Functionally Substituted Vinyl Carbanions, 32[1)]

Synthesis of 1,2-Oxaborole Betaines

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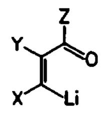
Reaction of β-lithiated functionally substituted acrylate derivatives **1** with triethylborane affords 1,2-oxaborole betaines **2** with a diethylborylene ring constituent. The structure of these compounds is assigned by ^{1}H-NMR data and by an X-ray analysis of **2c**.

Funktionell substituierte Vinylcarbanionen, 32[1)]. – Synthese von 1,2-Oxaborol-Betainen

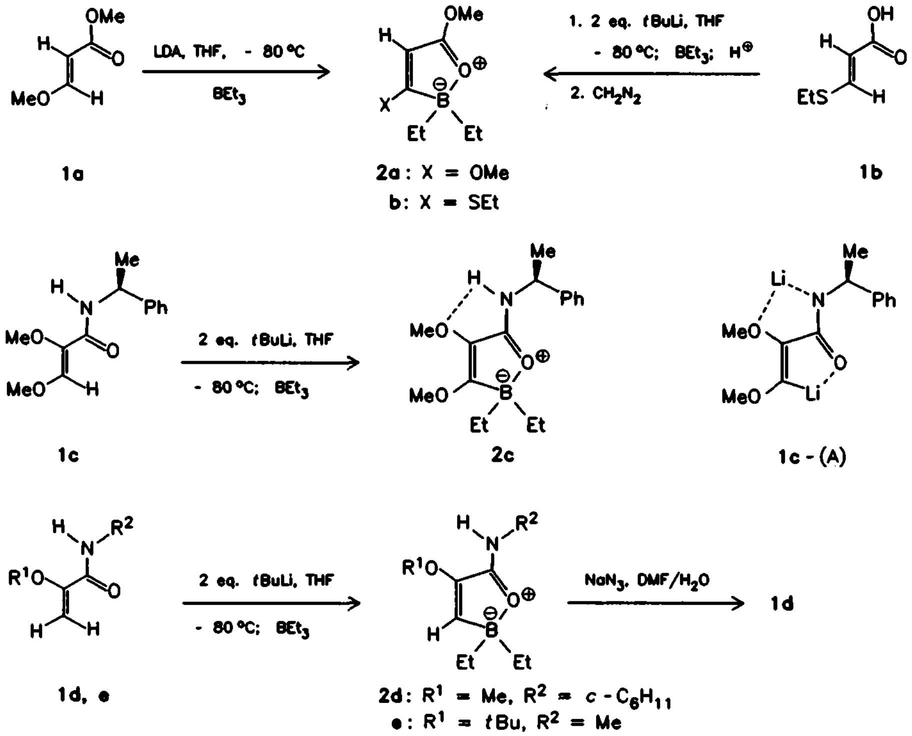
Die Umsetzung von β-lithiierten, funktionell substituierten Acrylsäurederivaten **1** mit Triethylbor liefert 1,2-Oxaborol-Betaine **2**, die eine Diethylborylen-Gruppe als Ringglied enthalten. Die Struktur dieser Verbindungen folgt aus den ^{1}H-NMR-Daten und vor allem aus der Röntgenstruktur-Analyse von **2c**.

β-Lithiated functionally substituted acrylates of structure **1**-(A) exhibit high nucleophilicity in reactions with various electrophiles thus yielding a variety of different products[2–4)]. With the aim to use trialkylborane compounds as electrophiles which upon reaction transfer alkyl substituents to the *C*-lithiated position[5,6)] we investigated the reaction of species **1**-(A) with triethylborane. The starting materials **1a–e** represent different substitution types, which have been transformed with base into the β-*C*-lithiated species **1a**-(A) – **1e**-(A)[2–4)].



