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

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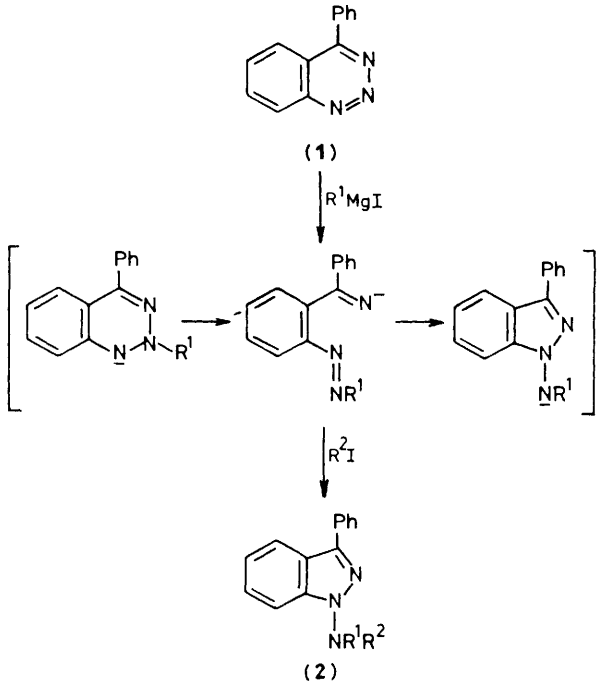
Attack of alkyl Grignard reagents on 4-substituted 1,2,3-benzotriazines occurs at N-2; ethylmagnesium iodide attacks at N-2 of 3-methyl-1,2,3-benzotriazin-4(3*H*)-one whereas methylmagnesium iodide adds at C-4 to give, after dehydration, 3,4-dihydro-4-methylene-3-methyl-1,2,3-benzotriazine.

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



Scheme 1

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**; R^1 = Me, R^2 = 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 ($CDCl_3$) 2.94 (s, 3H, CH_3), 3.23 (q, 2H, CH_2), and 0.83 (t, 3H, CH_3). Treatment with MeMgI followed by ethyl iodide gave the same ethylmethylaminoindazole (**2**; R^1 = Me, R^2 = Et), 23%, together with dimethylaminoindazole (**2**, R^1 = R^2 = 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 ^{13}C 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 dialkylaminoindazole structure (**2**) comes from flash pyrolytic decomposition (650 °C; 10^{-2} Torr) to give 3-phenylindazole, 65%. The assignment as the 1-dialkylaminoindazoles is based on the close similarity of the u.v. spectra and aromatic ^{13}C 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-dialkylaminoindazoles 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*-cyanobenzenediazonium 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 benzotriazines[1] but oxidation of 1-amino-3-chloroindazole in the presence of pyrrolidine, even at −80 °C, gives only the triazene (**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 triazenes (**8**) by attack at C-4.[5] Addition at C-4 of 3-methylbenzotriazin-4-(3*H*)-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**; R^1 = 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.

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