Tetrahedron. Vol. 27, pp. 367 to 374. Pergamon Press 1971 Printed in Great Britain

HETARYLNITRENES—IV
ANNELATED NITRENOAZINES

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(*Received in UK* 31 *July* 1970; *Accepted for publication* 20 *August* 1970)

Abstract—2-Quinolylnitrene (II) rearranges to 1-isoquinolylnitrene (IV) in the gas-phase: the products from either nitrene are *o*-cyanobenzylcyanide (IX) and 4-cyanoindole (X). 2-Quinoxalylnitrene (XVI) and 4-quinazolynitrene (XIV) likewise give identical products, 1-cyanobenzimidazole (XVIII) and N-cyanoanthranilonitrile (XX), formed by ring contraction and ring opening. Indole ring opens at 900° to give phenylacetonitrile. 9-Nitrenophenanthridine (XXIX) dimerises at 500°, but at 800° ring opens and recloses to give 4-cyanocarbazole (XXXII) and 9-cyanocarbazole (XXXI). The nitrenes were produced by N_2-elimination from the corresponding tetrazoles.

RESULTS AND DISCUSSION

IT WAS shown recently[1] that N-scrambling occurs in the products from 2-pyridylnitrene, due to ring expansion to 2,7-diazatropylidene. Similar reactions of nitrenobenzazines and -diazines are now reported.

Pyrolysis of tetrazolo[1.5-*a*]quinoline (I) in the interval 380–510°/10^{-3}-10^{-2} mm gave *o*-cyanobenzylcyanide (IX) and 4-cyanoindole (X; 40% and 25% respectively at 510°); the same products were obtained from tetrazolo[5.1-*a*]isoquinoline (V). The incomplete recovery was due to charring in the pyrolysis tube, a general tendency[1] for tetrazolopyridines. Formation of IX, which can be formally regarded as a glutacononitrile, is diagnostic[1] of ring isomerisation of 2-quinolylnitrene (II) to 1-isoquinolylnitrene (IV) by ring expansion, as shown in Scheme 1.* On the other hand there is no evidence to suggest that the reverse reaction (IV → II) takes place (such as, for example, 2-quinolylamine from IV). The reason for this may be that IV is easily converted to products, whereas quinolylnitrene (II) is not, thus making the ring expansion virtually irreversible (contrast Ref. 1).

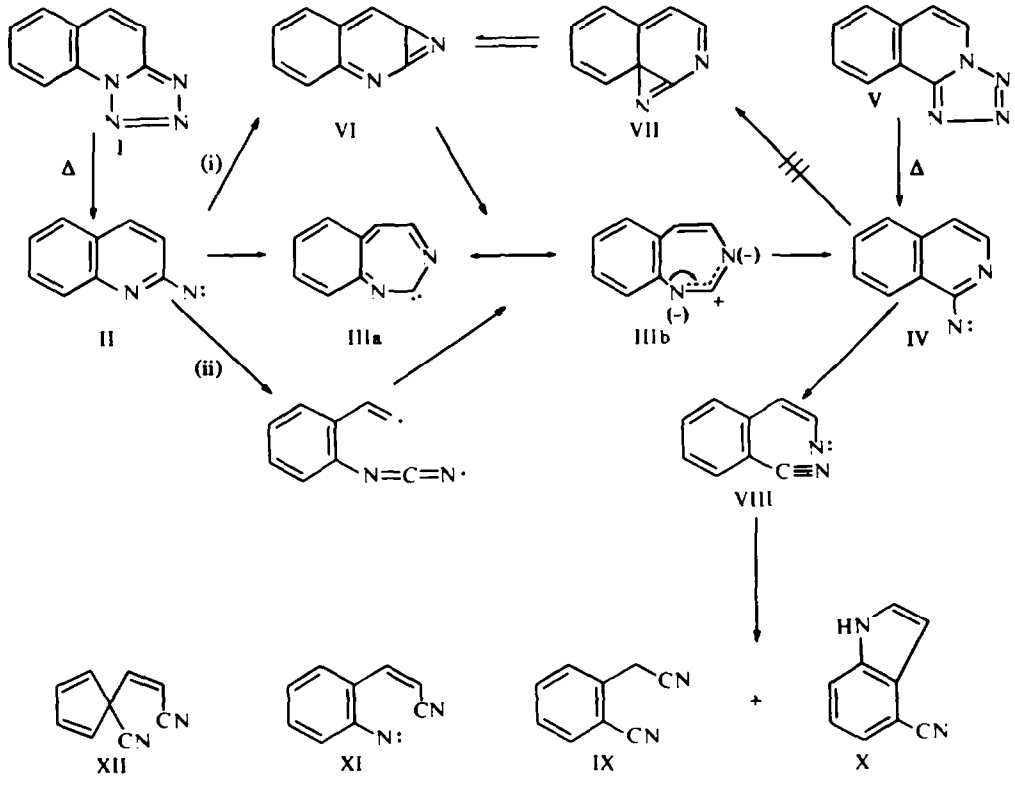
The involvement of azatropylidenes in ring isomerisations of this type[1-3] is corroborated by the analogous ring expansion of phenylcarbene to tropylidene.[4,5] The reaction II → III can proceed either *via* bicyclic intermediate[6] VI (route *i*), or *via* ring opening† (route *ii*). Cadogan[7] postulated an equilibrium analogous to VI ⇌ VII (but not involving tropylidenes) for the formation of pyridine derivatives in the deoxygenation of aromatic nitro compounds, a reaction which probably involves nitrenes.[8] The formation

