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[13] [Fe^{III}(TPP)]–imidazole complexation can be achieved either intramolecularly to form 1:1 complexes, or intermolecularly to form a lateral array. In both arrangements the porphyrin ring would be oriented perpendicular to the surface.

[14] Theoretic monolayer thicknesses were calculated from a model where the complexes or free ligands are oriented perpendicularly with respect to the surface.

[15] The coverage of monolayers of **1**, **2**, and their complexes was measured by Cu UPD[4a] (UPD = underpotential metal deposition) as 77–85%. The exposed surface is attributed to the relatively large space between the bound disulfides.

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[17] Prolonged rinsing in pure ethanol was ineffective, while the use of pure water caused the gold layer to exfoliate from the silicon surface.

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[20] Gold exposed to a [Fe^{III}(TPP)Cl] solution under the same conditions showed no voltammetric peak or a very weak peak > 100 mV negative of that of the complex monolayer, which is attributed to physisorbed porphyrins.

$[(Ph)_2(NMe_2)C(OLi)\cdot THF]_2$: Crystal Structure of the Tetrahedral Intermediate Formed in the Reaction of *N*,*N*-Dimethylbenzamide and Phenyllithium**

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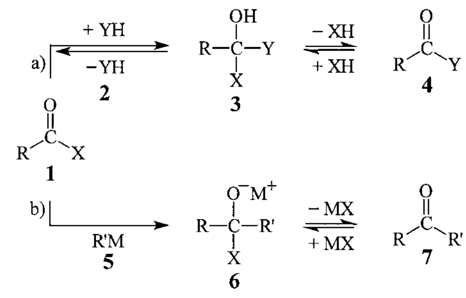
Norma Sbarbati Nudelman, and Gernot Boche*

*Dedicated to Professor Reiner Sustmann
on the occasion of his 60th birthday*

The tetrahedral intermediate RC(OH)XY (**3**) formed in reactions of carboxylic acid derivatives RC(O)X (**1**) with nucleophiles YH (**2**) to give RC(O)Y (**4**; Reaction a in Scheme 1) is of continued interest, for example, because of its significance for in vivo acylation rections.[1] Only recently, the solid-state structure of the (protonated) intramolecular amine adduct of a carboxylic acid was determined in a rather special case.[2]

Similarly, reactions of **1** with organometallic compounds R′M (**5**) proceed via a tetrahedral intermediate **6** (Reaction b in Scheme 1). In the case of X = Hal, SR, and OR, **6** undergoes a very fast 1,2-elimination of MX to give aldehyde or ketone **7**, which may react further with **5**. In the case of X = NR_2, **6** is more stable, a fact that has been utilized for the preparation of ketones **7** ($\mathbf{1}+\mathbf{5}\rightarrow\mathbf{6}$; $\mathbf{6}+H_3O^+\rightarrow\mathbf{7}$)[3] as well as for the protection of aldehydes and ketones ($\mathbf{7}+MNR_2\rightarrow\mathbf{6}$).[4] What is the structure of a compound of type **6**, and in particular what is the environment at the new tetrahedral carbon atom? The X-ray crystal structure of $[(Ph)_2(NMe_2)C(OLi)\cdot THF]_2$ (**10**),[5] which is prepared from *N*,*N*-dimethylbenzamide (**8**) and phenyllithium (**9**) and crystallized from tetrahydrofuran/diethyl ether [Eq. (1)], gives an answer to these questions (Figure 1).



Scheme 1. Reaction of carboxylic acid derivatives **1** with nucleophiles YH (**2**; a) and R′M (**5**; b). R = H, alkyl, aryl; X = Hal, SR, OR, NR_2; YH = R″SH, R″OH, R″NH_2; R″ = H, alkyl, aryl; R′ = alkyl, aryl; M = Li, MgX, etc.

$$\underset{\mathbf{8}}{PhC(O)NMe_2} + \underset{\mathbf{9}}{PhLi} \xrightarrow{THF/Et_2O} \underset{\mathbf{10}}{[(Ph)_2(NMe_2)C(OLi)\cdot THF]_2} \quad (1)$$