1 - (A)

	X	Y	Z
1a - (A)	MeO	H	MeO
b - (A)	EtS	H	LiO
c - (A)	MeO	MeO	PhCH(Me)–N(Li)–
d - (A)	H	MeO	$c-C_6H_{11}N(Li)$–
e - (A)	H	*t*BuO	$CH_3N(Li)$–



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A. Reactions with Triethylborane

Reactions of ester **1a** with lithium diisopropylamide (LDA) generates species **1a**-(A)[7] which afforded with triethylborane a new heterocyclic oxaborole betaine system **2a**[8] with a tetracoordinated boron atom as a ring constituent. Presumably due to the stability of this system intermolecular ethyl transfer to the medium takes place rather than intramolecular ethyl transfer to the carbon next to the boron atom. The structural assignment of betaine formation is supported by the ^{1}H-NMR data (see Table 3): The signals of both *O*-methyl-group protons and of the vinylic proton are shifted downfield as compared to the starting material and the ethyl resonances are shifted upfield. Final proof for this structure came from an X-ray analysis of compound **2c** (see below).

Generation of *O,C*-dilithiated species **1b**-(A) from 3-(ethylthio)acrylic acid (**1b**)[4a] and reaction with triethylborane afforded after acidic workup and subsequent diazomethane addition the corresponding compound **2b**. This result is again indicative of the preferred formation of these compounds. Similarly from the 2,3-dimethoxy-substituted acrylamide **1c**[2,9] compound **2c** was obtained as crystalline material. Compared with the starting material again the signals of both methoxy-group protons are shifted downfield in the ^{1}H-NMR spectrum. The X-ray analysis of this material (see below) clearly indicated a BO bond and in addition also hydrogen bonding of the NH group to the α-methoxy group. This finding also supports intramolecular complexation of the lithium ions in the dilithiated species as indicated in the formula **1c**-(A)[10]. Recently we were also able to generate β-*C*-lithiated species from α-methoxy-substituted acrylamides **1d, e** and similar types of compounds[3]. Although the reactivities of species **1a**-(A) – **1c**-(A) are quite different from the reactivity of species **1d, e**-(A)[2,3] they afforded the corresponding betaines **2d** and **2e**[11] with triethylborane as indicated by the ^{1}H-NMR data (Table 3). For further studies the observation is of interest that this reaction can be reversed with sodium azide in dimethylformamide containing traces of water.

B. Structure of Compound 2c

Compound **2c** crystallizes in the monoclinic system, polar space group $P2_1$ (no. 4[12]), with two molecules in the independent unit. The absolute configuration was inferred from the known stereochemistry of the amide group, since the accurracy of the data did not allow for enantiomeric discrimination by anomalous dispersion.

The essential part of the structure (Fig. 1) is the heterocyclic 1,2-oxaborole ring. The atoms B1, C1, C2, C3, and O3 form a planar five-membered ring with an approximately tetrahedral geometry around the boron atom and trigonal planar environment at the carbon atoms. The atoms O1, O2, N1 of the oxygen and nitrogen substituents are almost coplanar with the oxaborole ring (Tables 1,2).

Table 1. Selected bond distances (pm) for the two independent molecules of compound **2c** in the unit cell

B1–C1	158.5 (1.0)	158.3 (1.1)
C1–C2	134.6 (.9)	134.1 (.9)
C2–C3	140.9 (1.1)	141.2 (1.1)
C3–O3	126.4 (.8)	127.1 (.8)
O3–B1	159.5 (1.1)	159.0 (1.0)
C1–O1	133.5 (.9)	134.7 (.9)
C2–O2	135.5 (.8)	136.3 (.8)
C3–N1	131.7 (.9)	130.1 (.9)
$B-C_{Et}$	158.7	158.0
N1–H1	96.6	92.8
H1–O2	240.3	245.0

The bond distances in the ring indicate a CC-double bond between C1 and C2 [134.6(9) pm] and a somewhat lengthened CO-double bond between C3 and O3 [126.4(8) pm]. The B–O as well as the B–C distances are well within the

