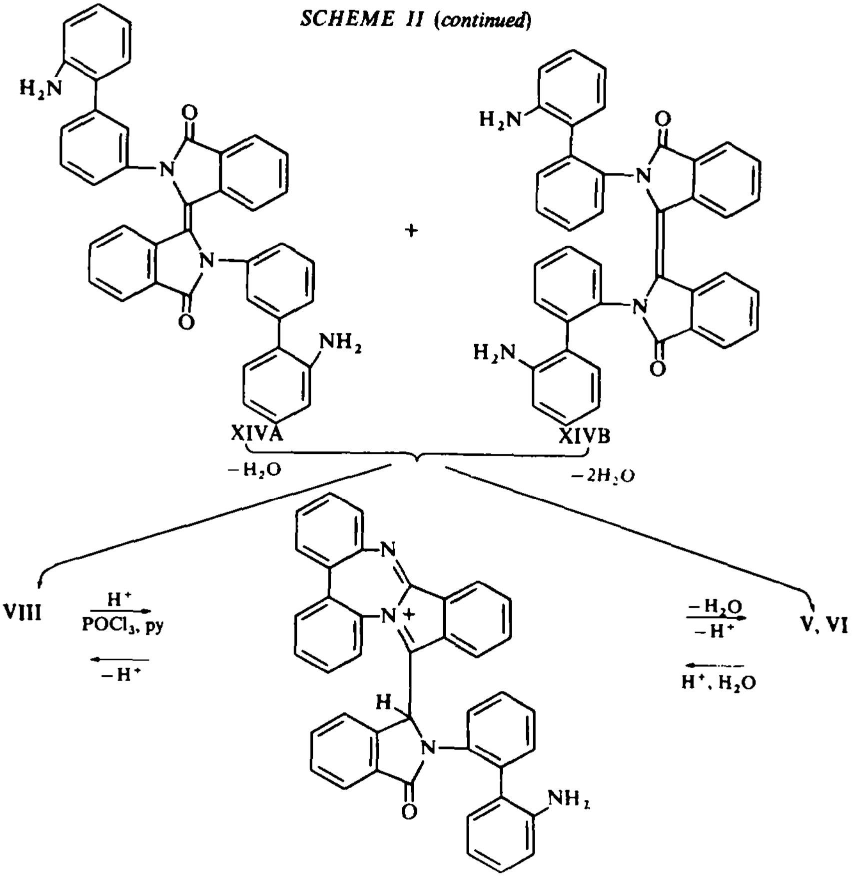


XII

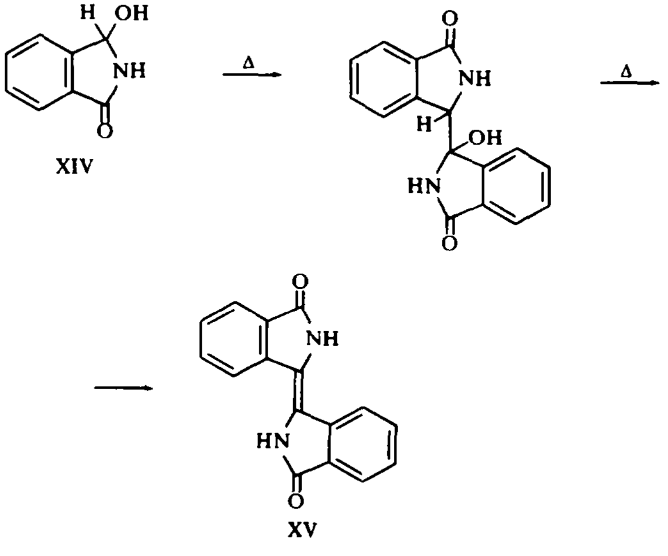
XIII

The oxidation of carbinolamines by one-electron oxidising agents is well established (e.g. with 5-hydroxy-2-pyrrolone[8]), so we propose that XII is susceptible to oxidation by the atmospheric oxygen present in the reaction system. The so-formed hydroxyphthalimidine (XIII) would then lead to the observed products V, VI and VII, VIII as shown. 3-hydroxyphalimidine (XIV) itself, is known to undergo a parallel conversion to β-isoindigo (XV) on heating[9] (see Scheme III).