* The same type of ring opening/re-closure as in the reaction IV → VIII → X has been observed in XXIX (*vide infra*).

† The ring opening pathway seems to be preferred in the case of 9-nitrenophenanthridine (XXIX) (*vide infra*).

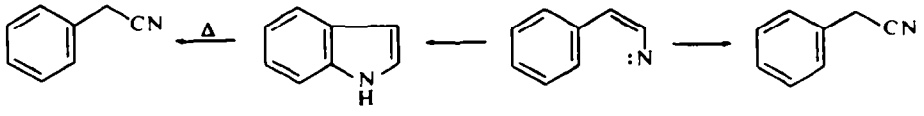
of VII would be particularly unfavourable in the present case, due to complete loss of aromaticity, and therefore provides an additional reason for the non-occurrence of the reaction IV → III.

SCHEME 1



Brown and Smith[9] reported recently the formation of the products IX and X by CO_2-elimination from the oxadiazolones, and proposed another intermediate (XII), supposedly formed by ring contraction[10, 11] in the new nitrene (XI) which would result from cleavage[12] of quinolylnitrene (II). It is highly unlikly[10, 11] that such an intermediate (XII) could be formed in the required[9] high yield (~ 100%).

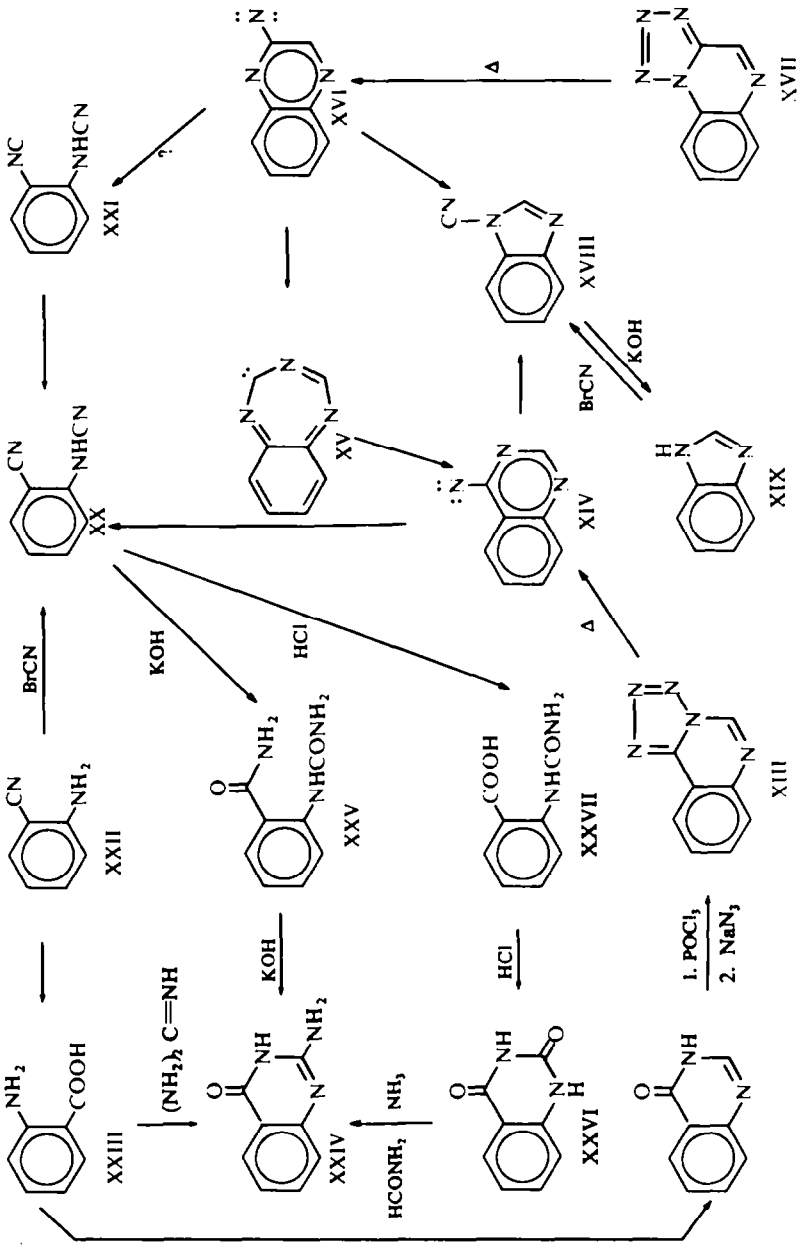
Although indole on pyrolysis gives phenylacetonitrile the reaction requires such



drastic conditions that the possibility (X→IX) can safely be excluded. Conversely, β-styrylnitrenes are known to give indoles[13] and phenylacetonitriles.[13]

Tetrazolo[1.5-*a*]quinoxaline (XVII) and tetrazolo[5.1-*c*]quinazoline (XIII) also gave identical products, namely 1-cyanobenzimidazole (XVIII) by ring contraction and N-cyanoanthranilonitrile (XX) by ring opening (Scheme 2), in near quantitative yield in both cases. Both the nitrenes (XIV and XVI) are able to ring contract[12] to XVIII,

