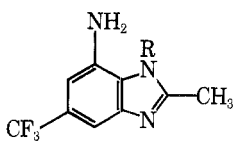
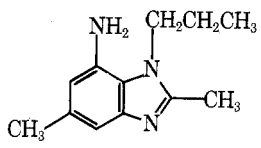
Benzimidazole Chemistry. II. Alkyl Migration of *N*-Alkyl-4-trifluoromethyl-2,6-dinitroanilines on Reduction with Tin

Summary: In reductions of certain *N*-alkyl-4-trifluoromethyl-2,6-dinitroanilines, migration of the alkyl group occurs simultaneously with formation of the triamines, probably by formation of a radical from the *N*-alkyl group followed by rearrangement.

Sir: A study of the syntheses of benzimidazoles[1] was initiated to provide compounds for comparison with the products of bacterial and atmospheric changes of the 2,6-dinitroaniline, agricultural chemicals.[2] The preparation of 1-propyl-7-amino-2-methyl-5-trifluoromethylbenzimidazole (**1c**) was required. The synthetic route that was chosen followed the method of preparation of the 5-methyl analog (**2**);[1] however, the intermediate triamine formed by the reduction of the 2,6-dinitroaniline (**3c**) with tin and hydrochloric acid was obviously not the expected symmetrical compound (**5c**), but the unsymmetrical triamine (**4c**). The unsymmetrical structure was evident from the nonidentity of the aromatic hydrogens in the NMR spectrum.



1a, R = *s*-C_4H_9
b, R = *n*-C_4H_9
c, R = *n*-C_3H_7



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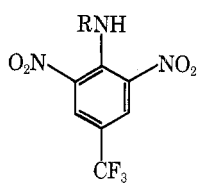
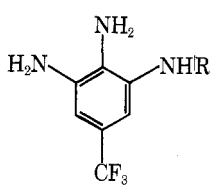
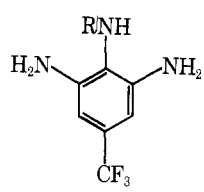


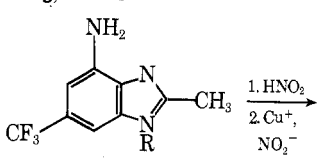
3a, R = *s*-C_4H_9
b, R = *n*-C_4H_9
c, R = *n*-C_3H_7
d, R = *t*-Bu
e, R = $PhCHCH_3$
f, R = C_6H_5
g, R = H

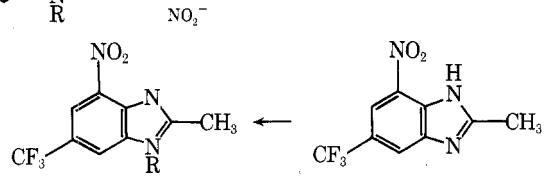


4a, R = *s*-C_4H_9
b, R = *n*-C_4H_9
c, R = *n*-C_3H_7



5a, R = *s*-C_4H_9
c, R = *n*-C_3H_7
g, R = H
f, R = C_6H_5





7 **8**

The structure of the triamine, **4c**, was confirmed by conversion via diazotization and the Sandmeyer reaction to the same alkyl nitrobenzimidazole (**7c**) formed by the alkylation of 2-methyl-7-nitro-5-trifluorobenzimidazole (**8**). The alkylation of such benzimidazoles as **8** has been shown to give the 1-alkyl-4-nitrobenzimidazole.[1] Thus **7** must have the structure 1-alkyl-2-methyl-4-nitro-6-trifluoromethylbenzimidazole. The symmetrical triamines (**5**) could be prepared by catalytic hydrogenation. Cyclization gave the 1-alkyl-7-amino-2-methyl-5-trifluoromethylbenzimidazoles (**1**) which were isomeric with the products of cyclization of the amines formed by the rearrangement.

Table I
Results of Tin and Acid Reduction of *N*-Alkyl-4-trifluoromethyl-2,6-dinitroanilines

	%			
3	**5**[a]	**4**[a]	**5g**[a]	Total yield
a	33	67		50
b	5	95		Quant
c		100		Quant
d			100	74
e			100	73
f	100			71

[a] The yields were determined by NMR analysis of the total product mixture.

