A Novel Series of Nitrosamino-tetrazoles

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Summary A new series of nitrosamino-tetrazoles, with a possible primary nitrosamino-structure, has been isolated as stable compounds.

THE reaction of primary arylamines (and heterocyclic amines) with nitrous acid, which leads to diazonium salts is normally regarded as proceeding through a nitrosamine stage. No such nitrosamines have been isolated, though in the case of 5-amino-1-methyltetrazole (I; $R^1 = Me$, $R^2 = H$), reaction with nitrous acid has been suggested[1,2] to lead to such a compound, (I; $R^1 = Me$, $R^2 = NO$). This reaction could not be repeated by us, or by others.[3] We now report the first isolation of a number of nitrosamines, compounds (I; $R^1 = CH_2Ph$ and Ph, $R^2 = NO$) and (II; R = NO) from the nitrosation of 5-amino-1-benzyl-, -1-phenyl-, and -2-benzyltetrazole respectively (see Table).

Nitrosamines

Compound	Yield %	M.p.
(I; $R^1 = CH_2Ph$, $R^2 = NO$) ..	84	56°
(I; $R^1 = Ph$, $R^2 = NO$)	51	110°
(II; R = NO)	*ca.* 50	—[a]

Hydrazones

Compound	Yield %	M.p.
(I; $R^1 = CH_2Ph$, $R^2 = N{=}CHPh$	75	208°
(I; $R^1 = Ph$, $R^2 = N{=}CHPh$) ..	89	212°
(II; $R = N{=}CHPh$)	32[b]	145°

[a] Isolated as a viscous oil which decomposed on heating. For the nitrosation reaction in this case, the quantity of hydrochloric acid was 1/5 of that described above and the sodium nitrite 1/2.

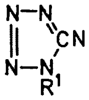
[b] Overall yield from amine.

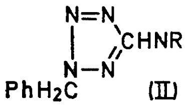
In a typical run 350 mM. of sodium nitrite in aqueous solution (3·5M) was added with stirring to a suspension of compound (I; $R^1 = CH_2Ph$, $R^2 = H$) (170 mM.) in 500 ml. of concentrated hydrochloric acid diluted with an approximately equal volume of crushed ice. The mixture was stirred for 2 hr. and the solid removed and stirred with cold ether (150 ml.). Evaporation of the ethereal solution, after drying, yielded compound (I; $R^1 = CH_2Ph$, $R^2 = NO$).

Reduction of the nitrosamines to the corresponding hydrazines which were characterised as benzaldehyde derivatives (I; $R^1 = CH_2Ph$ or Ph, $R^2 = N{=}CHPh$) and

(II; R = N=CHPh), was effected when the materials (I; R^1 = CH$_2$Ph or Ph, R^2 = NO) and (II; R = NO) were treated with zinc dust in acetic acid. The isomeric hydrazones (I; R^1 = CH$_2$Ph, R^2 = N=CHPh) and (II; R = N=CHPh) were also prepared by direct benzylation of the parent unsubstituted hydrazone. These two compounds were distinguished by the unequivocal preparation of one, *i.e.* compound (I; R^1 = CH$_2$Ph, R^2 = N=CHPh) by treating benzylidene-4-benzylthiosemicarbazone with litharge and sodium azide, a reaction of a type we have previously described.[4]

The ^{1}H n.m.r. spectra of the materials (I; R^1 = CH$_2$Ph, R$_2$ = NO) and (II; R = NO) (measured on a Varian H-A 100 spectrometer at 25° with deuteriochloroform as solvent) were consistent with their nitrosamine character. N.m.r. studies of isomerism due to restricted rotation about the N–N bond are well documented,[5] and it has been established that protons *cis* to the O atom resonate at higher fields than *trans*. The spectra of the materials (I; R^1 = CH$_2$Ph, R^2 = NO) and (II; R = NO), each showed two signals for the benzyl protons, as expected: (I; R^1 = CH$_2$Ph, R^2 = NO), τ *cis*, 4·56, *trans*, 4·36, isomer ratio *cis* : *trans*, *ca* 1 : 7; (II; R = NO), *cis*, 4·42, *trans*, 4·26, isomer ratio, *ca.* 1 : 1·5. The small separation of the *cis* and *trans* signals relative to that of *N*-alkyl-nitrosamines ($\Delta\tau$ *ca.* 0·8) is probably due to the greater distance of the alkyl groups from the nitrosamine unit in this instance. The model compound (III), prepared by nitrosation of 5-benzylaminotetrazole, also showed two benzyl signals, τ 4·70 and 3·94 ($\Delta\tau$ 0·76) in good agreement with other work.[5]


(I)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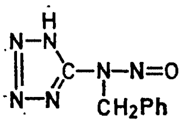
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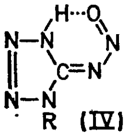
(IV)

The materials (I; R^1 = Me, CH$_2$Ph, and Ph, R^2 = NO) and (II; R = NO) may exist in the amino-tetrazole form shown or in a tautomeric imino-tetrazoline form (IV) which may be stabilised by intramolecular hydrogen bonding of the nitrosamine oxygen atom. Such tautomerism has been established for a number of substituted 5-aminotetrazoles.[6]

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