SCHEME 2


XXIII
XXII
XXI
XX
XIX
XVIII
XVII
XVI
XV
XIV
XIII
XXIV
XXV
XXVI
XXVII
BrCN
KOH
HCl
Δ
(NH2)2 C=NH
NH3
HCONH2
1. POCl3
2. NaN3

without intervention of a triazatropylidene (XV). The formation of XX from XVI may involve ring expansion to XV, but the reaction could also proceed by ring cleavage to *o*-isocyanophenylcyanamide (XXI). Similarly we found[14] that ring interconversion *via* ring expansion was a possibility but not a necessity in 4-pyrimidylnitrene and pyrazonylnitrene. The question must be further examined by labelling techniques.

1-Cyanobenzimidazole (XVIII) was also obtained from benzimidazole (XIX) and cyanogen bromide, and was hydrolysed again to benzimidazole by alkali. N-cyanoanthranilonitrile (XX) was similarly obtained from anthranilonitrile (XXII),[15] and it gave on alkaline hydrolysis 2-amino-4-quinazolinol* (XXIV), also obtainable[17] from anthranilic acid (XXIII) and guanidine. XXIV is presumably formed by cyclisation in an intermediate hydrolysis product (XXV). Acid hydrolysis of XX gave quinazolin-2,4-diol (XXVI), presumably *via* 2-ureido-benzoic acid[18] (XXVII). XXVI is converted to XXIV by ammonia.[19] Phenylcyanamide is known[20] to hydrolyse to phenylurea, and to trimerise on heating[21] to triphenylisomelamin. XX similarly resolidified quickly after melting, giving, according to the mass spectrum, a trimer.

