Efficient access to amides of the carborane carboxylic acid [1-(COOH)−CB_{11}H_{11}]^−

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The preparation of the carborane carboxylic acid chloride [1-(COCl)−CB_{11}H_{11}]^− from the carboxylic acid [1-(COOH)−CB_{11}H_{11}]^− is reported. This acid chloride exhibits remarkable inertness towards moisture and can be stored under ambient conditions for several months. Reaction with amines affords secondary and tertiary carborane amides [1-(CONR_{2})−CB_{11}H_{11}]^− in moderate to high yields under mild conditions. Two of the amide products were characterized by X-ray crystallography in addition to spectroscopic analysis. Preliminary studies show that the amides can be reduced to the corresponding amines and that the acid chloride has the potential to serve as a starting material for carborane ester formation.

Introduction

Owing to their unique steric and electronic properties, boron-based clusters have been the focus of a growing body of studies that are concerned with their fundamental properties, new methods of their preparation and their applications. Carboranes based on the scaffolds [CB_{11}H_{12}]^− and C_{2}B_{10}H_{12} are icosahedral clusters in which one or two B–H vertices are replaced by C–H (Fig. 1a). Their three-dimensional delocalization of electron density is frequently called σ aromaticity, in reference to the π aromaticity of organic arenes; it leads to exceptional chemical and thermal stability.1–2 A large number of applications of carboranes have emerged over the past decade; their utility has become evident in ligand design,3 functionalization of anionic carboranes led us to probe amide moieties as directing groups for B–H activation mediated by transition metals. We found that the carborane carboxylic acid [1-(COOH)−CB_{11}H_{11}]^− can be transformed to pyrrolidine and tosyl amides after activation by a combination of oxalyl chloride and dimethyl formamide (Fig. 1d).

In the current study we show that the corresponding acid chloride is an intermediate that can be isolated in high yield and stored for a prolonged time under ambient conditions. It undergoes substitution with a variety of amines to give secondary and tertiary amides in moderate to high yields (Fig. 1e). X-ray crystal structures and additional transformations are presented as well.
Results and discussion

At the outset of our study, we decided to investigate the activation of [1-(COOH)–CB$_{11}$H$_{11}$]/C$_{0}$ more thoroughly. Treatment of the acid with 1 equivalent of oxalyl chloride and catalytic amounts of dimethyl formamide in dichloromethane caused clean formation of the acid chloride within 30 min at 25°C, as indicated by $^{11}$B NMR spectroscopy and ESI-mass spectrometry (Scheme 1). This species was subsequently successfully isolated by either a classical work-up including removal of volatiles or by simple precipitation upon addition of hexane to the reaction mixture (see the ESI † for details). Both procedures furnished 1 in 87% yield. Acid chloride 1 exhibits high inertness towards moisture; [Et$_4$N][1], stored as a powder in a closed vial under air, remained unchanged over several months. The hydrolysis of [Et$_4$N][1] in a mixture of acetonitrile/water (5 : 1 v/v) was studied by NMR spectroscopy, and the details of the monitoring are provided in the ESI file (Fig. S1 and S2 †). A comparison of the $^{11}$B($^1$H) NMR spectra of [1-(COOH)–CB$_{11}$H$_{11}$]/C$_{0}$ and 1 showed that these two species can be distinguished clearly based on the chemical shifts of their B12 and B2–6/7–11 positions (Fig. 2a and b).

We next probed the reactivity of 1 towards amines with the aim to prepare a series of carborane amides. Reaction with amines took place at a much higher rate than with water. Addition of 1.5 equivalents of amine cleanly afforded the corresponding amide in dichloromethane within 20 min at 25°C; one equivalent of triethylamine was used to neutralize the $\text{HCl}$ byproduct (Scheme 1). Primary unbranched amines afforded products 2a–e in yields of 46–91%. Sterically more congested amines afforded the isopropyl, cyclohexyl and tert-butyl derivatives 2f–h, while pyrrolidine and piperidine gave tertiary amides 2i and 2j. Anilines proved to be viable substrates as well, as demonstrated by the formation of 2k–m. Compounds 2f–m were obtained in high yields of 84–92%. Isolation of

![Scheme 1 Preparation of carboxylic acid chloride 1 and subsequent synthesis of carborane amides 2. Yields are isolated yields with respect to 1.](image-url)

Fig. 1 General structure of icosahedral carboranes (a), reported carborane esters and carboxamides (b–d) and outline of the present study (e).

