utilized heavy-atom methods[22] and difference Fourier syntheses. Refinement was carried out as described for $[Cu(\mathbf{2d})]BF_4$. Final R_1 $[F \geq 4\sigma(F)] = 0.0416$, wR_2 [all data] $= 0.100$, S $[F^2] = 1.06$ for 310 refined parameters. The final ΔF synthesis showed no residual feature above $1.47\ e\,Å^{-3}$.[10c] c) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-111910 ($[Cu(\mathbf{2d})]BF_4$) and 111911 ($[Ag(\mathbf{2d})]BF_4$). 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).

[11] Data represent the ordered half-molecule in the asymmetric unit.

[12] Data represent one of two very similar half-molecules in the asymmetric unit.

[13] Cambridge Structural Database Version 5.16 (190307 structures, October 1998 release): F. H. Allen, O. Kennard, *Chem. Des. Automat. News* **1993**, *8*, 31–37.

[14] The United Kingdom Chemical Database Service: D. A. Fletcher, R. F. McMeeking, D. Parkin, *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 746–749.

[15] The query was constructed by defining three points on an aromatic ring: x, one C atom of the ring; o, the centroid of the ring; and y, the centroid of one of the C–C bonds parallel to xo. A metal atom at point m would have x,y coordinates $x_m = om\cos(x\hat{o}m)$ and $y_m = om\cos(y\hat{o}m)$. The radius of the cylinder (r) was defined by the relationship $x_m^2 + y_m^2 \leq r^2$, and the 5 Å height of the cylinder was limited by constraining om.

[16] CSD refcodes: DOCPAM, TEXZUR, YUHDEK, ZODZAT.

[17] H. Schmidbaur, *Angew. Chem.*, **1985**, *97*, 893–904; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 893–904.

[18] In all cases the benzene rings are associated independently to the metal. CSD refcodes: BEDBER, DEKMAH, FICXEU, HALVEV, JIVTEN, JIVTIR, SEJKAT, SIRROA.

[19] J. L. Atwood, W. E. Hunter, R. D. Rogers, J. A. Weeks, *J. Inclusion Phenom.* **1985**, *3*, 113–123.

[20] A total of 9141 crystal structures in the Cambridge Structural Database contain Cu and 1605 contain Ag, of which 104 (1.1%) and 32 (2.0%), respectively, exhibit the metal in a trigonal-planar ligand field (i.e., trivalent with bond angles between 115° and 125°). It must be noted that it is not possible using the CSD's QUEST-3D software to specify metal oxidation states, so the above figures for Cu include both Cu^{I} and Cu^{II}.

[21] Two examples are found in the literature where a crown ether incorporates a single benzene ring whose centroid is involved in bonding to Tl^{I} (metal–centroid, 2.96 Å) and Ag^{I} (metal–centroid, 2.89 Å): F. Fages, J.-P. Desvergne, H. Bouas-Laurent, J. Hinschberger, P. Marsau, M. Petraud, *Nouv. J. Chim.*, **1988**, *12*, 95–106; H. Andrianatoadndro, Y. Barrans, P. Marsau, J. P. Desvergne, F. Fages, H. Bouas-Laurent, *Acta Crystallogr. Sect. B* **1995**, *51*, 293–300, respectively.

[22] SHELXS-97: G. M. Sheldrick, *Acta Crystallogr. Sect. A* **1990**, *46*, 467–473.

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N-Oxidation of Epothilone A–C and *O*-Acyl Rearrangement to C-19- and C-21-Substituted Epothilones**

Gerhard Höfle,* Nicole Glaser, Michael Kiffe, Hans-Jürgen Hecht, Florenz Sasse, and Hans Reichenbach

Dedicated to Professor Wolfgang Steglich
on the occasion of his 65th birthday

Epothilone A (**1a**) and B (**1b**) form the parent compounds of a new family of cytotoxic and antifungal macrolides from the mycobacterium *Sorangium cellulosum*.[1] According to Bollag et al.,[2] their effect upon eucaryontic cells is based on the induction of tubulin polymerization and stabilization of microtubules, causing a massive disruption in mitosis and ultimately programmed cell death (apoptosis). This mechanism, which had been extremely rare for a long time, was first observed for taxol (paclitaxel),[3] and has recently been reported for discodermolide,[4] a polyketide from marine sponges, and eleutherobin,[5] a diterpene from soft coral. The high in vitro activity against multiresistant tumor cell lines[2, 6, 7] as well as other beneficial properties[1, 8] quickly made the epothilones interesting candidates for cancer chemotherapy and for total synthesis.[9]

