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BASE-INDUCED INTRAMOLECULAR CYCLISATION OF N-(o-AZIDOBENZOYL)-ARYLAMINES. A NEW SYNTHESIS OF 2-ARYL-1,2-DIHYDRO-3H-INDAZOLIN-3-ONES

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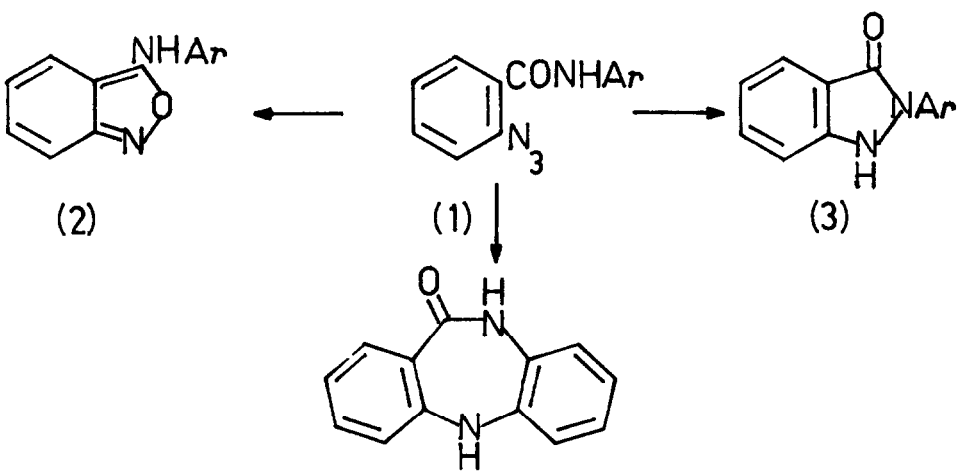
Summary In strong base, e.g. sodium hydride in dimethylformamide, N-(o-azidobenzoyl)arylamines cyclise in high yield to 2-aryl-1,2-dihydro-3H-indazolin-3-ones.

Recently we have become interested[1] in the chemistry of o-azidoanilides (1) and in particular their decomposition which offers various possibilities for cyclisation (see Scheme 1)[2]. However, attempts to bring about ring-closure to the 3-amino-2,1-benzisoxazoles (2) (rare species[3]) or to 2-aryl-1,2-dihydro-3H-indazolin-3-ones (3) by thermolysing the azidoanilides in boiling xylene or in boiling o-dichlorobenzene failed and yielded only high melting polymeric material from which no identifiable products have as yet been isolated.



(2) (1) (3) (4)

Scheme 1

As an alternative we have now looked at the decomposition of o-azidoanilides in the presence of strong base, since as the resonance stabilised anions (6⟷6a) these azides resemble o-nitrophenyl azides and hence by analogy to benzofuroxan formation[4] might be expected to undergo assisted cyclisation to 2-arylindazolin-3-ones under mild conditions.

Preliminary results were disappointing in that the azidoanilide (1; Ar = Ph) was recovered unchanged after treatment with sodium hydride in dimethylformamide, or sodium in dimethyl sulphoxide, at room temperature, and with hot or cold aqueous sodium hydroxide. However, on heating the azide (0.5 g.) with sodium hydride (0.5 g.) in dry dimethylformamide (15 ml.) at 80°C for three hours loss of nitrogen was observed and 2-phenyl-1,2-dihydro-3H-indazolin-3-one (3; Ar = Ph)[6] was obtained in virtually quantitative yield. Other 2-arylindazolin-3-ones were prepared similarly and details are listed in the Table. Cyclisation of (1; Ar = Ph) was also successful using sodium hydride in tetrahydrofuran, sodium in isopropanol, and potassium hydroxide in ethanol (all at reflux temperature). Yields, however, were lower (45-79%).

Table

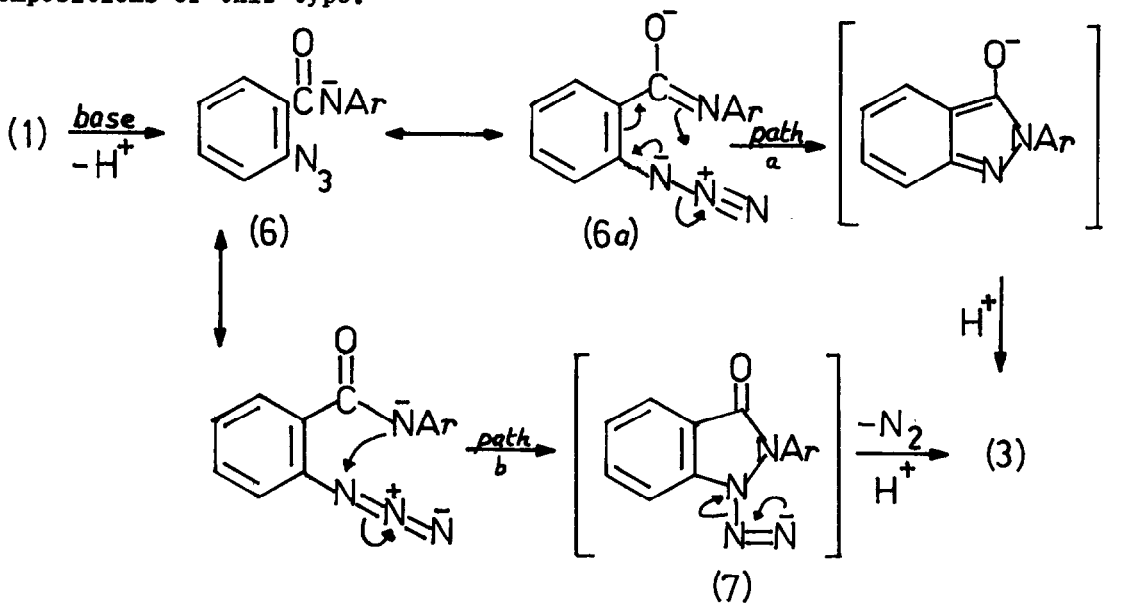
2-Aryl-1,2-dihydro-3H-indazolin-3-ones[7] (3)