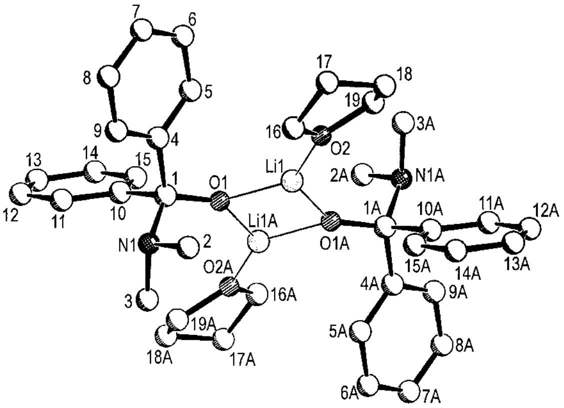


Figure 1. Crystal structure of **10**. Important bond lengths [pm] and bond angles [°]: C1−O1 137.1(2), C1−N1 150.0(3), C1−C4 154.8(3), C1−C10 154.9(3), Li1−N1 375.1(4), Li1−N1A 373.7(4); O1-C1-N1-C2 −58.4(2), O1-C1-N1-C3 63.8(2), C4-C1-N1-C2 65.3(2), C10-C1-N1-C3 −60.8(2).

In the dimeric structure the Li atoms Li1 and Li1A are bound to the anionic O atoms O1 and O1A and to the O atom of a THF molecule (O2 and O2A, respectively), leading to three-coordinate Li cations, which is rarely observed. The C1−O1 bond is 137.1(2) pm long, which corresponds to the C−O bond length in an α-alkoxyamine (137 pm).[6] In $(CH_3)_3C{-}OLi$ a length of 139.2 pm has been determined for

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[**] This work was supported by the Deutsche Forschungsgemeinschaft (SFB 260) and the Fonds der Chemischen Industrie.

the C–O bond.[7] In amides such as **8** the C=O bond measures 123.1 pm,[8] and in aromatic ketones 123.0 pm.[8] The C1–N1 bond is 150.0(3) pm long, which corresponds to the value of 149 pm determined for the above-mentioned α-alkoxyamine.[6] The mean value for C_{sp^3}–N bonds is 146.9 pm.[8] In carboxamides the C–N bond is even shorter (134.6 pm).[8] The bonds from C1 to C4 and C10 of the phenyl rings are 154.8(3) and 154.9(3) pm long. The mean value for C_{sp^3}–C_{aryl} bonds amounts to 151.3 pm.[8] Thus, the bonds C1–C4, C1–C10, and C1–N1 are slightly elongated, whereas the C1–O1 bond is somewhat shortened.

Dunitz, Bürgi, and Shefter investigated the geometrical reaction coordinates of the intramolecular addition of amine and alcohol nucleophiles to carbonyl groups finally leading to the tetrahedral intermediate (e.g. $\mathbf{1}+\mathbf{2} \rightleftharpoons \mathbf{3}$).[9] In agreement with their investigations, the structure of **10** indicates the beginning of the decomposition of an analogous tetrahedral intermediate, namely, the 1,2-elimination of $LiNMe_2$ (the best leaving group in **10**) to give benzophenone. This is shown by the bond lengths C1–N1 and C1–O1 discussed above. It is also in agreement with the angles between the C1-C4-C10 plane and the vectors C1–N1 (60.3°) and C1–O1 (52.8°): O1 is on the way towards the C1-C4-C10 plane, whereas N1 is removed from **10** along the trajectory.

A further point of interest is the conformation of the dimethylamino groups; their N atoms are not coordinated to the Li cations, which is normally very favorable.[10] In **10** the distances Li1···N1 and Li1···N1A are 375.1(4) and 373.7(4) pm, whereas normal Li–N bonds are approximately 200 pm long.[11] Bonding of N1 and N1A to Li1 and Li1A would require a rotation of the amino groups in **10** by about 180°, as shown by the torsional angles O1-C1-N1-C2 −58.4(2)°, O1-C1-N1-C3 63.8(2)°, C4-C1-N1-C2 65.3(2)°, and C10-C1-N1-C3 −60.8(2)°. This, however, would lead to unfavorable ecliptic conformations of the methyl groups at N1 and N1A with the phenyl groups at C1 and C1A. Furthermore, the electron lone pairs at the N atoms in **10** are perfectly placed for an interaction with the σ^* orbitals of the C–O bonds (anomeric effect[12]). The balance between N···Li complexation, conformational strain, and anomeric effect is shown by the data in Table 1, which summarizes the calculated bond lengths, bond angles, and relative energies of the compounds **11**–**15** in the conformations **A** and **B**.

