Tetrahedron Letters No. 45, pp 3973 - 3976, 1977. Pergamon Press. Printed in Great Britain.

DEAZIDATION OF ARYL AZIDES WITH HYDRAZINE HYDRATE. A NEW SYNTHESIS OF 3-AMINOINDAZOLE

Thomas McC. Paterson, Robert K. Smalley* and Hans Suschitzky

The Ramage Laboratories, Department of Chemistry and Applied Chemistry,

University of Salford, Salford M5 4WT, Lancashire

(Received in UK 5 September 1977; accepted for publication 22 September 1977)

o-Azidoketones react with hydrazine hydrate in boiling ethanol to give 3-substituted indazoles,[1] while benz(f)indazolin-3-one formation has been reported[2] on treating methyl 3-azido-2-naphthoate under similar conditions.

Independently, we have shown[3] that methyl o-azidobenzoate (1; X=CO_2Me) and o-azidobenzamide (1; X=$CONH_2$) yield indazolin-3-one (5) (90%) when treated with hydrazine hydrate, methyl hydrazine or phenyl hydrazine in hot ethanol or dimethylformamide solution. To gain insight into the as yet unresolved mechanism of this remarkably simple cyclisation, and also to explore its synthetic potential the action of ethanolic hydrazine hydrate on selected ortho-substituted aryl azides (1; X=CN, and SO_2NH_2) has been investigated.

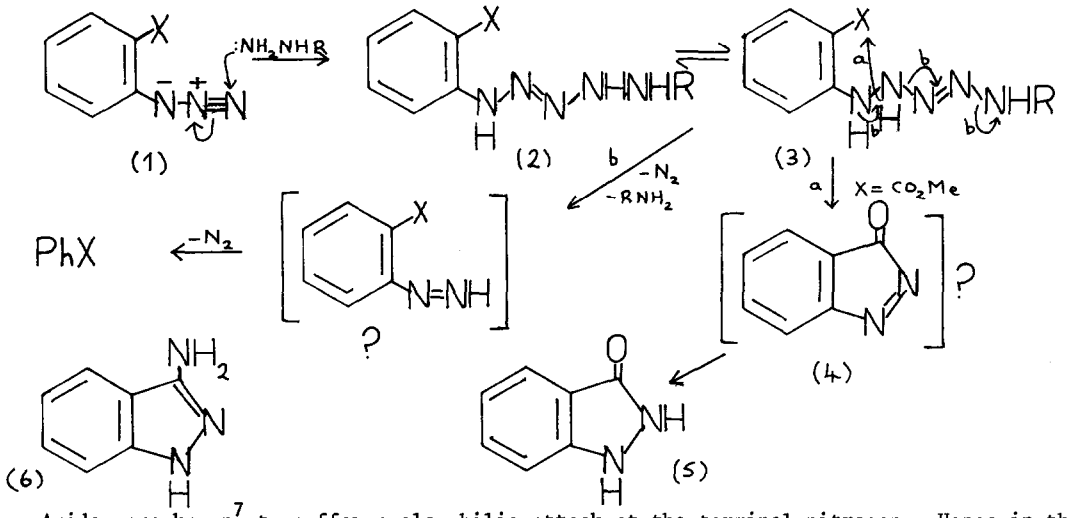
As anticipated the reaction with o-azidobenzonitrile paralleled those undergone by o-azido-ketones and -esters and gave 3-aminoindazole (6). The high yield (80-90%) makes this a useful synthetic method since other routes to 3-aminoindazole are somewhat tedious.[4] An identical reaction was observed with methylhydrazine, and precludes, as with the azido-esters,[2] any simple mechanistic explanation involving nucleophilic displacement of azide, or hydrazinolysis of the ester, followed by cyclisation.

By analogy with the cyclisation of o-azidobenzamide to indazolin-3-one it was hoped that o-azidobenzene sulphonamide (1; X=SO_2NH_2) would give the difficultly accessible benzyne precursor benzo-1,2,3-thiadiazoline-1,1-dioxide.[5] However, under the standard reaction conditions (see footnote to Table), the sulphonamide suffered deazidation to benzene sulphonamide in high yield (85%).

Deazidation of aryl azides is rare[6] and this unexpected result prompted us to examine the action of hydrazine hydrate on other simple aryl and heteroaryl azides. Results are gathered in the Table.

Except in clearly defined cases (i.e. where cyclisation, or attack by hydrazine at the side-chain - reactions e and f - takes place) loss of azide, although varying in degree appears to be a general process. A notable exception is o-azidobenzoic acid (reaction d), which undergoes neither cyclisation (to indazolin-3-one) nor deazidation, but reduces to anthranilic acid in high yield. Azide to amine reduction is observed in other instances (reactions a, b, c, j, k, l) although generally in minor amounts.

