Conjugated N-Isocyanides; a Reassessment and a Correction of Claimed Stable Conjugated N-Isocyanides. Stable *N*-Formyltriazenes; a Confirmation

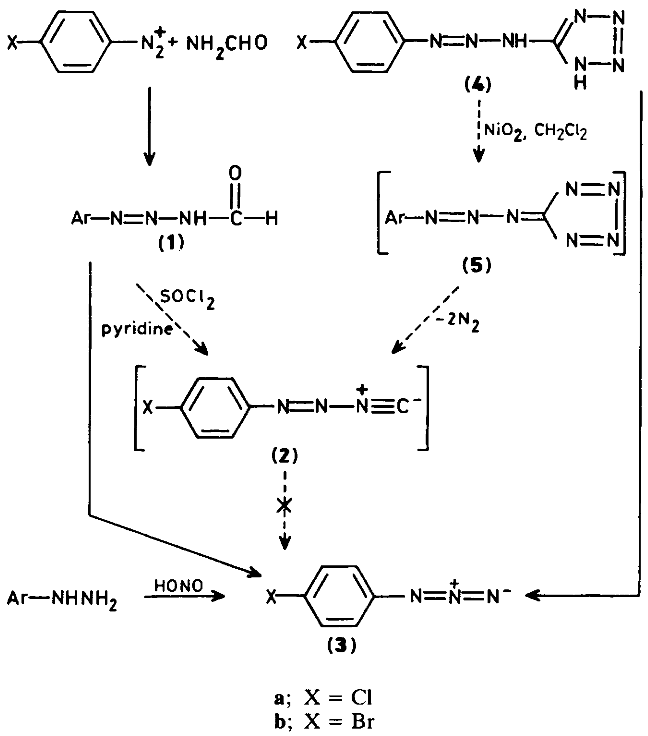
Richard N. Butler,*[a] **Paul D. O'Shea,**[a] **and Luke A. Burke**[b]

[a] *Chemistry Department, University College, Galway, Ireland*

[b] *Chemistry Department, Rutgers University, Camden College of Arts and Science, Camden, New Jersey 08102, U.S.A.*

Previously claimed stable solid aryldiazoisocyanides were found to be crude arylazides, and dehydration of formamides as a route to stable N-isocyanides must be viewed with caution; stable *N*-formyltriazenes are confirmed and literature difficulties with reproducible syntheses are explained.

The synthetic importance of isocyanides has resulted in major attention on these compounds.[1,2] Within this class there has been considerable interest[1,2] in isocyanides bonded to nitrogen such as (I) and (II) since they are isomeric with the thermodynamically more stable cyanamide structure (III) and nitrogen containing molecules often rearrange readily in order to replace N–N bonds with stronger N–C or C–C bonds. There are a number of reports[3—6] of the isolation of compounds containing the functional group (I). Some of these compounds have been described[3] as 'highly reactive, unstable, evil smelling liquids.' The isolation of crystals of compound (IIa) has been claimed.[4] In other reports N-isocyanides have been

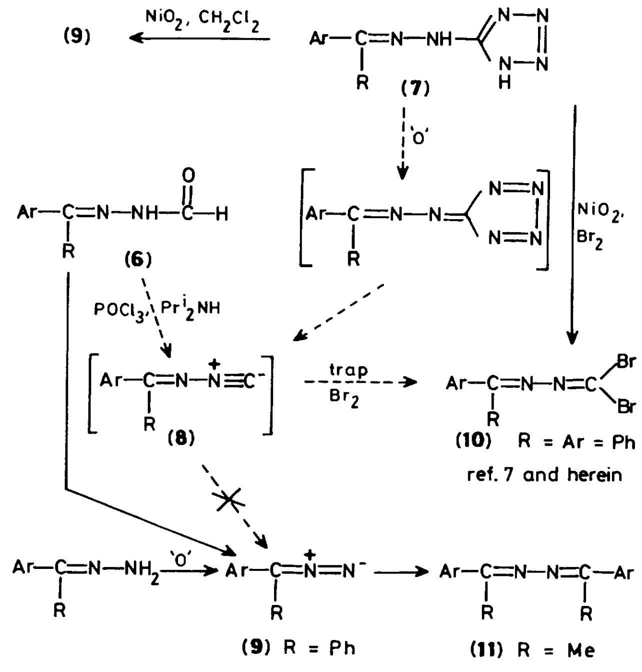


Scheme 1. (**2a**), lit.[10] m.p. 21 °C; (**2b**), lit.[10] m.p. 28 °C. (**3a**), m.p. 19—20 °C; (**3b**), m.p. 20 °C.