Ar	m.p. (°C)	Yield (%)
C_6H_5	216[a]	99
o-MeC_6H_4	229	59
p-MeC_6H_4	214	47
p-$MeOC_6H_4$	170	67
o-ClC_6H_4	172	45
p-ClC_6H_4	224	86
2,4,6-$Me_3C_6H_2$	210	89
2-pyridyl	190	70

[a] Lit.[8] m.p. 217°C

The relative ease of these base-induced cyclisations together with our failure to effect thermal ring-closure under neutral conditions suggests that indazolinone formation is the result of an assisted nitrogen loss from the anion (6⟷6a) rather than a nitrene reaction. The exact nature

of this anchimeric assistance, which is common in the production of heterocycles by decomposition of aryl azides bearing an α,β-unsaturated side-chain, has been the subject of a recent debate. Dyall and his co-workers[9], on the basis of kinetic data for the decomposition of azides of type o-$XC_6H_4N_3$ (5; X = RCO, ArCO, NO_2, and N=NAr) have proposed a concerted pericyclic process. In contrast, Hall and his co-workers[10,11], although concurring with Dyall for azides (5; X = NO_2), interpret their kinetic results in favour of an intramolecular 1,3-dipolar cycloaddition mechanism, particularly for azides (5; X = ArCO[10] and N=NAr[11]). Of these two possibilities, we favour the concerted pericyclic pathway (Scheme 2; path a) for base induced indazolinone formation, similar to that proposed[4,9] for the cyclisation of o-nitroaryl azides. An alternative view of the reaction (Scheme 2; path b) involves intramolecular nucleophilic attack by the amide anion at N-1 of the azide function. Structure (7) is equivalent to one of the several possible transition states considered by Hall and his co-workers[10] for assisted azide decompositions of this type.



Scheme 2

The reactions described herein constitute a remarkably simple procedure for the synthesis of the hitherto not too readily available[12] 2-aryl-1,2-dihydro-3H-indazolin-3-ones, and represent rare examples[13] of the base-induced

cyclisation of o-substituted aryl azides. Further studies are in progress to determine the scope of this new type of azide reaction.[14]

References and notes.

1. M. A. Ardakani, R. K. Smalley, and R. H. Smith, Synthesis, 1979, 308.
2. Nitrene attack at the amine-bearing benzene ring to give a dibenzodiazepinone (4) although feasible, is less likely in view of the known propensity of aryl nitrenes to yield 5- rather than 6- or 7-membered rings.[5]
3. M. S. Chauhan and D. M. McKinnon, Canad. J. Chem., 1975, 53, 1336, and references cited therein.
4. G. L'Abbé, Chem. Rev., 1969, 69, 345, and references cited therein.
5. P. A. S. Smith in 'Nitrenes', ed. W. Lwowski, Interscience Publishers, New York, 1970, p. 99.
6. Structure confirmed by comparison (mixed m.p. and superimposable i.r. spectra) with an authentic sample.
7. All new compounds gave satisfactory elemental analysis and spectroscopic (i.r. and mass) data.
8. G. Heller, Ber., 1916, 49, 2757.
9. L. K. Dyall, Austral. J. Chem., 1977, 30, 2669, and references cited therein.
10. J. H. Hall, F. E. Behr, and R. L. Reed, J. Amer. Chem. Soc., 1972, 94, 4952
11. J. H. Hall and F. W. Dolan, J. Org. Chem., 1978, 43, 4608.
12. L. Baiocchi, G. Corsi, and G. Palazzo, Synthesis, 1978, 633.
13. Most aryl azides are stable towards bases. However, 2,1-benzisoxazole has been cited as a possible intermediate in the decomposition of o-azidobenzaldehyde in boiling aqueous sodium hydroxide, and 2-hydroxy-2H-indazole has been obtained as one of several products from the decomposition of o-azidobenzaldoxime under similar conditions.[15]
14. See following letter.
15. J. H. Boyer and F. C. Canter, Chem. Rev., 1954, 54, 1, and references cited therein.

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