![Fig. 2 $^{11}$B($^1$H) NMR spectra of [Et$_4$N][1-(COOH)–CB$_{11}$H$_{11}$] (a), [Et$_4$N][1] (b) and [Et$_4$N][2a] (c) (acetone-$d_6$, 22 °C, 160 MHz for $^{11}$B).](image-url)
amides 2 involved either simple precipitation or purification by silica gel column chromatography. In their $^{11}$B NMR spectra, all products exhibited a characteristic B12 resonance at −6 to −7 ppm; as a representative example, the $^{11}$B{¹H} NMR spectrum of 2a is depicted in Fig. 2c.

Cage halogenation affects the properties of boron clusters (e.g., polarity, coordinating ability, solubility) and offers the possibility of further functionalization by transition metal-catalyzed cross coupling. Amide formation was probed starting from brominated and iodinated carborane carboxylic acids 3 (Scheme 2). Applying reaction conditions identical to the ones for the synthesis of 2, amides 4a–d were obtained in yields of 81–91%. In these cases, the acid chloride was precipitated from the initial reaction mixture, collected by filtration and used directly in the amide formation step.

X-ray crystallography revealed the solid-state structures of 2e and 2m. Single crystals of the composition [Na][Et₄N][2e]₂, were obtained from an acetonitrile solution in the presence of one equivalent of Na⁺ by slow evaporation (see the ESI† for details). The unit cell contains two [{Na}[Et₄N][2e]₂]₄ dimers, both of which feature a center of inversion and coordination of the Na⁺ centers by oxygen and nitrogen atoms (Fig. 3 and S1†). The [Et₄N]⁺ cations are well-separated from the anions. The different carboxamides exhibit similar geometries, and the structural parameters of one of them will be summarized (Fig. 4a). Generally, there is a pronounced resemblance to typical organic amides. Observed distances (Å) for 2e are C1–C2 1.525(8), C2–O1 1.214(8), and C2–N1 1.339(9). The sum of angles around C2 is 360.0(6)°, and the torsion angle O2–N1–C2–C1 of 177.1(5)° indicates coplanarity of the entire amide moiety. Solvent layering of an acetone solution of 2m with hexane gave single crystals of the composition [Et₄N][2m] (Fig. 4b and S2†). The distances (Å) and angles are similar to those of 2e, namely, C1–C2 1.506(8), C2–O1 1.214(8), C2–N1 1.339(9). The sum of angles around C2 360.0(6)° and torsion angle C3–N1–C2–C1 178.7(6)°.

Finally, the potential of 1 as a precursor of carborane esters and the reduction of two selected amides 2i and 2j were investigated. As anticipated from the slow reaction of 1 with water, ester formation required more forcing conditions than amide formation. Heating a solution of 1 in methanol at 50 °C for 5 h gave methyl ester 5 in 91% yield (Scheme 3a). Treatment of 2i and 2j with an excess of lithium aluminum hydride caused

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**Scheme 2** Synthesis of carborane amides 4 starting from halogenated carborane precursors. Yields are isolated yields with respect to 3.

**Scheme 3** Ester formation starting from 1 (a) and reduction of amides 2i and 2j (b).
clean reduction to the corresponding amines (Scheme 3b). Isolation under acidic conditions afforded products 6a and 6b in as N-protonated zwitterions in yields of 88% and 91%, respectively.

Conclusions
In conclusion, the results of this study demonstrate that the carboxamide chloride 1 can be conveniently prepared and stored in the form of [\(\text{Et}_4\text{N}\)][\(\text{I}\)] under ambient conditions without noticeable decomposition. In combination with amines it affords secondary and tertiary carboxamide amides 2 under mild conditions and generally in high yields. Additional transformations such as ester formation and reduction of products 2 to amines underscore the potential of 1 as a versatile starting material towards C1-substituted derivatives of the monocarboxylic-dodecarboxylic anion. We are currently exploring transformations of 1 with other nucleophiles.

Conflicts of interest
There are no conflicts to declare.

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