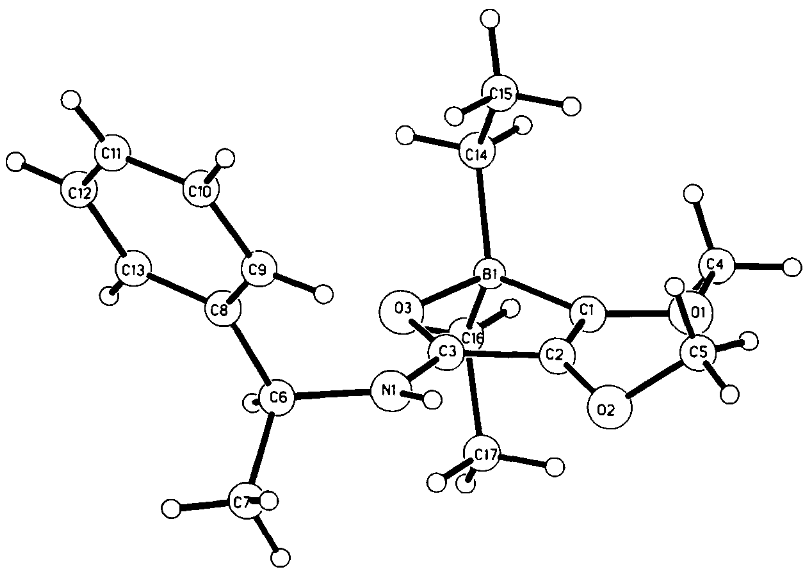

Fig. 1. Molecular structure of oxoniaboratacyclopentadiene **2c**

range of normal B—O and B—C bond lengths[11]; as expected the bond length between C2 and C3 is shorter than a CC-single bond [140.9(1.1) pm].

The rotational position of the amide group is fixed by a hydrogen bond between N1 and O2. The rotational position of the methoxy group at C2 corresponds to this interaction.

Table 2. Selected bond angles (°) and torsional angles (°) of compound **2c**

O3	B1	C1	96.7 (0.5)	B1	C1	O1	130.8 (0.6)
B1	C1	C2	110.3 (0.6)	C1	C2	O2	133.1 (0.7)
C1	C2	C3	108.0 (0.6)	C2	C3	N1	122.6 (0.6)
C2	C3	O3	115.6 (0.6)	O3	C3	N1	121.7 (0.7)
C3	O3	B1	109.2 (0.6)	C14	B1	C1	116.4 (0.7)
C14	B1	C16	114.8 (0.6)	C14	B1	O3	106.4 (0.7)

B1	C1	C2	C3	2.6 (0.8)
C1	C2	C3	O3	−0.2 (0.9)
C2	C3	O3	B1	−2.3 (0.9)
C14	B1	C1	C2	108.6 (0.7)
C16	B1	C1	C2	−113.1 (0.7)
C3	C2	C1	O1	−177.5 (0.6)
O3	C3	C2	O2	−174.2 (0.6)
C1	C2	C3	N1	177.8 (0.7)
C6	N1	C3	O3	5.0 (1.1)

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Experimental Part

Synthesis of the Starting Materials **1a–e**: Compounds **1a, b**, and **1d, e** were obtained as previously described[2,3,4a,7].

(S)-2,3-Dimethoxy-N-(1-phenylethyl)acrylamide (**1c**)[9,13]: A solution of 2,3-dimethoxyacrylic acid (3.3 g, 25 mmol) in dichloromethane (10 ml) was treated with thionyl chloride (2.9 ml, 40 mmol) at room temp. for 2 h. The solvent and excess thionyl chloride were evaporated under reduced pressure and then anhydrous tetrahydrofuran (10 ml) was added. To this solution was added a solution of (*S*)-1-phenylethylamine (6.4 ml, 50 mmol) in anhydrous tetrahydrofuran (10 ml) at room temperature. After 2 h the precipitate was filtered off, the organic phase was treated with ice water, which was acidified with HCl to pH 1. The product was extracted with ether (3 x 25 ml), the ether phase was washed with $NaHCO_3$ solution, then dried with Na_2SO_4, and evaporated. The solid material obtained was recrystallized from water. Yield 25 g (42%) colorless needles; m.p. 86–88°C; $[\alpha]_D^{23} = -126$ (c = 1, $CHCl_3$).