First results of in vivo studies on mouse models were reported by Danishefsky et al. In these studies, not epothilone B (**1b**), which demonstrated the highest in vitro activity, but the significantly less active deoxyepothilone B (= epothilone D, **1d**) showed a promising therapeutic range with good activity against sensitive and multiresistant tumors up to the point of complete remission.[10]

In the search for possible clinically suitable derivatives, we have concentrated our efforts on the isolation of natural structural variations[11] and the chemical modification of the epothilones obtained by fermentation.[12] We report herein the unexpectedly simple functionalization of the thiazol moiety.

During the preparation of epothilones by fermentation from *Sorangium cellulosum*, numerous structural variants from biosynthesis and biotransformation were obtained in addition to the main components A and B. Particularly

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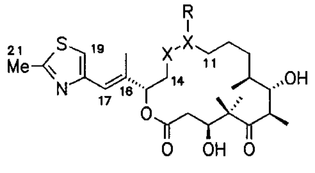
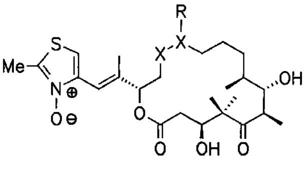
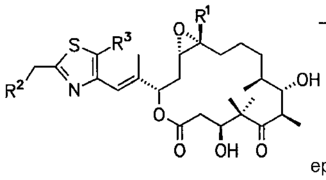
interesting are the epothilones C (**1c**) and D (**1d**),[11] as they represent the last intermediates in both the biosynthesis and several total syntheses.[9] In contrast to the biotransformation of **1c** and **1d**, which leads exclusively to **1a** and **1b**,[13] chemical epoxidation proceeds with only low chemo- and stereoselectivity. Whereas epoxidation with *m*-chloroperbenzoic acid at −20 °C leads to the formation of **1a** and **1b** in at least 40 and 70 % yield,[14] respectively, new compounds **2a–c** dominate when the same reaction is carried out at room temperature. The HPLC studies of these new compounds attracted attention as they show a band at $\lambda_{max} = 236$ nm in the UV spectrum, which is uncharacteristic for epothilones. The main components **2a** and **2b** can also be obtained from the reaction of **1a** and **1b** with *m*-chloroperbenzoic acid, thus making them easily accessible in large amounts.



		R	X—X
epothilone A	**1a**	H	$\overset{O}{\triangle}$
epothilone B	**1b**	CH_3	$\overset{O}{\triangle}$
epothilone C	**1c**	H	$=$
epothilone D	**1d**	CH_3	$=$



	R	X—X
2a	H	$\overset{O}{\triangle}$
2b	CH_3	$\overset{O}{\triangle}$
2c	H	$=$



		R1	R2	R3
	4a	H	CH_3CO_2	H
	4b	CH_3	CH_3CO_2	H
	4c	H	Cl	H
	4d	H	H	Cl
	4e	H	H	TosO
epothilone E	**4f**	H	OH	H
epothilone F	**4g**	CH_3	OH	H

According to HPLC/ESI-MS and elemental analysis, **2a** contains one oxygen atom more than **1a** and differs only in the thiazol side chain, as can be seen in the respective ^1H and ^{13}C NMR spectra. As expected for a thiazol-*N*-oxide,[15] the signals for C-18, C-19, and C-20 are shifted towards higher field by $\Delta\delta = 9.8$ and 20. It could be confirmed by crystal structure analysis[16] that an *N*-oxide, and not an *S*-oxide, was actually formed (Figure 1).[17] The oxygen atom of the *N*-oxide is involved in strong hydrogen-bonding interactions to the OH group at C-3 (N−O 274 pm). Based on the structure of **1a**, this arrangement requires rotations around the C-1/C-2, C-2/C-3, and C-3/C-4 bonds by +148°, +31°, and −132°,[18] respectively, as well as minor changes in the torsion angles of the thiazol side chain. This conformation also exists in solution, as can be seen by the NOE effect between the axial 3-H atom and 17-H, as well as the chemical shift of the 3-OH proton at $\delta = 6.48$ (d, $J_{3\text{-H},3\text{-OH}} = 5.6$ Hz).

