

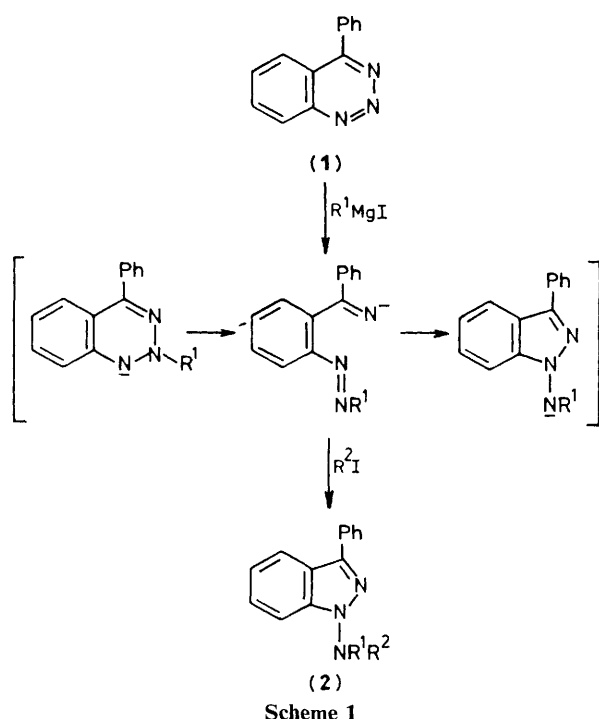
The Reaction of 1,2,3-Benzotriazines with Grignard Reagents

James J. A. Campbell, Stephen J. Noyce, and Richard C. Storr*

Robert Robinson Laboratories, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, U.K.

Attack of alkyl Grignard reagents on 4-substituted 1,2,3-benzotriazines occurs at N-2; ethylmagnesium iodide attacks at N-2 of 3-methyl-1,2,3-benzotriazin-4(3*H*)-one whereas methylmagnesium iodide adds at C-4 to give, after dehydration, 3,4-dihydro-4-methylene-3-methyl-1,2,3-benzotriazine.

Nucleophilic attack by water and hydrazine occurs at C-4 of 4-phenyl-1,2,3-benzotriazine.¹ Therefore nucleophilic addition of alkyl Grignard reagents to 4-phenylbenzotriazine (**1**), followed by quenching of the resulting anion with alkyl

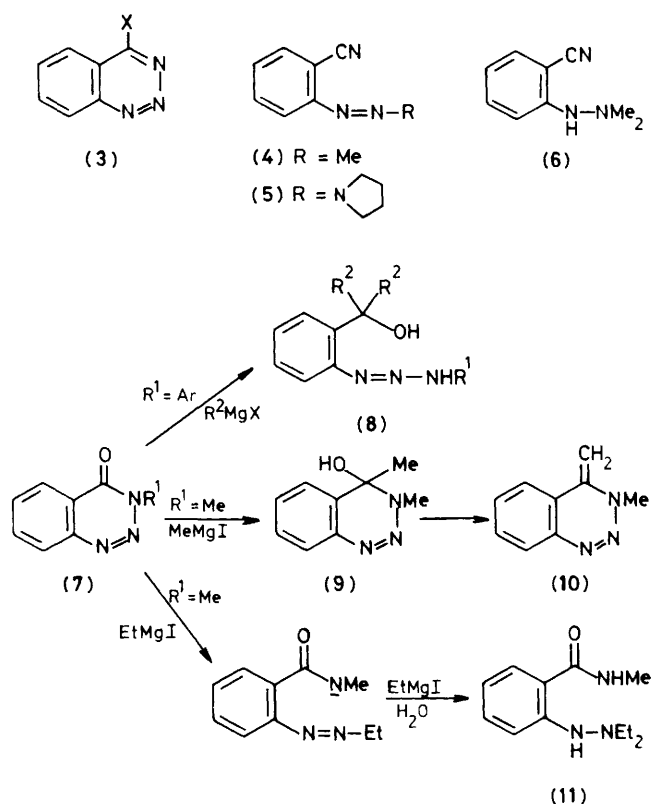


iodide, seemed to offer a simple route to 3,4-dialkyl-3,4-dihydro-1,2,3-benzotriazines or their 1,4-isomers.[†] However this sequence of reactions, unexpectedly, gives 1-dialkylamino-3-phenylindazoles (2).

Thus treatment of the triazine (1) with EtMgI (2 equiv.) in ether followed, after 1 h, by methyl iodide gave the indazole (2; R¹ = Me, R² = Et),[‡] 44%, as a pale yellow oil, b.p. 112 °C at 1.5 × 10⁻¹ Torr, λ_{max} 216 (ε 24 234), 247 (8121), 272.6 (5049), and 311.5 (9665) nm, δ (CDCl₃) 2.94 (s, 3H, CH₃), 3.23 (q, 2H, CH₂), and 0.83 (t, 3H, CH₃). Treatment with MeMgI followed by ethyl iodide gave the same ethylmethylaminindazole (2; R¹ = Me, R² = Et), 23%, together with dimethylaminindazole (2, R¹ = R² = Me), 11%; this latter product presumably arises because exchange between the residual MeMgI and added ethyl iodide leads to the presence of methyl iodide. This dimethylamino compound was also obtained by treatment of the triazine (1) with MeMgI and then methyl iodide and showed only one methyl absorption in both its ¹H and ¹³C n.m.r. spectra. This fact, together with formation of the same ethylmethyl derivative from both MeMgI/EtI and EtMgI/MeI, eliminates the expected 3,4- or 1,4-dihydrobenzotriazine structures. Chemical support for the dialkylaminindazole structure (2) comes from flash pyrolytic decomposition (650 °C; 10⁻² Torr) to give 3-phenylindazole, 65%. The assignment as the 1-dialkylaminindazoles is based on the close similarity of the u.v. spectra and aromatic ¹³C n.m.r. absorptions of both compounds to those of 1-amino-3-phenylindazole, which are significantly different from those of 2-amino-3-phenylindazole.¹