Pyrolysis of 9,10-tetrazolophenanthridine (XXVIII; Scheme 3) at 500° gave a colourless dimer of the nitrene, presumably the dihydrotetrazine derivative (XXX). At 800° two other products, 9-cyanocarbazole (XXXI) and 4-cyano-carbazole (XXXII) were formed, presumably by ring opening and recyclisation as shown in Scheme 3. This is in marked contrast to the 2-pyridylnitrenes[1, 12] where ring contraction to cyanopyrroles occurs readily at 380°. It was postulated[12] that the latter reaction proceeds *via* a nitreno-azaprefulvene† intermediate (XXXIV). Such an intermediate would be particularly unfavourable for 9-nitrenophenanthridene (XXIX) as it destroys aromatic stability.

We have noted previously[14] that the thermal reactions of nitrenoazines bear formal resemblance to the photochemical reactions of azine N-oxides. The postulated ring opening of 9-nitrenophenanthridene (XXIX) to the biradical (XXXIII) and re-cyclisation to 9-cyanocarbazole (XXXI) is likewise in complete accord with the scheme put forward[23] for the formation of 9-acylcarbazoles (XXXVI) by photolysis of phenanthridene N-oxides (XXXV) (Scheme 3). Most interestingly, Buchardt and Kumler[24] have of late come to consider a nitrene mechanism in the reactions of azine N-oxides. This would correspond to the ring opening[12] of pyridylnitrenes which leads to glutacononitriles, as in the reaction IV → VIII → IX + X.

9,10-tetrazolophenanthridene (XXVIII) was originally obtained[45] in an attempt to prepare 4-cyanocarbazole (XXXII) from 2-azido-2′-cyanobiphenyl in an ordinary nitrene reaction. As the azido-group underwent 1,3-addition to the cyano-group instead, an attempt was made, without success, to pyrolyse the product, (XXVIII).