detected as highly reactive transient intermediates,[7,8] and PhNH-N$^+$≡C$^-$ has recently been reported[9] to rearrange to the corresponding cyanamide at −100 °C. The most recent report[10] of stable N-isocyanides describes the compounds (**2**) (Scheme 1) as unreactive crystalline solids with low melting points. Hence the reported N-isocyanides may be divided into two main groups (I) and (II), the latter of which are considered to be especially stable owing to conjugation with the X=N moiety. This paper is concerned with this group containing the structure unit (II).

$>\mathrm{N{-}\overset{+}{N}{\equiv}C^-}$	$\mathrm{X{=}N{-}\overset{+}{N}{\equiv}C^-}$	$>\mathrm{N{-}C{\equiv}}$	$p\text{-}\mathrm{MeOC_6H_4C(Me){=}N{-}\overset{+}{N}{\equiv}C^-}$
(I)	(II)	(III)	(IIa), ν_{NC} 2080 cm^{-1}

Our work[11,12] on tetrazol-5-yltriazenes (**4**) (Scheme 1) should provide a good route to these systems by oxidation to penta-azafulvenes (**5**) which should fragment to the diazoisocyanides (**2**). Normal oxidations of 5-substituted aminotetrazoles, RNH$\overline{\mathrm{C{=}NN{=}N}}$NH readily give isocyanides, R-NC.[13] However the triazenes (**4**) proved to be highly susceptible to N-N bond fragmentation giving diazonium ions in the presence of acidic electrophiles such as Pb(OAc)$_4$, H$^+$, AcOAc, and Br$_2$.[11,12] We have now achieved the oxidation† of the compounds (**4**) without fragmentation of the triazene chain by carefully excluding acid using either Et$_3$N with Br$_2$ or NiO$_2$ in dichloromethane (the Br$_2$–Et$_3$N system did not give a clean oxidation, and the fragmentation path[11,12] competed to the extent of 30—40%). The oxidation products were the azidobenzenes (**3**). The failure of this reaction to give the supposedly stable products (**2**) compelled us to make them by the reported[10] procedures. We encountered considerable initial difficulties in obtaining the precursory *N*-formyltriazenes (**1**). Others[14,15] have also had difficulties with *N*-formyltriazenes and there is confusion in the literature concerning the reproducible synthesis and stability of these compounds, probably owing to inadequate description of experiments. We found that in order to achieve the coupling‡ with formamide solid diazonium salt must be quickly filtered off and transferred to the ethereal formamide solution. If this diazonium salt is pure (>90% yield in a separate coupling with β-naphthol) stable *N*-formyltriazenes are formed and we confirm the m.p.s. and properties reported.[10] However, the diazonium salt may often be severely contaminated with the triazene, Ar–N=N–NHAr, from self-coupling. When this occurs *N*-formyltriazenes are not obtained.



Scheme 2

The evidence[10] for the structure of the diazoisocyanides (**2**) was provided by i.r. and u.v. spectra, cryoscopic molecular