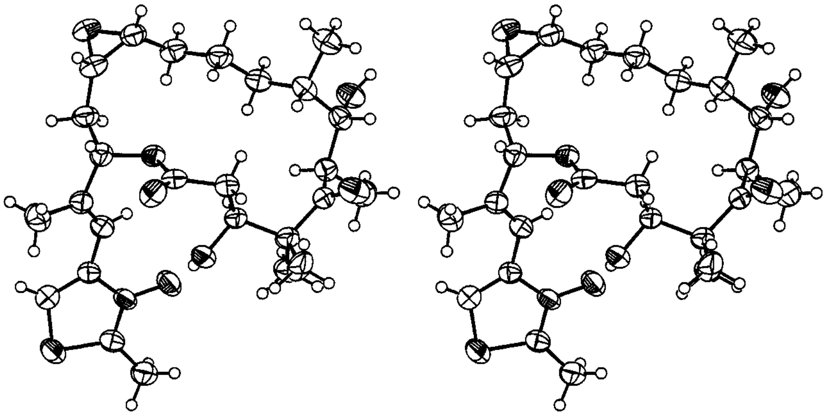
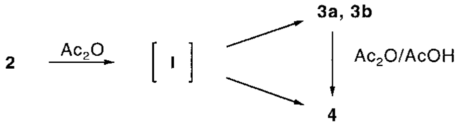


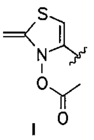
Figure 1. Stereo representation of the structure of **2a** in the crystal. The heteroaoatoms S, N, and O are indicated by shaded ellipsoids, and two methanol molecules are omitted for clarity.

In line with rearrangements reported for *α*-picoline and quinaldine *N*-oxide with carboxylic acid anhydrides,[20] we have investigated the behavior of the *N*-oxides **2** towards acetic anhydride. When an excess of acetic anhydride was used, a 1:1:2 mixture of **3a**, **3b**, and **4a** (^1H NMR) was obtained from **2a** within a few minutes at 75 °C. After 10–20 min this mixture converted completely into compound **4a** (Scheme 1). Depending on the timing of the workup, either all three compounds or only **4a** can be obtained by silica gel chromatography. The 21-acetoxythiazol structure of **4a** can be concluded from spectroscopic data (21-CH_2O: $\delta_H = 5.34$ and $\delta_C = 62.5$ (m)), and also from the observation that reaction with ammonia in methanol leads to epothilone E (**4f**).[11, 19]

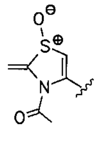


Scheme 1. Reaction of the thiazol-*N*-oxide **2** with acetic anhydride.

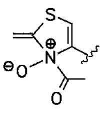
The MS and NMR spectra reveal that **3a** and **3b** are very similar isomers of **4a**. Given the specific rotation values of −185.1 and 119.6, **3a** and **3b** appear to be diastereomers that differ from **4a** only by the presence of a 20-*exo* methylene group (20-CH_2: $\delta_H = 5.2$ and 5.7, $\delta_C = 107$). This information leads to the proposed structures **I–III**. Structure **I**, an expected intermediate of the total reaction,[20] can certainly be excluded since **3a** and **3b** do not undergo a change in configuration when heated to 140 °C in toluene. Since structure **II**, which contains a cross-conjugated chromophore, is not compatible with the observed UV spectrum ($\lambda_{max} = 267$ and 315 nm), only the structure of an *N*-acetylammonium-*N*-oxide (**III**) remains as a feasible option. However, there appears to be no precedent for this type of structure.[21]



I



II



III

Important for preparative applications of this *N*-oxide rearrangement is that not only other carboxylic acid anhydrides but also activated carboxylic acid derivates such as acid chlorides can be used in the presence of 2,6-lutidine. In contrast to the case of anhydrides, the 19-chloro-, 21-chloro-, and 19-sulfonyloxy-epothilones **4c**, **4d**, and **4e** were obtained with *p*-tosyl chloride and mesyl chloride/1,4-lutidine (tosyl = $H_3CC_6H_4SO_2$; mesyl = H_3CSO_2) in dichloromethane.