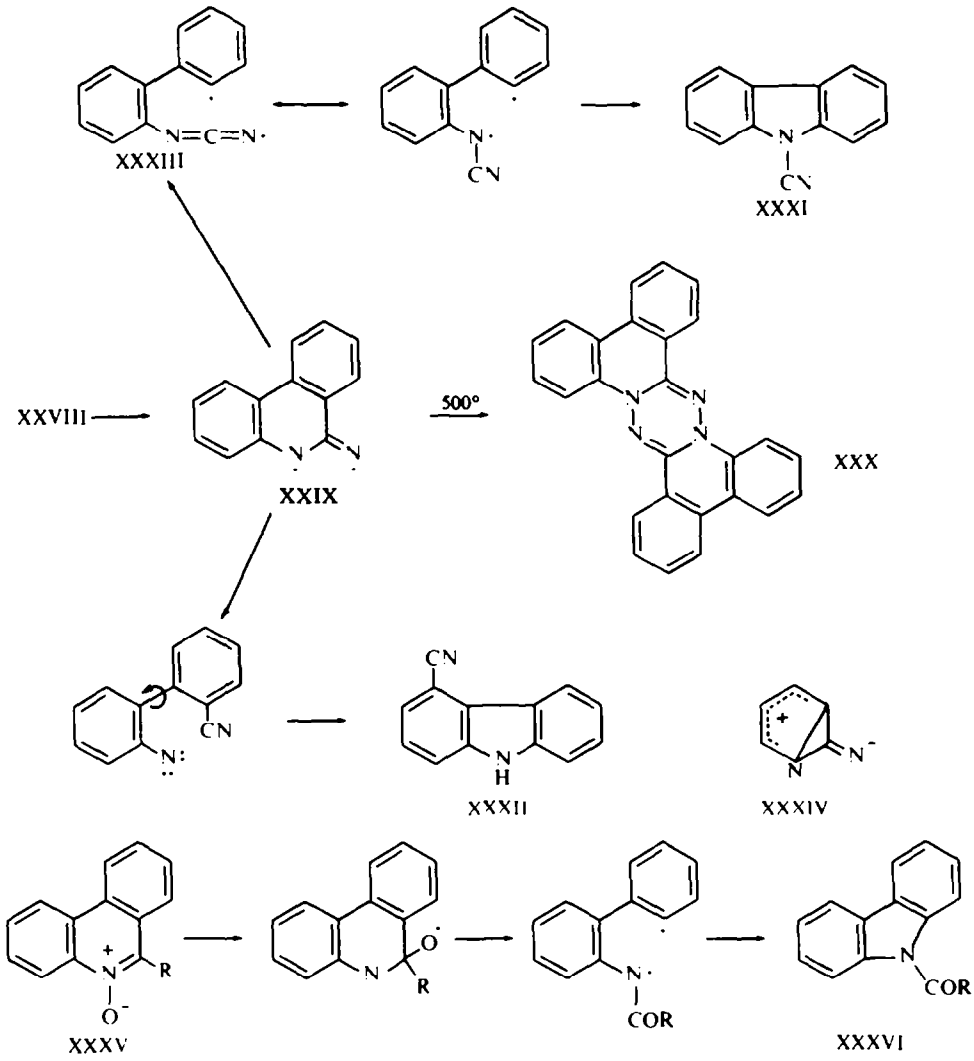
EXPERIMENTAL

Pyrolyses were performed in an unpacked pyrex tube (compounds I, V, XIII, and XVII) or a packed silica tube (compounds XXVIII and indole), held under an ultimate vacuum of 10^{-5} mm Hg. Samples were sublimed in below their mps, and the products collected in one trap cooled in liquid N_2. Mass spectra were recorded on an A.E.I. MS 902 or a CEC 21–490 with direct inlet, and nmr spectra were recorded on a Perkin–Elmer R 10 or a Varian A-60 spectrometer. Mps are uncorrected.

* The aromatic nomenclature is used, although the formulae are drawn in the keto-form, *cf* Armarego.[16]

† The name "prefulvene" was introduced by Bryce-Smith and Longuet-Higgins.[22]

SCHEME 3



(i) *Tetrazolo*[1.5-a]*quinoline*[26] (I) or *tetrazolo*[5.1-a]*isoquinoline*[27] (V) (1·00 g) was pyrolysed at 510°/10^{-2} mm in 6 hr (subl in at 135°) with some carbonisation inside the tube. The white crystalline product was chromatographed on alumina. CCl_4 eluted IX, mp 80–81°, lit.[28] 81°; ir (KBr): 2250 m (unconj *CN*) and 2225s (*conj CN*) cm^{-1}; NMR ($CDCl_3$): τ 2·85 (m, 4H), 6·02 (s, 2H); M⁺ 142. Chloroform eluted X, m.p. after recrystallization from water: 121°, lit[29] 120–121°, picrate: m.p. 164° from water, lit[29] 164–165°. acid from alkaline hydrolysis:[29] m.p. 213–214°, lit[29] 213–214°; IR (KBr): 3320 s (NH), 2225 s (CN) cm^{-1}; NMR ($CDCl_3$): τ 0·9 (broad, NH), 2·60 (centre of 10 multiplets, 4H), 3·25 (long-range coupled triplet, 1H); M⁺ 142. The yields were determined by NMR of the crude pyrolysate and were close to identical from either I or V: 40%IX and 25%X.

At 380°/10^{-3} *mm (subl in at 100–135°; 12 h) 25% IX and 15% X were obtained.*

(ii) *Tetrazolo*[5.1-c]*quinazoline* (XIII). 4-Chloroquinazoline[30] (2·0 g) and sodium azide (1·6 g) in abs EtOH (30 ml) was stirred at 20° for 1 hr, evaporated to dryness, extracted with benzene, and the extract

evaporated to give XIII (2·08 g), m.p. (dec subl) 195–205°. Recrystallisation from benzene gave colourless prisms, m.p. 211–212° (lit[31a] 205°;[31b] 208–209°); mass spectrum: (CEC, source 210°, probe 80°): M^+ 171 (28), 143 (100, m^* 120), 116 (40·5, m^* 94), 89 (12·5, m^* 68·2).

0·05 g XIII was pyrolysed at 450°/10^{-3} mm (subl in at 130° in 12 hr). The products were separated by fractional sublimation (60°/0·5 mm), giving 0·21 g (50%) slightly lachrymatory[14] XVIII as the most volatile, and 0·19 g (45·5%) XX as the least volatile component. At 380°/10^{-3} mm 53% XVIII and 46% XX were obtained. Identification is described under (iv) and (v).