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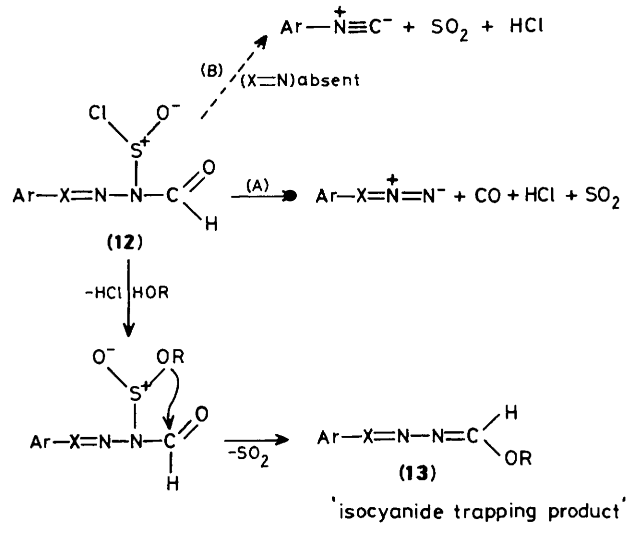
† Typically: a suspension of the triazene (**4**) (5 mmol) in dry dichloromethane was treated with NiO$_2$ (4 g), stirred at ambient temperature for 24 h, and filtered. The filter cake was washed thoroughly with dichloromethane, the combined washings and filtrate were evaporated, and the residue was chromatographed on a silica gel column [eluant, 3 : 1 v/v light petroleum (b.p. 40—60 °C)–dichloromethane] to give in the first fractions compound (**3a**) (43%) m.p. 19—20 °C and (**3b**) (41%), m.p. 20 °C.

‡ Typically: a solution of *p*-chloroaniline (13 mmol) in absolute ethanol (9.6 ml) was treated with 0.5 ml of saturated ethanolic hydrogen chloride (prepared by bubbling dry HCl gas through ethanol), then slowly treated with n-pentyl nitrite (16 mmol) at 20—25 °C, and set aside for 30 min at ambient temperature. Sufficient diethyl ether to precipitate the diazonium salt was added and the salt was filtered off under gravity, washed with ether till white, suspended in ether (25 ml), treated with formamide (27 mmol) with vigorous stirring and the mixture heated to reflux and then while under reflux treated slowly with 7% sodium hydrogen carbonate solution (5 ml) over 30 min. The mixture was cooled and the ethereal layer separated. The aqueous layer was mixed with further ether (25 ml), heated to reflux and treated again with the sodium hydrogen carbonate solution (5 ml) as before and this process repeated twice more. The combined ethereal extract was dried and evaporated, and the residue washed with cold ether–hexane (1 : 1 v/v) and recrystallised from hexane to give compound (**1a**), m.p. 130—131 °C (55%), lit.[10] m.p. 130—131 °C.



Scheme 3

weights, and microanalysis. Their stability was ascribed to special resonance and it was pointed out that they gave an i.r. band similar to the azide group doublet. Our treatment of the triazene (**1**) with thionyl chloride gave stable solid products which were identical to those reported.[10] These products proved to be crude samples of the azides (**3a**) and (**3b**) (Scheme 1). Their ^{13}C n.m.r. spectra showed four aromatic signals and no isocyanide signal. They were identical (m.p., mixture m.p., i.r., u.v., ^{1}H n.m.r., ^{13}C n.m.r.) with the compounds obtained by the oxidation of the triazenes (**4**) (Scheme 1) and with authentic samples separately prepared by treating *p*-chloro- and *p*-bromo-phenylhydrazines with nitrous acid. We conclude that diazoisocyanides are at present unknown and that they are not involved in these reactions. They may not exist at all. Preliminary MNDO calculations showed that the heat of reaction for the rearrangement from diazoisocyanide to diazocyanide involves a release of *ca.* 40 kcal mol^{-1} (cal = 4.184 J) and the barrier to interconversion is small ($\sim$20 kcal mol^{-1}).

