Tetrahedron Letters No.47, pp. 4079-4082, 1970. Pergamon Press. Printed in Great Britain.

SYNTHESIS AND REACTIONS OF TRIHALOGENO-DIAZABUTADIENES[1]- NEW VERSATILE SYNTHETIC INTERMEDIATES

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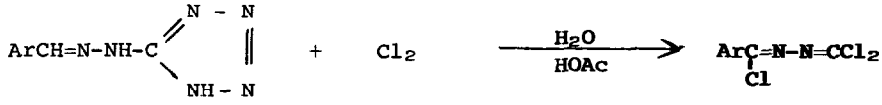
(Received in UK 25 August 1970; accepted for publication 10 September 1970)

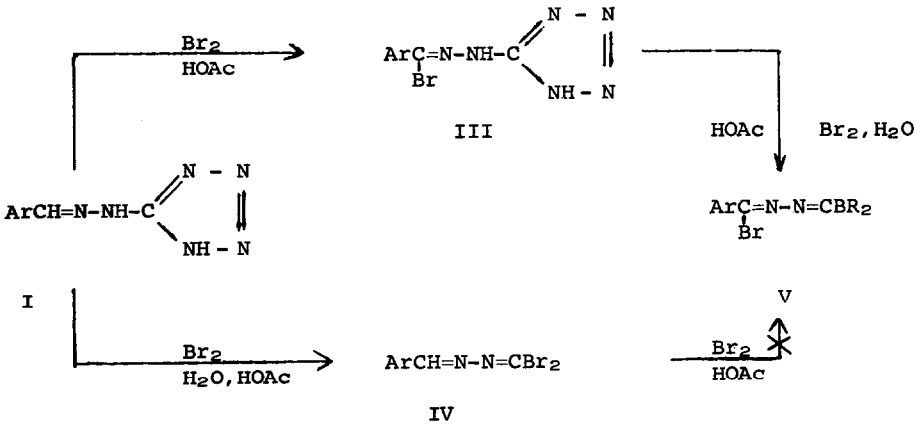
Some time ago[2] we reported an oxidative cleavage of substituted arylidene hydrazinotetrazoles (I) to form the substituted dibromo-diazabutadienes (IV) and we have commented subsequently[3] on the wide synthetic utility of these materials. We now report another tetrazolyl ring cleavage which this time produces the novel and even more synthetically useful compounds the substituted trihalogeno-diazabutadienes (II).



I II

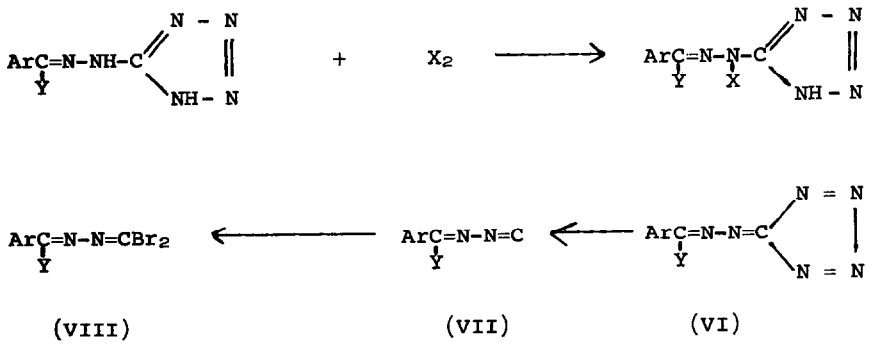
Reaction of the tetrazolyl hydrazones (I) with chlorine in 90% aqueous acetic acid yields the trichloro compounds (II) in good (65-75%) yields. Our work on the analogous bromo compounds throws further light on the mechanism of this process. As summarised in Scheme 1 reaction of the hydrazones (I) with bromine in anhydrous acetic acid yields the tetrazolyl hydrazidic bromides (III). Further reaction of these hydrazidic halides with bromine in 50% aqueous acetic acid yields the desired tribromo materials (V). In our hands the reverse sequence did not work. While oxidative cleavage of compounds (I) to the dibromo compounds (IV) was smooth, compounds (IV) did not brominate further under our normal conditions. Interestingly, in the chlorination reactions, a dichloro stage was bypassed (and could not be intercepted) - compounds (II) being the sole reaction products.