$C_{13}H_{17}NO_3$ (235.3)	Calcd. C 66.37	H 7.28	N 5.95
	Found C 66.60	H 7.38	N 5.80

General Procedure for the Synthesis of Compounds **2a–e**[14]: The β-lithiated species **1a**-(A)–**1e**-(A) were generated from compounds **1a–e** according to literature procedures[3,4a,7]. After completion of the lithiation 1 equivalent of triethylborane (1 M solution in *n*-hexane) was introduced into the reaction flask with a syringe against a flow of nitrogen. After 0.5 h at −80°C the reaction mixture was poured into water, acidified with 1 N HCl to pH 1, and extracted with dichloromethane. In case of compound **1a** the reaction mixture is poured into saturated ammonium chloride solution and then extracted with dichloromethane. The extract is dried over sodium sulfate, evaporated under reduced pressure and the residue in case of compound **1b** treated with excess diazomethane in ether and then evaporated again. The products were purified by flash chromatography on silica gel (Merck, 230–400 mesh ASTM) with petroleum ether (b.p. 35–80°C)/ethyl acetate (2:1) as solvent system. For yields, elemental analyses, and ^{1}H-NMR data see Table 3.

Formation of Compound **1d** *from* **2d**: To a solution of **2d** (0.12 g, 0.47 mmol) in dry dimethylformamide (10 ml) and one drop of

Table 3. Analytical and physical data of compounds **2a–e**

-1-oxonia-2-borata-3,5-cyclopentadiene	Yield[a] (%)	M.p. (°C)	Molecular Formula (Weight)		Analysis C	H	N	^{1}H NMR (250 MHz, $CDCl_3$, TMS int.)[b] δ Values
2,2-Diethyl-3,5-dimethoxy- (**2a**)	48	oil	$C_9H_{17}BO_3$ (184.0)	Calcd. Found	58.74 58.79	9.31 9.15		5.32 (s, 1H, 4-H), 4.20 (s, 3H, 5-CH_3O), 3.95 (s, 3H, 3-CH_3O), 0.7–0.4 (m, 10H, 2 C_2H_5)
2,2-Diethyl-3-(ethylthio)-5-methoxy- (**2b**)	75	oil	$C_{10}H_{19}BO_2S$ (214.1)	Calcd. Found	[c]			5.80 (s, 1H, 4-H), 4.01 (s, 3H, CH_3O), 2.85 (q; 2H, CH_2S, J = 7.6 Hz), 1.35 (t, 3H, SCH_2CH_3, J = 7.6 Hz), 0.65 (m, 6H, 2 BCH_2CH_3), 0.55 (mc, 2H, 2 BCH), 0.4 (m, 2H, 2 BCH)
(*S*)-2,2-Diethyl-3,4-dimethoxy-5-[(1-phenylethyl)amino]- (**2c**)	63	56	$C_{17}H_{26}BNO_3$ (303.2)	Calcd. Found	67.34 67.27	8.63 8.61	4.61 4.61	7.35 (m, 5H, C_6H_5), 6.10 (d, 1H, NH, J = 7.9 Hz), 5.19 (dq, 1H, NHCH, J = 7.9; 6.7 Hz), 3.95 (s, 3H, 3-CH_3O), 3.70 (s, 3H, 4-CH_3O), 1.60 (d, 3H, −CHCH_3, J = 6.7 Hz), 0.75–0.40 (m, 10H, 2 C_2H_5)
5-(Cyclohexylamino)-2,2-diethyl-4-methoxy- (**2d**)	52	66	$C_{14}H_{26}BNO_2$ (251.2)	Calcd. Found	66.95 66.67	10.42 10.35	5.57 5.50	6.32 (s, 1H, 3-H), 6.18 (sb, 1H, NH), 3.85 (m, 1H, NHCH), 3.65 (s, 3H, CH_3O), 2.1–1.1 (m, 10H, cyclohexyl-CH_2), 0.68 (mc, 6H, 2 BCH_2CH_3), 0.4 (mc, 4H, 2 BCH_2)
4-*tert*-Butoxy-2,2-diethyl-5-(methylamino)- (**2e**)	49	20	$C_{12}H_{24}NBO_2$ (225.1)	Calcd. Found	64.02 63.84	10.74 10.92	6.22 6.05	6.56 (s, 1H, 3-H), 6.32 (sb, 1H, NH), 3.05 (d, 3H, NHCH_3, J = 5.2 Hz), 1.38 (s, 9H, C(CH_3)$_3$), 0.66 (mc, 6H, 2 CH_2CH_3), 0.43 (mc, 4H, 2 CH_2CH_3)