(iii) *Tetrazolo*[1.5-a]*quinoxaline*[32] (XVII; 0·475 g) was pyrolysed at 500°/0·05 mm in 12 hr (subl in at 130–150°). The products (0·38 g; 95·5%) were separated by fractional sublimation (60°/0·5 mm), giving 0·16 g (40·0%) of XVIII and 0·22 g (55·5%) XX. Identification: see (iv) and (v).

At 450°/10^{-3} mm (subl in at 120–145° in 12 hr) 57·5% (XVIII) and 33·5% (XX) were obtained.

(iv) *1-Cyanobenzimidazole* (XVIII). Cyanogen bromide (0·1 mole) in benzene (10 ml) was added dropwise to benzimidazole (0·2 mole) in benzene (100 ml) at 60°. The sol was evaporated after filtering, giving an 88% yield of XVIII, m.p. after sublimation (60°/0·5 mm) 104–5°, IR (KBr): 3000m, 2255s (CN), 1510 s, 1450 s, 1370 s, 1200 vs; NMR ($CDCl_3$): τ 1·83 (s, 1H, H_2), 2·0–2·67 (4 aromatic H); M^+ 143 (100), M–27 (47), M–27–26 (18). (Source 210°, probe 90°).

Alkaline hydrolysis (4N KOH; 100°; 12 hr) gave benzimidazole, m.p. 170°, undepressed on admixture with authentic sample; NMR identical with that of authentic sample.

(v) *N-Cyanoanthranilonitrile* (XX) was obtained from anthranilonitrile[15] (0·2 mole) and cyanogen bromide (0·1 mole) in ether, *cf* Baum.[33] It had m.p. 116–17° (from chloroform), turning yellow in the melt. The cooled, crystallised melt melted again at 135° and was, according to the mass spectrum a trimer: M^+ 429. The monomer had the following properties: IR (KBr): 3225 s (broad, NH), 2250–2200 s (broad, CN), 1605 m, 1590 s, 1510 s, 1450 s, 1295 s, 1250 s, 760 vs; NMR ($CDCl_3$): τ 2·50 (centre of multiplet, 4H), 3·22 (broad, 1H, exchangeable with D_2O): M^+ 143 (100), M–27 (21), M–41 (1·7, m^*94), *m/e* 90 (2·9), 89 (3·4), 76 (1·9), 75 (2·3) (Source 210° Probe 80°).

Alkaline hydrolysis of XX (4N KOH; 100°; 12 hr) gave after acidification with AcOH a ppt of XXIV m.p. (dec) 320°, identical (IR, UV) with a sample prepared according to Verkade and Breukink,[17] and distinctly different from 4-amino-2-quinazolinol.[17, 34]

Acid hydrolysis of XX (4N HCl; 100°; 12 hr) gave XXVI, m.p. > 350°, identical with a sample prepared from anthranilic acid and potassium cyanate, followed by acidification.[18]

(vi) 9,10-*Tetrazolophenanthridine* (XXVIII). 9-Chlorophenanthridine (6·4 g; 0·03 mole) and sodium azide (7·8 g; 0·12 mole) in EtOH (125 ml) containing HCl (0·12 mole) was refluxed for 66 hr. The solid was filtered off, washed with water, and recrystallized from 90% aqueous EtOH giving colourless needles, m.p. 222·5–223·5° (lit[25] 221·5–223·5°), yield 3·75 g (57%).

Compound XXVII (0·50 g) was pyrolysed at 500°/0·01–0·05 mm (subl in at 196°) to give 0·22 g of a white solid which did not melt at 360° but sublimed slowly. The mass spectrum (M^+ 384 (70%); M/2 192 (100%), m^* 96) indicated a dimer of the nitrene; thus the yield was 50·5%.