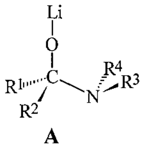
Thus, **11B** is 8.0 kcal mol^{-1} higher in energy than **11A**, whose conformation at the C–N bond corresponds to that in **10**. The anomeric effect in **11A** is nicely shown by the bond lengths: The C–O bond is longer (137.0 pm) and the C–N bond is shorter (153.2 pm) than in **11B** (135.9 and 159.0 pm, respectively). A similar effect is observed in compounds **12**–**15**.[13] Interestingly the torsional angles O-C-N-R^3 (−158.0°) and O-C-N-R^4 (73.3°) in **11B** are almost equal to the corresponding angles in a recently investigated α-aminolithium alkoxide (158.9/−71.7° and 154.9/−73.9°, respectively).[14] Apparently, to avoid ecliptic interactions, rotation about the C–N bond takes place if a Li-O-C-N four-membered ring is formed. A decrease in conformational strain (**11**→**12**→**13**→**14**) provides a reduction in the destabilization of conformers **B** from 4.3 kcal mol^{-1} (**12B**) to 1.5 kcal mol^{-1} (**13B**). In the case of **14** the **B** isomer is −2.7 kcal mol^{-1} more stable than **14A**, and the torsional angles O-C-N-R^3 and O-C-N-R^4 ideally amount to −120.1° and 121.1°. Isomer **15B** is even more stable than **15A** (−4.5 kcal mol^{-1}). In the case of **15** the energies and geometries of the conformers **A** and **B** were also determined by the MP2 method, and the results confirm the tendency shown in Table 1.

In conclusion, the bond lengths and bond angles at the tetrahedral C1(C1A) atom in **10** indicate the tendency for 1,2-elimination of $LiNMe_2$ to give benzophenone, even though the anomeric effect stabilizes **10**.

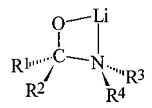
Experimental Section

10: A solution of *N*,*N*-dimethylbenzamide (500 mg, 3.35 mmol) in diethyl ether (60 mL) was allowed to react with 1.8 N phenyllithium in cyclohexane/diethyl ether (1.86 mL, 3.35 mmol) at room temperature under an argon atmosphere. The white precipitate was washed with diethyl ether (2 × 10 mL) under argon and dissolved in THF (10 mL). A 4-mL aliquot of this solution was treated with diethyl ether (2 mL) and kept at −16 °C for 8 h. Colorless rhombic crystals were obtained (121 mg, 44 % yield).

Table 1. Calculated bond lengths [pm], torsion angles [°], and relative energies [kcal mol^{-1}] of the conformers **A** and **B** of compounds **11**–**15** (RHF/3–21G//PM3). The MP2/6-31+G*//MP2/6-31+G* values of **15** are given in parentheses.



A



B

Compd	R^1	R^2	R^3	R^4	C–O	C–N	O-C-N-R^3	O-C-N-R^4	E_{rel}
11A	Ph	Ph	Me	Me	137.0	153.2	58.4	−70.9	0.0
11B	Ph	Ph	Me	Me	135.9	159.0	−158.0	73.3	8.0
12A	Ph	H	Me	Me	136.7	152.0	59.2	−71.1	0.0
12B	Ph	H	Me	Me	135.4	157.2	−146.4	86.0	4.3
13A	H	H	Me	Me	136.5	150.4	64.9	−65.8	0.0
13B	H	H	Me	Me	134.9	156.7	−117.3	116.6	1.5
14A	H	H	H	H	136.9	148.4	58.7	−61.3	0.0
14B	H	H	H	H	135.2	154.5	−120.1	121.1	−2.7
15A	Me	Me	H	H	138.3	150.4	59.9	−60.2	0.0
					(139.3)	(147.1)	(56.7)	(−56.7)	(0.0)
15B	Me	Me	H	H	136.2	155.9	−126.0	115.2	−4.5
					(137.3)	(154.8)	(−129.7)	(112.5)	(−6.0)

1433-7851/99/3809-1262 $ 17.50+.50/0

^{1}H NMR (200 MHz, [D$_8$]THF, 298 K): $\delta = 7.78$ (4H), 7.12 (4H), 6.93 (2H), 2.20 (6H); ^{13}C NMR (50 MHz, [D$_8$]THF, 298 K): $\delta = 154.6$, 128.0, 127.6, 125.2, 94.3,[16] 39.7.