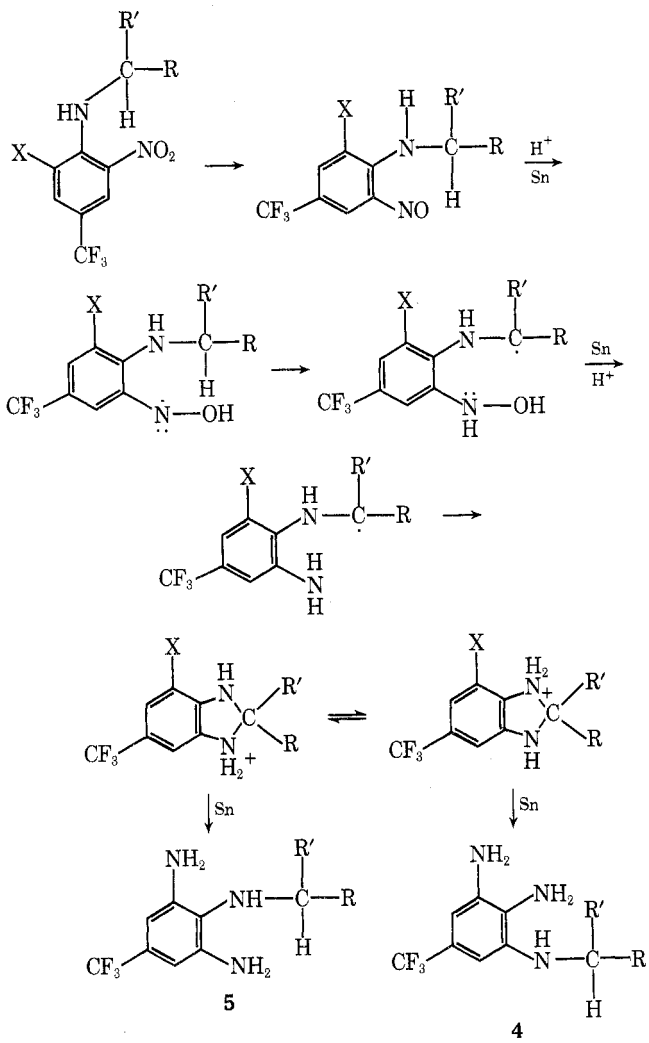
The same rearrangement was observed during the reduction of the dinitroanilines **3a** (R = *s*-butyl), **3b** (R = *n*-butyl), and **3c**, (R = *n*-propyl) to give the corresponding triamine **4**. With the *N*-alkyl groups which are easily eliminated such as *tert*-butyl (**3d**) or α-phenethyl (**3e**), reduction with tin gave the unsubstituted triamine, **5g** (R = H). When the substituent was phenyl no rearrangement or elimination was observed, and the product was 2,6-diamine-1-anilino-4-trifluoromethylbenzene (**5f**). See Table I for a summary of these data.

To determine whether the migration occurred by an internal nucleophile displacement or some intermediate, **3a** ($[\alpha]^{20}D$ +22.0°) was prepared with *S-sec*-butylamine. The reduction, however, gave N-*sec*-butyl-2,3-diamino-5-trifluoromethylaniline (**4a**) with no optical activity. For comparison the reduction of **3a** was accomplished with catalytic hydrogenation over platinum to give **5a** ($[\alpha]^{19}D$ −25.3°). These data suggested that the chiral carbon was converted to a carbonium ion[2d] or a radical[2a,c] during the reduction.

There are reported rearrangement of groups from one ortho nitrogen to another. In all previous cases, however, the group is unsaturated and an obvious intermediate heterocycle can be envisioned.[3] No previous migration of a saturated group, such as an alkyl group, between adjacent nitrogens has been reported, and for identification this reaction was called the UNH[4] rearrangement.

A consideration of the experimental data suggests that the reduction of the nitro function with tin produces a radical[5] which abstracts a hydrogen from the *N*-alkyl group and cyclization then occurs. Carbonium ions have also been proposed for these reductions[2d] and cannot be eliminated by this study. Radicals formed from the nitro group by photochemical reactions give benzimidazoles;[2] however, if the nitro group is reduced to the nitroso function prior to alkyl radical formation (Scheme I), the dihydro benzimidazole should be formed. Reduction of this intermediate occurs with C–N bond cleavage to form the symmetrical triamine or with formation of the unsymmetrically substituted triamine **4** giving the UNH[4] rearrangement (see Table I

Scheme I



for relative importance of these two pathways). Similar mechanisms have been proposed for the formation of benzimidazoles by the reductive photolysis of dinitroanilines; however, no rearrangement of the alkyl group has been reported. It is probable, however, that such rearrangement products may be formed but not previously detected.