At 800°/0·05 mm *ca* 10 mg carbazole deposited at the *entrance* to the furnace. At the exit end deposited two fairly distinct bands of crystals. Those which had sublimed farthest (*ca* 10%) were in all respects identical with the sample of 9-cyanocarbazole described in (vii). The combined crystals were chromatographed on alumina (wet ether, followed by chloroform) which removed 9-cyanocarbazole (*cf* vii) and left as the major product XXXII (60% yield), m.p. 153–55°. Alkaline hydrolysis[36] of 0·10 g nitrile gave 0·08 g carbazole-4-carboxylic acid, m.p. 244–45° from benzene (lit[35] 244–45°); ν_{max} 3400, 2600, 2500, 1700 cm^{-1}; the nitrile had ν_{max} 3320, 2230, 1615 cm^{-1}, and mass spectrum identical with that of 9-cyanocarbazole (see vii).

The mass spectrum of 9,10-tetrazolophenanthridine was, below M^+, identical with that of the nitrile(s); (M–28) was the base peak, and only at 12 eV did M^+ and M–28) attain equal intensities. The fragmentation was accompanied by a prominent meta-stable peak, excluding the possibility of thermal decomposition.

(vii) 9-*Cyanocarbazole* (XXXI). To carbazole (5·2 g; 0·0311 mole) in dry ether (100 ml) was added sodium hydride (0·75 g, 0·0312 mole), with a trace of NaOMe as catalyst, and the mixture refluxed for 12 hr, then cooled to −30°. Cyanogen bromide (5 g; 0·047 mole) in ether was added, the mixture was allowed to warm and then refluxed for 1 hr, filtered, and concentrated *in vacuo*. 9-Cyanocarbazole (5·3 g; 89%) containing a trace of carbazole resulted. It was purified by chromatography on a short column (10 cm) of dry alumina/dry ether [the alumina and ether must be dry, otherwise hydrolysis takes place, giving carbazole]. IR (Nujol) 2235 cm^{-1} (CN); no NH in the spectrum; Calc. mass: 192·06875; Found: 192·06932; M^+ 192 (100), M—HCN (5, m^*), M—H_2CN (8), M^{2+} (10), the spectrum was identical with

that of 4-cyanocarbazole. Alkaline hydrolysis[36] or chromatography on alumina/wet ether afforded carbazole (94%). Pyrolysis at 700–900° gave increasing amounts of carbazole, as judged from the IR and UV spectra.

(viii) *Pyrolysis of indole.* Indole (1·0 g) was pyrolysed at 960°/0·10–0·01 mm, and the products separated by GLC (silicone rubber, SE 30; 150°; 60 ml He/min). The three major compounds were indole, phenylacetonrile, and *o*-toluntrile (25 : 1 : 1·5, relative peak areas), identified by comparison of their spectra with those of authentic samples. Phenylacetonrile is known to give *o*-tolunitrile on pyrolysis[37] but not in as high yield as recorded here. It appears that indole gives *o*-tolunitrile directly.

Acknowledgements—I thank Dr. J. K. McLeod, Research School of Chemistry, A.N.U., for mass spectrometric data, and Professor Dr. P. E. Verkade, The Technical University, Delft, for providing IR spectra of the samples of 2-amino-4-quinazolinol and 4-amino-2-quinazolinol prepared by Breukink and Verkade.[17] The award of an A.N.U. Postgraduate Scholarship is gratefully acknowledged.

