A simple, effective synthesis of carborane nitriles

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Lithium- and bromomagnesium-carboranes are readily converted into the nitriles by reaction with *p*-toluenesulfonyl cyanide.

The syntheses of different functionally-substituted carboranes are of great importance due to their possible application in the Boron Neutron Capture Therapy (BNCT) of cancer.[1] The direct synthesis of carboranes from acetylenes and decaborane is used for obtaining limited functionalities.[2]

We have paid special attention to carborane nitriles for the following reasons. On the one hand, carborane nitriles are of interest as synthons for the preparation of water soluble carboranes for BNCT (salts of acids and amines); on the other hand, the nitrile group may take part in effective stabilisation of carbonucleophiles with a carboranyl group like the methoxycarbonyl group in carboranylacetic methyl esters.[3] Thus, successful preparation of carboranylmethylnitriles extends the synthetic possibilites of carborane chemistry to a considerable degree. At present a number of procedures for the synthesis of nitriles from organometallic derivatives of carboranes are known.

The interaction of lithium-*o*-carborane with ClCN to form a mixture of cyano- and chloro-*o*-carboranes has no synthetic utility.[4] The reactions of lithium- and bromomagnesium-carboranes with PhOCN[5] and sodium carboranes with $ClCH_2CN$[6] have limited application. It is possible to obtain nitriles from amides of carboranyl carboxylic acids[2] and by direct cyanoethylation of carboranes.[7] At present *p*-toluenesulfonyl cyanide (TosCN) is recommended for the preparation of various nitriles by reaction with organometallics.[8]

The application of lithium- and bromomagnesium-carboranes in the reaction with TosCN has proved to be effective in obtaining carborane nitriles in good to excellent yields,[†] Scheme 1.

$$o\text{-},m\text{-}RCB_{10}H_{10}CLi \xrightarrow[\substack{\text{ether}\\ -78\,^{\circ}\text{C to r.t.}\\ 5\text{–}6\text{ h}}]{\text{TosCN}} o\text{-},m\text{-}RCB_{10}H_{10}CCN$$

o-carboranes: R = Me (91%), Ph (87%)
m-carboranes: R = Me (92%), Ph (86%)

$$o\text{-}RCB_{10}H_{10}CCH_2MgBr \xrightarrow[\substack{\text{ether}\\ -78\,^{\circ}\text{C to r.t.}\\ 6\text{ h}}]{\text{TosCN}} o\text{-}RCB_{10}H_{10}CCH_2CN$$

R = H (70%), Me (88%), Ph (90%)

Scheme 1

The reactions investigated have general utility and may be applied to different carboranes.

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References

1 R. F. Barth, A. H. Soloway, R. G. Fairchild and R. M. Brugger, *Cancer*, 1992, **70**, 2995; M. F. Hawthorne, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 950.
2 R. N. Grimes, *Carboranes*, Academic Press, New York, 1970.
3 Sang Chul Shim, Jae Goo Shim, Shin Yae Chae, Seung Yub Lee and V. N. Kalinin, *J. Organomet. Chem.*, 1993, **443**, C22.
4 L. I. Zakharkin and A. I. L'vov, *Zh. Obshch. Khim.*, 1966, **36**, 761 [*J. Gen. Chem. USSR (Engl. Transl.)*, 1966, **36**, 777].
5 L. I. Zakharkin, V. N. Kalinin, V. A. Pankratov and V. V. Korshak, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1976, 217 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1976, **25**, 210).
6 L. I. Zakharkin, V. N. Kalinin and V. A. Pankratov, *Zh. Vses. Khim. O-va im D.I.Mendeleeva*, 1978, 227 (in Russian).
7 V. N. Kalinin, O. M. Zurlova and L. I. Zakharkin, *J. Organomet. Chem.*, 1979, **166**, C37.
8 K. J. Rutan, F. J. Heldrich and L. F. Borges, *J. Org. Chem.*, 1995, **60**, 2948 and references therein.

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[†] *Typical experimental procedures.*
Method 1. A two-necked flask equipped a thermometer and addition funnel connected with an N_2-system was charged with the appropriate carborane (10 mmol) in ether (10 ml) and cooled to 0 °C, and Bu^nLi (8.5 ml, 10.2 mmol, 1.2 mol dm^{-3} in hexane) was added over 10 min, then the solution was stirred for 30 min at 0 °C and cooled to −78 °C. *p*-Toluenesulfonyl cyanide (1.9 g, 10.5 mmol) in ether (15 ml) was added, and the reaction mixture was warmed to room temperature and stirred for 5 h, poured into 100 ml of 5% HCl and extracted with Et_2O (3 × 30 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After the usual work-up and evaporation of the solvent, the crude residue was purified by column chromatography, yielding the product. This method was used for obtaining: *o*-$MeB_{10}H_{10}CN$, mp 195–196 °C; *o*-$PhCB_{10}H_{10}CCN$, mp 104–105 °C; *m*-$MeCB_{10}H_{10}CN$, mp 130 °C; *m*-$PhCB_{10}H_{10}CCN$, mp 107 °C.
Method 2. *p*-Toluenesulfonyl cyanide (1.9 g, 10.5 mmol) in ether (15 ml) was added at −70 to −78 °C to bromomagnesium carborane [from bromomethylcarborane (10 mmol) and Mg (0.3 g, 13 mmol) in ether (40 ml)] with stirring. The solution was maintained at −70 °C for 30 min. The resulting mixture was warmed to room temperature and worked-up as in Method 1. The following carborane nitriles were obtained: *o*-$HCB_{10}H_{10}CCH_2CN$, mp 113–114 °C; *o*-$MeCB_{10}H_{10}CCH_2CN$, mp 138 °C; *o*-$PhCB_{10}H_{10}CCH_2CN$, mp 115 °C.
Melting points of products were in accordance with literature data. All products were also characterized by IR and MS spectra and comparison with earlier prepared samples.