[a] Yields refer to pure isolated products. — [b] Bruker WM 250 Cryospectrometer. — [c] Not analyzed.

water was added sodium azide (60 mg, 0.94 mmol). The reaction mixture was heated to 110°C for 2 h, then it was poured into water. The organic material was extracted with dichloromethane (3 × 50 ml), the extract washed with water, dried over sodium sulfate, and evaporated. The residue, recrystallized from ethyl acetate, was found to be identical with compound **1d** (m.p. and ^{1}H NMR). Yield 78 mg (91%).

X-ray Structure Analysis of **2c**[15]: $C_{17}H_{26}BNO_3$, monoclinic, space group $P2_1$ (no. 4[12]), a = 1082.6(7), b = 1226.3(9), c = 1315.8(9) pm, β = 103.57(5)°, V = 1698(2) · 10^6 pm^3, d_{calc} = 1.18 gcm^{-3}, Z = 4, μMo-K_α = 0.8 cm^{-1}, T = 238 K, ω-scan, $\Delta\omega$ = 1°, $1.9 \leq \dot{\omega} \leq 29.3°$ mm^{-1}, $2 \leq 2\Theta \leq 45°$.

The cell constants and the reflections were measured on a Syntex (Nicolet) P3 diffractometer with a graphite monochromator λMo-K_α = 71.069 pm. The structure was solved by direct methods (SHEL-XTL[16]) on the basis of 2017 independent reflexions ($I \geq 2\sigma(I)$) and refined in a partially anisotropic model by least square techniques (216 parameters; R = 0.07) with a maximum residual electron density between −0.35 and 0.48 $e \cdot Å^{-3}$. Hydrogen atoms, with the exception of H1 (bound to N1) and H6 (bound to C6), were fixed in geometrically ideal positions; the coordinates of H1 and H6 were inferred from difference Fourier syntheses but not refined.

CAS Registry Numbers

1a: 34846-90-7 / **1b**: 103755-64-2 / **1c**: 105858-45-5 / **1d**: 98083-80-8 / **1e**: 105858-46-6 / **2a** (B III): 105858-47-7 / **2a**: 105858-53-5 / **2b** (B III): 105858-48-8 / **2b**: 105858-54-6 / **2c** (B III): 105858-49-9 / **2c**: 105858-55-7 / **2d** (B III): : 105858-50-2 / **2d**: 105858-56-8 / **2e** (B III): 105858-51-3 / **2e**: 105858-57-9 / 2,3-dimethoxyacrylic acid: 105858-52-4 / (*S*)-1-phenylethylamine: 2627-86-3 / triethylborane: 97-94-9

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[14] Compound **2e** was synthesized by A. Enhsen.
[15] Further details and basic data concerning the X-ray analysis may be obtained from Fachinformationszentrum Energie Physik Mathematik, D-7514 Eggenstein-Leopoldshafen 2 (W.-Germany), by specifying the registry number CSD 52093 authors, and source.
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