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References and Notes

(1) R. E. Lyle and J. L. LaMattina, *J. Org. Chem.*, **40**, 438 (1975).
(2) (a) E. Leitis and D. Crosby, *J. Agr. Food Chem.*, **22**, 842 (1974); (b) P. C. Kearney, J. Plimmer, and U. Klingebiel, the 166th National Meeting of the American Chemical Society, Chicago, Ill., Aug. 27–31, 1973, PEST-3; (c) C. P. Nilles and M. J. Zabik, *J. Agr. Food Chem.*, **22**, 684 (1974); (d) O-Meth-Cohn and H. Suschitzky, *Adv. Heterocycl. Chem.*, **14**, 211 (1972).
(3) For example see (a) A. J. Boulton and P. B. Ghosh, *Adv. Heterocycl. Chem.*, **10**, 1 (1969); (b) F. Galbraith and S. Smiles, *J. Chem. Soc.* (*London*), 1234 (1935).
(4) Since the rearrangement led from a symmetrical to an unsymmetrical product, the reaction is called the "Unsymmetrical Nitrogen Hop" to summarize this process.
(5) H. O. House, "Modern Synthetic Reactions", Second ed, W. A. Benjamin, Inc., Menlo Park, Calif., 1972, pp 148, 211.

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9-Borabicyclo[3.3.1]nonane as A Highly Selective Reducing Agent for the Facile Conversion of α,β-Unsaturated Aldehydes and Ketones to the Corresponding Allylic Alcohols in the Presence of Other Functional Groups[1]

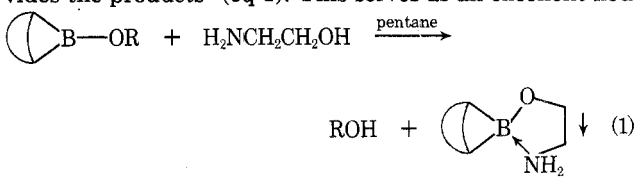
Summary: Reduction of α,β-unsaturated aldehydes and ketones with 9-borabicyclo[3.3.1]nonane proceeds selectively and cleanly to the corresponding allylic alcohols in excellent yield in the presence of many other functional groups.

Sir: 9-Borabicyclo[3.3.1]nonane (9-BBN) is an exceptionally stable bicyclic dialkylborane[2] and hydroborates olefins with very high regio- and stereoselectivity, far greater than those observed with borane and other dialkylboranes.[3] These remarkable characteristics and its commercial availability[4] prompted us to examine the behavior of 9-BBN as a reducing agent toward representative organic functional groups in tetrahydrofuran[5] (THF).

In the course of this investigation we found that 9-BBN reduces aldehydes and ketones rapidly and cleanly (to alcohols) even faster than it hydroborates olefins. For example, $k_{\text{cyclohexanone}}/k_{\text{cyclopentene}}$ was found to be 37 in competition experiments. Thus, the reaction of 2-cyclohexenone with 4 molar equiv of 9-BBN at 25° proceeds rapidly, using 1 equiv of 9-BBN in 10 min, while the uptake of the second equivalent requires 3 days. GLC analysis of the reaction mixture, following hydrolysis at the end of 10 min, indicated the presence of 2-cyclohexenol in 100% yield. Consequently, the reaction involves a rapid initial reduction of the carbonyl group followed by very sluggish subsequent hydroboration. The clean reduction of α,β-unsaturated aldehydes and ketones by hydride reagents has offered considerable difficulty.[6,7] Accordingly, it appeared desirable to examine this reaction in detail.

The reductions were carried out by the dropwise addition of an essentially stoichiometric quantity of 9-BBN solution in THF (3–5% excess) to the ketone in THF solution at 0°. The reaction mixtures were stirred for 2–4 hr at 0° and 1 hr at 25°.

Two procedures can be used to isolate the product. The reaction mixture can be treated with alkaline hydrogen peroxide to oxidize the 9-BBN moiety and the allylic alcohol separated by distillation from the 1,5-cyclooctanediol. More conveniently, the THF can be removed under vacuum from the reaction mixture and then pentane added. Addition of 1 mol of ethanolamine then precipitates 9-BBN as the adduct. Distillation of the pentane solution then provides the products[8] (eq 1). This serves as an excellent neutral work-up procedure for compounds containing acid- and base-sensitive groups.



Simple conjugated aldehydes, such as crotonaldehyde and cinnamaldehyde, are converted into crotyl alcohol and cinnamyl alcohol in yields of 98 and 99%, respectively (eq 2).