SCHEME II (continued)



SCHEME III



Alternatively, XII may undergo dehydration to give a phalimidine via the tautomeric hydroxyisoindole, and this compound may subsequently be oxidatively dimerised to the isoindigo intermediates (XIV).

EXPERIMENTAL

IR spectra were recorded on a Unicam model S.P. 200G spectrometer and NMR spectra on a Perkin–Elmer R-10 spectrometer. Chemical shifts were measured on the τ-scale relative to TMS as internal standard (τ = 10·0). Mass spectra were recorded on a MS-9 spectrometer. M.ps are uncorrected. All chromatograms were carried out on thick layer plates (100 × 20 × 0·1 cm) using alumina (Merck G) as adsorbent.

Condensation of 2,2′-diaminophenyl with o*-phthalaldehyde.* 2,2′-Diaminobiphenyl (0·55 g, 3·0 m mole) and *o*-phthalaldehyde (0·40 g, 3·0 m mole) were dissolved in MeOH (100 ml) and permitted to stand at room temp overnight. The MeOH was then distilled under reduced press and the residue chromatographed using light petroleum (b.p. 40–60°)–CH_2Cl_2 (ratio 2:1) as eluent. Three distinct major orange-red bands could be detected. Each band was removed separately, extracted with $CHCl_3$, and the $CHCl_3$ soln concentrated. Each fraction so obtained was then purified further by repeated chromatography on similar plates. By this means the third band could be further resolved into a faster moving red band, and a slower pink band.

The initial orange band contained V (17 mg, 2·0%) which crystallized from EtOH as orange needles, m.p. 276–280° (dec); UV λ_{max} (90% EtOH) 212 nm (log ε 4·88), 251 (4·86), 320 (4·28) and 454 (4·12); NMR (CCl_4) τ 2·30–2·85 (complex multiplet); IR ν_{max} (CCl_4) 1725 cm^{-1} (N—C=C—N), 1650 (C=N); mass spec. *m/e* 560·1994, all other peaks <5% of M^+ peak ($C_{40}H_{24}N_4$ required M = 560·2000).

The second band (red) yielded VI (19 mg, 2·3%) which crystallized from EtOH as red needles, m.p. 267–268°; UV λ_{max} (90% EtOH) 214 nm (log ε 4·89), 253 (4·81) 258 sh (4·80), 304 sh (4·49), 333 sh (4·19), 383 (3·95) and 476 (4·10); NMR ($CDCl_3$) τ 1·35–3·60 (complex multiplet); IR ν_{max} 1715 cm^{-1} (N—C=C—N), 1645 (C=N); mass spec. *m/e* 560·1996, all other peaks <5% M^+ peak ($C_{40}H_{24}N_4$ requires M, 560·2000).

The third band (red) was extracted and concentrated to give VII (80 mg, 9·2%) which crystallized from EtOH in bright red needles m.p. 262°; UV λ_{max} (90% EtOH) 212 nm (log ε 4·83), 360 sh (3·90) and 482 (4·13); NMR ($CDCl_3$) τ 1·70–3·80 (24 H, m), 6·90–7·30 (2H, broad, exchange with D_2O); IR ν_{max} ($CHCl_3$) 3450 cm^{-1} (N—H), 3360 (N—H), 1710, 1690 (C=O, N—C=C—N), and 1645 (C=N); mass spec. *m/e* 579 (52%), 578 (100%), 560 (23%), 395 (36%), 297 (30%), 296 (64%), 282 (62%), 281 (46%) and 254 (17%) were the major peaks. (Found: M, 578·2107. $C_{40}H_{26}N_4O$ requires: M, 578·2106).

The fourth band (pink) yielded VIII (3·5 mg, 0·4%) as a pink solid; UV λ_{max} (90% EtOH) 225 nm (log ε 4·83), 300 sh (4·17), 340 sh (3·89) and 504 (3·62); mass spec. *m/e* 578 (2%), 560 (3%) 463 (12%), 462 (30%), 461 (20%), 283 (22%), 282 (100%), 281 (56%) and 254 (11%) were the major peaks (Found: M, 578·2108. $C_{40}H_{26}N_4O$ requires: M, 578·2106).