REFERENCES

[1] W. D. Crow and C. Wentrup, *Chem. Commun.* 1387 (1969)
[2] W. D. Crow and C. Wentrup, *Tetrahedron Letters* 6149 (1968)
[3] C. Wentrup, *Chem. Commun.* 1386 (1969)
[4] R. C. Joines, A. B. Turner and W. M. Jones, *J. Am. Chem. Soc.* **91**, 7754 (1969)
[5] C. Wentrup and K. Wilczek, *Helv. Chim. Acta* **53**, 1459 (1970)
[6] *Cf.* R. Huisgen, D. Vossius and M. Appl, *Chem. Ber.* **91**, 1 (1958); R. Huisgen and M. Appl, *Ibid.* **91**, 12 (1958); M. Appl and R. Huisgen, Ibid. **92**, 2961 (1959)
[7] J. I. C. Cadogan, *Chem. Revs* **22**, 222 (1968)
[8] R. J. Sundberg, W. G. Adams, R. H. Smith and D. E. Blackburn, *Tetrahedron Letters* 777 (1968); R. J. Sundberg, B. P. Das and R. H. Smith, *J. Am. Chem. Soc.* **91**, 658 (1969)
[9] R. F. C. Brown and R. J. Smith, *Chem. Commun.* 795 (1969)
[10] W. D. Crow and C. Wentrup, *Tetrahedron Letters* 4379 (1967)
[11] W. D. Crow and C. Wentrup, *Ibid.* 5569 (1968)
[12] W. D. Crow and C. Wentrup, *Chem. Commun.* 1082 (1968)
[13] G. Smolinsky and C. A. Pryde, *J. Org. Chem.* **33**, 2411 (1968); K. Isomura, S. Kobayashi and H. Taniguchi, *Tetrahedron Letters* 3499 (1968)
[14] C. Wentrup and W. D. Crow, *Tetrahedron* (Hetarylnitrenes Part I)
[15] G. R. Bedford and M. W. Partridge, *J. Chem. Soc.* 1633 (1959)
[16] W. L. F. Armarego, *Adv. Heterocycl. Chem.* **1**, 253 (1963)
[17] K. E. Breukink and P. E. Verkade, *Rec. Trav. Chim.* **79**, 443 (1960); F. Kunckell, *Ber. Dtsch. Chem. Ges.* **38**, 1212 (1905)
[18] O. Diels and A Wagner, *Ibid.* **45**, 874 (1912)
[19] P. Griess, *Ibid.* **2**, 417 (1869)
[20] A. Cahours and S. Cloëz, *C. R. Acad. Sci., Paris*, **38**, 354 (1851); *Liebigs. Ann.* **90**, 91 (1854)
[21] F. Arndt, *Ibid.* **384**, 350(**1964**); A. W. Hoffmann, *Ber. Dtsch. Chem. Ges.* **18**, 3223 (1885)
[22] D. Bryce-Smith and H. C. Longuet-Higgins, *Chem. Commun.* 593 (1966); D. Bryce-Smith, *Pure Appl. Chem.* **16**, 47 (1968)
[23] E. C. Taylor and G. C. Spence, *Chem Commun.* 1037 (1968)
[24] O. Buchardt and P. L. Kumler, *Ibid.* 1321 (1968); O. Buchardt, P. L. Kumler and C. Lohse, *Acta Chem. Scand.* **23**, 2149 (1969)
[25] P. A. S. Smith, J. M. Glegg and J. H. Hall, *J. Org. Chem.* **23**, 524 (1958)
[26] G. A. Raynolds and J. A. Van Allen, *Ibid.* **24**, 1478 (1959)
[27] D. Nair and S. R. Mehta, *Indian J. Chem.* **5**, 403 (1967)
[28] S. Gabriel and R. Otto, *Ber Dtsch. Chem. Ges.* **20**, 2222 (1887)
[29] F. C. Uhle, *J. Am. Chem. Soc.* **71**, 761 (1949)
[30] T. Stephen and H. Stephen, *J. Chem. Soc.* 4178 (1956)
[31] [a] G. S. Sidhy, G. Thyagarajan and N. Rao, *Naturwissenschaften* **50**, 732 (1963)
[b] I. Ya. Postovskii and S. L. Mertsalov, *Khim. Geterotsikl. Soedin.* 1096 (1967); *Chem. Absts.* **69**, 59188 (1968)
[32] D. I. Shino and S. Tagami, *J. Am. Chem. Soc.* **82**, 4044 (1960)

[33] F. Baum, *Ber. Dtsch. Chem Ges.* **41**, 524 (1908)
[34] R. B. Trattner, G. B. Elion, G. H. Hitchings and D. M. Sharefkin, *J. Org. Chem.* **29**, 2674 (1964)
[35] P. H. Carter, S. G. P. Plant and M. Tomlinson, *J. Chem. Soc.* 2210 (1957)
[36] T. R. Govindachari, S. Rajappa and V. Sudarsanan, *Indian J. Chem.* **1**, 247 (1963)
[37] C. Wentrup and W. D. Crow, *Tetrahedron* **26**, 3965 (1970)