Received: December 8, 1998 [Z12756IE]
German version: *Angew. Chem.* **1999**, *111*, 1345–1347

Keywords: carbonyl compounds · intermediates · nucleophilic additions

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[5] a) Crystal structure analysis of **10** (C$_{19}$H$_{24}$LiNO$_2$, $M_r = 305.33$): monoclinic, space group $P2_1/c$, $a = 1059.4(1)$, $b = 928.5(1)$, $c = 1775.4(1)$ pm, $\beta = 93.927(5)^\circ$, $V = 1742.3(2) \times 10^{-30}$ m^3, $Z = 4$, $\rho_{calcd} = 1.164$ Mg m^{-3}, $\mu(Cu_{K\alpha}) = 1.542$ mm^{-1}. Data collection on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated Cu$_{K\alpha}$ radiation at $T = 213(2)$ K. Of 3063 reflections collected, 2954 were unique ($R_{int} = 0.0260$). The structure was solved with direct methods (SHELXS-97)[5b] and refined on F^2 with all reflections (SHELXL-97).[5c] Non-hydrogen atoms were anisotropic, and hydrogen atoms were placed at calculated positions with fixed isotropic temperature factors. Parameters for the weighting scheme calculated by the program: 0.0856, 0.8018; $R1 = 0.0547$ (2446 reflections with $I > 2\sigma(I)$), $wR2 = 0.1602$, GOF = 1.044; a total of 211 refined parameters. All calculations were performed on DEC Alpha Stations with VMS.[5d–f] b) G. M. Sheldrick, SHELXS-97, *Program for the Solution of Crystal Structures*, Göttingen, **1997**; c) G. M. Sheldrick, SHELXL-97, *Program for the Refinement of Crystal Structures*, Göttingen, **1997**; d) A. L. Spek, Platon 94, *Program for Geometrical Analysis of Crystal Structures*, Utrecht, **1994**; e) E. Keller, SCHAKAL-88B, *A FORTRAN Program for the Graphic Representation of Molecular and Crystallographic Models*, Freiburg, **1988**. f) Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-111982. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[10] $[CH_3O^-Li^+ \cdot THF] + NH_3 \rightarrow [CH_3O^-Li^+ \cdot THF \cdot NH_3]$ leads to a stabilization of −20.0 kcal mol^{-1} (RHF/3-21G//PM3).

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[13] Therefore, without an anomeric effect in **10**, C1−N1 should be longer and C1−O1 shorter.

[14] After we started our investigations on α-aminolithium alkoxides,[15] the first solid-state structure of such a compound was published by J. E. Davies, P. R. Raithby, R. Snaith, and A. E. H. Wheatley (*Chem. Commun.* **1997**, 1721–1722). However, they discussed neither C−C, C−O, or C−N bond lengths nor the bond angles of these atoms. They were only interested in O−Li and N−Li interactions. This is also the case in a recent paper: D. R. Armstrong, J. E. Davies, R. P. Davies, P. R. Raithby, R. Snaith, A. E. H. Wheatley, *New J. Chem.* **1999**, 35–41.

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[16] The chemical shift of C1 in the ^{13}C spectrum ($\delta = 94.3$) corresponds to those of related tetrahedral carbon atoms: $\delta = 88.6$[14] and 105.9.[15]

Total Synthesis of (−)-Mucocin[**]

Stefan Bäurle, Sabine Hoppen, and Ulrich Koert*

The acetogenins of *Annonaceae* are characterized by their variety in structure and their potent biological features, for example, as antitumor agents or immunosuppressants.[1] Therefore, this class of compounds is subject to intensive synthetic efforts.[2] Within the acetogenins a group of compounds exists that also bear a tetrahydropyran (THP) ring additional to the usual tetrahydrofuran rings in the molecular scaffold. A representative member of that group is (−)-mucocin, which was isolated from *Rollinia Mucosa*.[3] The molecule shows a highly selective inhibitory effect against A-549 (lung cancer) and PACA-2 (pancreatic cancer) cell lines with a selectivity up to 10000 times that of the known antitumor agent adriamycin. A blockage of the mitochondrial complex I is discussed as the mode of action.[1]

Here we report on a total synthesis of (−)-mucocin that follows a highly convergent synthetic strategy.[4] According to our retrosynthetic analysis (disconnection at C16−C17) mucocin could be constructed by the addition of a THP organometallic compound **1** to a THF aldehyde **2** (Scheme 1).

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[**] This work was supported by the Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie, Schering AG, and Asta-Medica. We thank Wacker AG for gifts of chemicals. Dipl.-Chem. S. Fietz-Razavian is acknowledged for support in the beginning of this project.

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