Dehydration of VII *and* VIII. The keto-amine VII (10 mg) was dissolved in benzene (20 ml) containing pyridine (1 ml) and $POCl_3$ (0·5 ml) was added. The reaction mixture was then boiled under reflux (1 hr), cooled, poured onto ice-water and then extracted with $CHCl_3$. The $CHCl_3$ extract was dried ($MgSO_4$) and concentrated to give a red solid (6 mg). This product was shown to contain approximately equal equantities of V and VI, the identity of which was confirmed by comparing the R_f values and the ultraviolet spectra with that of the authentic samples.

The keto-amine (VIII) was dehydrated under identical conditions, to furnish a similar mixture of V and VI.

Equilibration of V *and* VI. $POCl_3$ (0·5 ml) was added to a soln of V (2 mg) in benzene (10 ml) containing pyridine (1·0 ml), and the reaction mixture boiled under reflux (1 hr). The cooled soln was poured onto ice, extracted with $CHCl_3$ and the $CHCl_3$ soln was dried and concentrated. The product (1·5 mg) was analysed by TLC and UV spectroscopy and shown to containing approximately equal quantities of V and VI. The compound VI could be equilibrated under identical conditions.

Hydrolysis of V *and* VI. A soln of V (1·0 mg) in $CHCl_3$ (5 ml) was exposed to the atmosphere, and permitted to stand at room temp overnight. The product (1·0 mg) obtained on concentration was shown to contain mainly VII with traces of VIII (and V, VI), the identity of which was confirmed by comparing the R_f values and ultraviolet spectra with that of the authentic samples.

Oxidation of VI. VI (5 mg) was dissolved in glacial AcOH (5 ml), warmed to 100° and treated with 3% $KMnO_4$aq (5 ml). The reaction mixture was then warmed on a water bath (5 min) and a second portion of

$KMnO_4$aq (2 ml) was added. After the reaction mixture had been permitted to stand at room temp (15 min), it was cooled in an ice-bath, and decolourized with a stream of SO_2. The soln was diluted with water (10 ml) and extracted with $CHCl_3$. The $CHCl_3$ soln was washed repeatedly with water, dried ($MgSO_4$) and concentrated. The residue obtained was adsorbed onto a silica gel plate (20 × 20 × 0·1 cm, Merck HF 254 + 366) and eluted with light petroleum (b.p. 40–60°) ether (2 : 1). Only one major band could be detected under low wavelength UV light. This band was removed, extracted into $CHCl_3$ and the $CHCl_3$ soln concentrated to yield a trace of pale yellow solid (XI); mass spec. *m/e* 344·0789 (M^+), 298·0872 ($M^+—NO_2$). $C_{20}H_{12}N_2O_4$ requires M, 344·0797; IR ν_{max} ($CHCl_3$) 1786 (C═O), 1720 (C═O), 1530 (NO_2), 1350 (NO_2).

REFERENCES

[1] E. E. van Tamelen and T. L. Burkoth, *J. Am. Chem. Soc.* **89**, 151 (1967); S. Masamune and R. T. Seidner, *Chem. Commun.* 542 (1969).

[2] E. Vogel, *Chem. Soc. Special Publ.* No. 21, 113 (1967).

[3] F. Sondheimer and A. Shani, *J. Am. Chem. Soc.* **89**, 6310 (1967).

[4] K. Grohmann and F. Sondheimer, *Ibid.* **89**, 7119 (1967); R. H. Mitchell and F. Sondheimer, *Ibid.* **90**, 530 (1968).

[5] A. P. Bindra, J. A. Elix and M. V. Sargent, *Tetrahedron Letters* 4335 (1968).

[6] A. E. Blood and C. R. Noller, *J. Org. Chem.* **22**, 873 (1957).

[7] J. A. Elvidge and J. H. Golden, *J. Chem. Soc.* 4144 (1956).

[8] P. De Mayo and S. T. Reid, *Chem. & Ind.* 1576 (1962).

[9] A. Dunet and A. Willemart, *C.R. Acad. Sci., Paris*, **226**, 1286 (1948).