Synthesis of 3-Monosubstituted *s*-Tetrazines and Their Reactions with Monosubstituted Acetylenes

By OTTO MERESZ* and PATRICIA A. FOSTER-VERNER

(*Lash Miller Chemical Laboratories, Department of Chemistry, University of Toronto, Toronto* 181, *Ontario, Canada*)

Summary In the inverse Diels–Alder reactions of monosubstituted *s*-tetrazines, 3-*p*-tolyltetrazine and phenylacetylene gave 3,4-diphenylpyridazine, while the same tetrazine and methylacetylene gave the 3,5-disubstituted product.

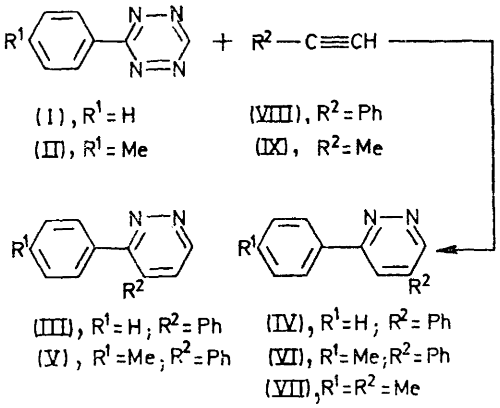
WHILE the stereo- and regio-chemistry of the Diels–Alder reaction has been extensively investigated, no information is available on related aspects of the addition reactions of *s*-tetrazines.[1]† We have therefore synthesised monosubstituted tetrazines and studied their reactions with monosubstituted ethylenes and acetylenes. The published route[2] to 3-phenyltetrazine appeared to be rather tedious and we have explored the possibility of obtaining monoaryltetrazines by modifying Pinner's original[3] method.

Reaction of a mixture of methyl iminobenzoate hydrochloride and formamidine acetate (1:3 molar ratio) with hydrazine hydrate (85%) at room temperature for 2 h, followed by the oxidation of the precipitating solid dihydrotetrazine with sodium nitrite and acetic acid gave almost pure 3-phenyltetrazine (I) (75%). 3-*p*-Tolyltetrazine (II) was similarly prepared (84%) from methyl imino-*p*-toluate hydrochloride, as magenta crystals, m.p. 84·5—85°.

Styrene reacted rapidly with (I) to give a complicated mixture, oxidation of which gave a black tar containing (t.l.c.) among other products both (III) and (IV), characterised below. The reaction of (I) with (VIII) in toluene solution was very slow [it took one week at room temperature for the colour of (I) to disappear], but gave a mixture of diphenylpyridazines (III) and (IV) (95:5) in 76% yield. Compounds (III) and (IV) were identical in all respects with authentic samples.[4]

When (II) and (VIII) treated in toluene solution at room temperature over a period of two weeks, the crude product (78%) was shown to be (V) and a trace of a second component, possibly (VI). Pure (V) formed colourless crystals, m.p. 136—137°. Methylacetylene (IX) did not react with (I) and only extremely slowly (3 weeks in a toluene solution stirred in a methylacetylene atmosphere at room temperature) with (II) to give, in addition to polymers, only one product (20%), m.p. 115·5—117°, characterised as (VII).

Structures (V) and (VII) were assigned to the above products mainly on the basis of their ^{1}H n.m.r. spectra, in comparison with those of authenticated (III) and (IV).



(I), $R^1 = H$
(II), $R^1 = Me$
(VIII), $R^2 = Ph$
(IX), $R^2 = Me$
(III), $R^1 = H$; $R^2 = Ph$
(V), $R^1 = Me$; $R^2 = Ph$
(IV), $R^1 = H$; $R^2 = Ph$
(VI), $R^1 = Me$; $R^2 = Ph$
(VII), $R^1 = R^2 = Me$

The 6-H resonance in (III) appears at δ 9·2 p.p.m. (1H, d, *J* 2·5 Hz), while in (IV) at δ 9·5 (1H, d, *J* 0·5 Hz). Compound (V) gave this signal at δ 9·1 (1H, d, *J* 2·5 Hz) and (VII) at δ 8·95 (1H, d, *J* 0·5 Hz). Mass spectral data were also in agreement with the assigned structures.

Thus it appears that the inverse Diels–Alder process is highly regioselective and follows the pattern of the normal reaction. The role of secondary orbital overlap effects in determining the stereochemistry in Diels–Alder reactions has been disputed.[5] Unfortunately, the symmetry of the tetra-azabarelene type intermediates rules out the addition reactions of tetrazines as models for the study of *exo*- or *endo*-additions. However, the complete change of regio-

---

† *s*-Tetrazines, *i.e.* 1,2,4,5-tetrazines, will be referred to as tetrazines in this communication.

specificity in the reactions of (II) with (VIII) and (IX), respectively, indicates that, here, secondary orbital overlap effects may be important. Our EHMO calculations on (I) and (VIII) support this hypothesis.

We thank the donors of the L. V. Redman Fellowship (to P.A.F.), the National Research Council of Canada for financial support, and Professor A. G. Brook for his interest in this work.

(*Received*, 22*nd May* 1972; *Com.* 867.)

[1] R. A. Carboni and R. V. Lindsey, *J. Amer. Chem. Soc.*, 1958, **80**, 5793, **81**, 4342; J. Sauer and D. Lang, *Angew. Chem.*, 1964, **76**, 603.

[2] V. A. Grakuskas, A. J. Tomasewski, and J. P. Horwitz, *J. Amer. Chem. Soc.*, 1958, **80**, 3155.

[3] A. Pinner, *Ber.*, 1893, **26**, 2126; 1894, **27**, 984.

[4] P. Schmidt and J. Druey, *Helv. Chim. Acta*, 1954, **37**, 134; R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Amer. Chem. Soc.*, 1965, **87**, 1320.

[5] R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, 1965, **87**, 4388; W. C. Herndon and L. H. Hall, *Tetrahedron Letters*, 1967, 3095.