Although the detailed reaction mechanism is not established, formation of these 1-dialkylaminindazoles appears to require unprecedented nucleophilic attack at N-2 of the triazine ring (Scheme 1).

Nucleophilic attack also occurs at N-2 of 4-methoxy- and



4-methylthiobenzotriazines (3; X = MeO or MeS) which give the cyanohydrazine (6) (34 and 38% respectively), b.p. 40 °C at 5 × 10⁻² Torr, ν_{max} 3300 (NH) and 2210 cm⁻¹ (CN), on treatment with an excess of MeMgI in ether. In this case initial attack leads to displacement of a good leaving group producing the cyanoazo compound (4) which suffers further nucleophilic addition. This behaviour contrasts with that with N and O nucleophiles where displacement of the 4-substituent by attack at C-4 leaves the triazine ring intact.^{1,3}

The formation of products derived from *o*-cyanobenzene-diazonium chloride in attempts to obtain 4-chlorobenzotriazine (3; X = Cl) by chlorination of 4-hydroxybenzotriazine (3; X = OH)⁴ provides an extreme example of formal attack by a nucleophile at the 2-position of a benzotriazine. It seems reasonable that the chlorine in 4-chlorobenzotriazine should be very labile and that fragmentation occurs to give the cyanodiazonium compound which then suffers attack by the nucleophile. There is no evidence for such prior fragmentation in the case of benzotriazines with poorer leaving groups (3; X = Ph, MeO, or MeS); these are inert in the absence of Grignard reagent. An alternative approach to 4-chlorobenzotriazine underlines the extreme instability of this unknown compound. Thus oxidation of 1-aminoindazoles is an established route to benzotriazines¹ but oxidation of 1-amino-3-chloroindazole in the presence of pyrrolidine, even at -80 °C, gives only the triazine (5) derived from the *o*-cyanodiazonium compound.

Reaction of 3-aryl-1,2,3-benzotriazin-4-ones (7; R = Ar) with Grignard reagents is reported to give the triazines (8) by attack at C-4.⁵ Addition at C-4 of 3-methylbenzotriazin-4-(3H)-one (7; R = Me) also occurs on treatment with MeMgI (ca. 3 equiv. in ether), but in this case spontaneous dehydration of the intermediate (9) provides a new route to 3,4-dihydro-3-methyl-4-methylene-1,2,3-benzotriazine (10),⁶ 68%. In surprising contrast reaction of the methylbenzotriazinone (7; R¹ = Me) with EtMgI under identical conditions gives the

[†] Only one claim for a 1,4-dihydro-1,2,3-benzotriazine has appeared: ref. 2.

[‡] All new compounds were fully characterised by analysis and spectral data.

amidohydrazine (**11**), m.p. 96 °C, ν_{max} 3470, 3410 (NH), 1635 cm^{-1} (C=O), δ (CDCl_3) 7.98 (1H, s), 6.15 (1H, br., amide), 2.90 (3H, d, NHMe), 2.69 (4H, q, CH_2), and 0.98 (6H, t, CH_3), in 35% yield. Although benzotriazin-4-ones are known to act as ring-opened diazonium compounds under acidic or vigorous thermal conditions and hence give products formally derived from attack by nucleophiles on N-2,^{3,7,8} this appears to be the first example of ring cleavage of a benzotriazin-4-one which is initiated by nucleophilic attack at N-2.

We thank Dr. M. T. Williams for synthesis of 1-amino-3-chloroindazole, Dr. K. Vaughan (St. Mary's University, Nova Scotia) for stimulating discussion, and the S.E.R.C. for support (S. J. N.).

Received, 15th July 1983; Com. 946

References

- 1 B. M. Adger, S. Bradbury, M. Keating, C. W. Rees, R. C. Storr, and M. T. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1975, 31.
- 2 H. Igeta, T. Tsuchiya, and T. Nakai, *Tetrahedron Lett.*, 1971, 3117.
- 3 H. Neunhoeffer, 'The Chemistry of Heterocyclic Compounds,' Vol. 33, Wiley, New York, 1978.
- 4 D. Buckley and M. S. Gibson, *J. Chem. Soc.*, 1956, 3242.
- 5 A. Mustafa, W. Asker, A. M. Fleifel, S. Khattab, and S. Sherif, *J. Org. Chem.*, 1960, **25**, 1501.
- 6 H. Fong and K. Vaughan, *Can. J. Chem.*, 1978, **53**, 3714.
- 7 R. J. Kobylecki and A. McKillop, *Adv. Heterocycl. Chem.*, 1976, **19**, 215.
- 8 M. S. S. Siddique and M. F. G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2482.