We have also clarified the mechanism of the tetrazolyl ring cleavage - a reaction which has been cited as a mechanistic enigma.[4] We regard this ring cleavage as involving first N-halogenation, followed by tetrazafulvene



Scheme 1

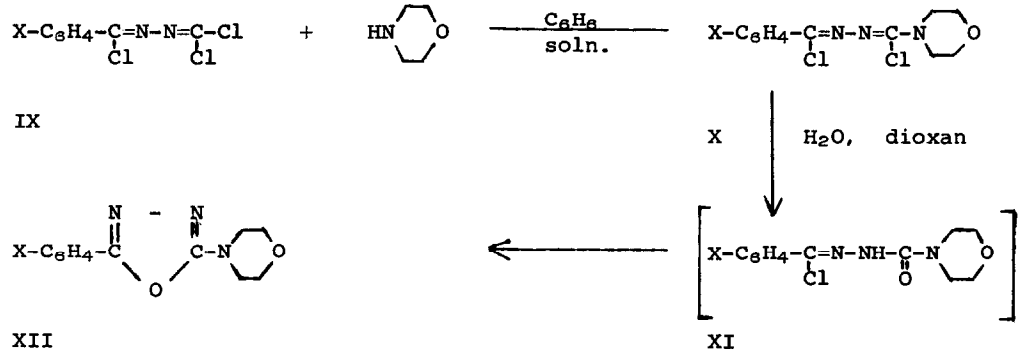
(VI) formation; this then yields the isonitrilic compound (VII) and thence compound (VIII) - Scheme 2.[5] In support of this mechanism we have generated compound (VII, Ar=Y=C_6H_5) via the reaction of benzophenone hydrazone in chloroform with ethanolic potassium hydroxide. After the mixture was allowed to stand at room temperature for 10 minutes, addition of bromine in 50% aqueous acetic acid gave the dibromo compound (VIII, Ar=Y=C_6H_5) (in 9% yield) which was identical with the product obtained from the reaction of benzophenone tetrazolyl hydrazone with bromine in aqueous acetic acid.



Scheme 2

We have examined the reactivity of the trihalogeno compounds (II and V) towards a wide variety of nucleophilic reagents and have found that the three

halogen atoms may be sequentially replaced. We have unequivocal evidence[6] that the first to react is one of the geminal ($-N=CX_2$) pair; in the product the second geminal halogen ($-N=CXY$, Y being the nucleophile) is generally more reactive than the one replaced and finally the methine ($ArCX=N-$) halogen is replaced. As an example of this stepwise technique the reactions outlined in Scheme 3 were performed. The trichloro compounds (IX) were reacted with two equivalents[7] of morpholine in benzene and yielded the dichloro compounds (X) in good yield. These materials when refluxed in 80% aqueous dioxan hydrolysed to yield the hydrazidic halides (XI) in situ and these then



Scheme 3

cyclised to form the oxadiazoles (XII). We prepared these oxadiazoles unambiguously by oxidative cyclisation of the corresponding 4-morpholino substituted semicarbazones ($ArCH=N-NHCONC_4H_8O$) with bromine in acetic acid containing sodium acetate.

Table 1

Conversion of Compounds (IX) to (XII)

X	Substrate (IX) m.p. (b.p.)°C	Compound (X) m.p.°C	Compound (XII) m.p.°C	Overall Yield %
H	162-4 (b.p.1mm)	81-3	135-7	85
CH_3	173-4 (b.p.1mm)	131-3	139-41	90
$(CH_3)_2CH$	192-4 (b.p.1mm)	66-8	142-3	95
Cl	52-4	98-9	146-7	92
Br	54-6	112-3	143-4	90
NO_2	79-80	159-60	151-3	88

For this latter oxidative cyclisation a nitrilimine[7a], or a perbromide[7b] have been variously suggested as intermediates. Our present work shows that under non-oxidative conditions a hydrazidic halide can also function as a precursor to oxadiazoles.

One of us (J.K.O'H) is indebted for a state maintenance grant for research.

References

1. We had originally based our naming system for compounds (II) and (IV) on Thiele's system (J. Thiele, Ann. 303, 57, 70 (1898)) i.e. naming them as derivatives of isocyanogen (C=N-N=C). As a referee has pointed out this system can be misleading and difficult to use. Accordingly, we are shifting to the nomenclature used by Mitsch (R. A. Mitsch and P. H. Ogden, J. Org. Chem., 31, 3833, (1966)) i.e. the compounds are regarded as derivatives of 2,3-diaza-1,3-butadiene $XYC=N-N=CX^1Y^1$.

2. F. L. Scott and D. A. Cronin, Chem. and Ind., 1757 (1964).

3. F. L. Scott, J. A. Cronin and J. Donovan, Tetrahedron Letters, 4615 (1969) and subsequent papers.

4. S. Ranganathan, 'Fascinating Problems in Organic Reaction Mechanisms' Holden-Day Inc. San Francisco (1967).

5. This scheme is related to that suggested by Behringer for a pyrolytic cleavage of tetrazoles, see e.g. H. Behringer and M. Matner, Tetrahedron Letters, 1663 (1966).

6. This evidence is based on both kinetic and synthetic data and will be described in the full paper.

7. A morpholine to halide ratio of 6:1 results in complete halogen replacement.

8. (a) M. S. Gibson, Tetrahedron, 18, 1337 (1962); (b) G. Werber, M. C. Aversa and F. Buccheri, Annali Di Chimica, 59, 912 (1969).