These results cast doubt on the validity of dehydration of *N*-formylhydrazines as a route to stable conjugated N-isocyanides. The experimental details by which compound (IIa) was obtained[4] by dehydration of the *N*-formylhydrazone of *p*-methoxyacetophenone were not disclosed. We have attempted to make compound (IIa) by dehydration of the *N*-formylhydrazone (**6**) (Ar = *p*-$MeOC_6H_4$, R = Me) with $POCl_3$ and di-isopropylamine[16] and also by oxidation of the corresponding tetrazol-5-ylhydrazone (**7**) (Scheme 2). The same yellow solid ($\nu_{max.}$ 2079 cm^{-1}) was obtained from each reaction and this was identical to a yellow solid obtained on attempted synthesis of *p*-anisylmethyldiazomethane (**9**, Ar = *p*-$MeOC_6H_4$, R = Me) by oxidation of *p*-methoxyacetophenone hydrazone (Scheme 2). This yellow solid was mainly azine (**11**) contaminated with a small amount of compound (**9**; R = Me). Similar results were obtained on dehydration of *N*-formylhydrazones and oxidation of tetrazol-5-ylhydrazones of other aryl ketones which also gave aryldiazomethanes (**9**) ($\sim$80%) (Scheme 2). Oxidation of compound (**7**; Ar = R = Ph) in the presence of bromine gave the known compound (**10**) (66%). The formation of compounds such as (**10**) and (**13**) (Scheme 3) (supposedly derived from trapping of conjugated N-isocyanides) had led to claims of the existence of these N-isocyanides and to their supposed isolation when the reactions were carried out in the absence of trapping agents. The dashed lines in Schemes 1 and 2 represent current literature understanding of these reactions. This must now be fundamentally reassessed. The common factor in these reactions is not necessarily an isocyanide but more likely a different intermediate from which arylazides and diazomethanes may fragment but which may also fragment to an isocyanide. We tenatively propose the species (**12**) which could fragment by paths (A) or (B) (Scheme 3). Path A probably occurs when the group $-X{=}N^+{=}N^-$ constitutes a better leaving group than the isocyanide. When the reaction of the substrates (**1**) with $SOCl_2$ was carried out under a positive pressure of N_2 and the gases evolved were collected in an evacuated i.r. gas cell strong absorptions from carbon monoxide (2143 cm^{-1}), HCl, and sulphur dioxide were detected (and confirmed with authentic samples). This supports fragmentation (A) which is complicated and may involve moisture. It is likely that low yields of arylamines also reported[10] in this reaction, and confirmed herein, arise from unstable monosubstituted triazine, $ArN{=}N{-}NH_2$. External attack by alcohols could give compounds of type (**13**) by routes not involving N-isocyanides (Scheme 3). This mechanism suggests that the dehydration of formamides would be a 'safe' route to N-isocyanides of type (I) since there is no alternative stable leaving group. Necessary further mechanistic work will be undertaken and will include a theoretical study of the conjugated isocyanide moiety, $-X{=}N{-}N^+{\equiv}C^-$, and the postulated[7,13] penta-azafulvene intermediates from the tetrazole derivatives.

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References

1 I. Ugi, 'Isonitrile Chemistry,' Academic Press, New York, 1971; H. Walborsky and M. P. Perlasmay, 'The Chemistry of Triple-Bonded Functional Groups,' eds. S. Patai and Z. Rappoport, Wiley, New York, 1983, Part 2, p. 835.

2 J.-P. Anselme, *J. Chem. Educ.*, 1977, **54**, 296.

3 H. Bredereck, B. Fohlisch, and K. Walz, *Angew. Chem., Int. Ed. Engl.*, 1962, **1**, 334; *Liebigs Ann. Chem.*, 1965, **686**, 92.

4 I. Hagedorn and U. Eholzer, *Angew. Chem., Int. Ed. Engl.*, 1962, **1**, 514.

5 I. Hagedorn and H.-D. Winkelmann, *Chem. Ber.*, 1966, **99**, 850.

6 E. Muller, R. Beutler, and B. Zeeh, *Liebigs Ann. Chem.*, 1968, **719**, 72.

7 F. L. Scott, J. Donovan, and J. K. O'Halloran, *Tetrahedron Lett.*, 1970, 4079.

8 A. F. Hegarty and I. Cunningham, *J. Chem. Soc., Chem. Commun.*, 1986, 1196.

9 C. Wentrup and H.-W. Winter, *J. Org. Chem.*, 1981, **46**, 1045.

10 T. Ignasiak, J. Suszko, and B. Ignasiak, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2122; J. Suszko and T. Ignasiak, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, 1970, **18**, 671, 673.

11 R. N. Butler, P. D. O'Shea, and D. P. Shelly, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1039.

12 R. N. Butler and D. P. Shelly, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1101.

13 G. Hoffle and B. Lange, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 113.

14 S. Treppendahl, P. Jacobsen, and J. Wieczorkowski, *Acta Chem. Scand., Ser. B*, 1983, **37**, 155.

15 M. D. Threadgill and A. P. Gledhill, *J. Chem. Soc., Perkin Trans. 1*, 1986, 873.

16 R. Obrecht, R. Herrmann, and I. Ugi, *Synthesis*, 1985, 400.