A speculative mechanistic rationale is outlined in the Scheme.



Azides are known[7] to suffer nucleophilic attack at the terminal nitrogen. Hence in the absence of a more easily attacked ortho substituent e.g. (1; X=COCl or CHO), attack by the hydrazine yields the tautomeric pentazene (2 ⇄ 3). When X is CO_2Me (or CN) intramolecular nucleophilic attack (path a) followed (or accompanied) by loss of N_2 and RNH_2, and reduction of the resulting cyclic azo-carbonyl compound (4) by the excess of hydrazine present[8] leads to indazolin-3-one formation. A similar mechanism applies to o-azidobenzonitrile.

Alternatively, if intramolecular attack is unlikely (i.e. reactions b, c, h, i) or impossible (reactions a, j, k, l, m) then deazidation (path b) is preferred. The difference in behaviour between o-azidobenzamide and o-azidobenzene sulphonamide is possibly due to the easier displacement of NH_2 from carboxyamides than sulphonamides. Presumably, cyclisation of o-azidobenzoic acid is prevented by the "poor-leaving group" character of the OH group. However, its preference for reduction rather than deazidation is not clear, as is the formation in a few cases (reactions c, j, l) of aryl hydrazines.

Table: Reaction of Aryl and Heteroaryl Azides With Ethanolic Hydrazine Hydrate

Reaction*	Azide	Reaction Time (h)	Products (% yield)
a[10]	PhN_3	24	PhH (17%); $PhNH_2$ (71%)
b	o-$NO_2C_6H_4N_3$	2	$PhNO_2$ (15%); o-$NO_2C_6H_4NH_2$ (17%); o-$NH_2C_6H_4NH_2$ (37%)
c	o-$ClC_6H_4N_3$	4	PhCl (30%); o-$ClC_6H_4NH_2$ (17%); o-$ClC_6H_4NHNH_2$ (14%)
d	o-$N_3C_6H_4CO_2H$	2	o-$NH_2C_6H_4CO_2H$ (80%)
e[11]	o-$N_3C_6H_4COCl$	1/4	(o-$N_3C_6H_4CONH$)$_2$ (85%)
f	o-$N_3C_6H_4CHO$	2	(o-$N_3C_6H_4CH{=}N$)$_2$ (85%)
g	o-$N_3C_6H_4SO_2NH_2$	1/2	$PhSO_2NH_2$ (84%)
h	o-$N_3C_6H_4SO_2Ph$	1	$PhSO_2Ph$ (92%)
i	o-$N_3C_6H_4SOPh$	1	PhSOPh + PhSPh (80%)
j	p-$N_3C_6H_4CN$	1	PhCN (52%); p-$NCC_6H_4NH_2$ (6%); p-$NCC_6H_4NHNH_2$ (13%)
k	p-$N_3C_6H_4Cl$	5	PhCl (40%); p-$ClC_6H_4NH_2$ (14%)
l	3-N_3-quinoline	1	quinoline (70%); 3-NH_2-quinoline (6%); 3-NH_2NH-quinoline (13%)
m	p-N_3-$C_6H_4CO_2Me$		$PhCONHNH_2$ (81.5%)

* Standard conditions involved heating a solution of azide (2 g) in ethanol (25 ml) and hydrazine hydrate (5 ml) under reflux for the time stated.

References

1. S. Bradbury, M. Keating, C.W. Rees, and R.C. Storr, J.C.S. Chem. Comm., 1971, 827.

2. M.E. Peek, C.W. Rees, and R.C. Storr, J.C.S. Perkin I, 1974, 1260.

3. W.A. Strachan, Ph.D. Thesis, University of Salford, 1974.

4. L.C. Behr, in "The Chemistry of Heterocyclic Compounds", ed. R.H. Wiley, Interscience Publishers, New York, 1967, Vol. 22, p.344.

5. G. Wittig and R.W. Hoffmann, Chem. Ber., 1962, 95, 2718.

6. R.A. Abramovitch, S.R. Challand, and E.F.V. Scriven, J. Org. Chem., 1972, 37, 2705.

7. G. L'Abbe, Ind. Chim. Belg, 1969, 34, 519.

8. E. Fahr and H. Lind, Angew. Chem. Internat. Edn., 1966, 5, 372.

9. Yields not optimised - products sometimes precipitated from mixture but in general were obtained by either chromatographic separation or extraction of the residue after removal of ethanol and excess of hydrazine.

10. This reaction has also been observed by Dr. M.F.G. Stevens, University of Aston in Birmingham - personal communication.

11. Reaction carried out at room temperature.