Biological testing of the easily accessible thiazol derivatives of type **4** confirm earlier results,[11, 12] which suggest that structure modifications at C-21 but not at C-19 are tolerated (Table 1). The studies also reflect the trend towards higher activities of the epothilones of the B series as compared to those of the A series. For the *N*-oxides **2a** and **2b**, for instance, even a difference by a factor of 50 to 100 can be observed. Epothilone F (**4g**),[11] in vitro the most effective derivative after epothilone B, can be prepared with particular ease with the procedures presented herein starting from **1b**, which is obtained by fermentation. Furthermore, the route via the *N*-oxides **2** offers access to a variety of other derivatization and degradation reactions at C-21. It is furthermore noteworthy that the *N*-oxide rearrangement[22] which has hardly been used on thiazoles was employed for the first time on a complex natural product in the presence of sensitive functional groups.

Table 1. Comparison of in vitro activities of the epothilone derivatives **2a–c** and **4a–g** with those of paclitaxel and epothilone A–D (**1a–d**).

Compound	Cell line L929[a] IC_{50} [nM]	KB-3.1[b] IC_{50} [nM]	A-549[c] IC_{50} [nM][d]
paclitaxel (taxol)	80	12	4
epothilone A (**1a**)	8	2	1.4
epothilone B (**1b**)	1.4	1.2	0.2
epothilone C (**1c**)	100	40	60
epothilone D (**1d**)	20	24	20
2a	200	100	160
2b	4	2	1.5
2c	1400	200	600
4a	30	10	5
4c	400	130	20
4d	1100	600	1100
4e	1800	1500	1500
epothilone E (**4f**)	40	10	6
epothilone F (**4g**)	3	1.0	0.2

[a] Mouse fibroblasts (ATCC CCL 1). [B] Cervix carcinoma (human; DSM ACC 158). [C] Lung carcinoma (human; DSM ACC 107). [D] The growth was determined by the tetrazolium reduction test.

Experimental Section

General procedure for the preparation of the epothilone-*N*-oxides **2**: A solution of *m*-chloroperbenzoic acid (2 mmol) in dichloromethane (10 mL) was added to a stirred solution of **1** (1 mmol) in dichloromethane (0.5 mL). After 3 h the reaction was quenched with an aqueous Na_2SO_3 solution, and the resulting mixture distributed between an aqueous saturated $NaHCO_3$ solution and ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue (0.6–0.7 g) was separated by chromatography using RP-18 silica gel with acetonitrile/0.05 M ammonium acetate (pH 7.5, 35/65). Yield **2a**: 40%, **2b**: 48%, **2c**: 20%.

2a: Colorless crystals from methanol; m.p. 115 °C; TLC: $R_f = 0.15$ (silica gel Si60, dichloromethane/methanol (95/5), detection with vanillin/sulfuric acid, bluish gray stain upon heating to 120 °C); HPLC: $R_t = 2.2$ min (HD-Sil 100, C-18, 5 μm, 125 × 4-mm column, acetonitrile/water (40/60), 1.5 mL min^{-1}, detection at 254 nm); UV (MeOH): λ_{max} (ε) = 283 sh (1700), 264 sh (4700), 236 nm (17000); $[\alpha]_D^{21} = -114.0$ ($c = 0.9$ in methanol); IR (KBr): $\tilde{\nu} = 3430, 2966, 2933, 2879, 1741, 1688$ cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 2.16 (dd, J = 13.0, 2.6 Hz, 2-H_a), 2.46 (t, J = 12.0 Hz, 2-H_b), 4.54 (br d, J = 12.0 Hz, 3-H), 6.65 (d, J = 5.6 Hz, 3-OH), 3.22 (dq, J = 2.3, 5.0 Hz, 6-H), 3.72 (d, J = 5.0 Hz, 7-H), 1.26–1.86 (m, 8-H, 9-H_2, 10-H_2, 11-H_2), 2.91 (m, 12-H), 2.96 (m, 13-H), 1.66 (ddd, J = 15.2, 11.2, 9.7 Hz, 14-H_a), 2.23 (br d, J = 15.2 Hz, 14-H_b), 5.32 (d, J = 11.2 Hz, 15-H), 6.81 (br s, 17-H), 7.08 (s, 19-H), 2.59 (s, 21-H_3), 1.02 (s, 22-H_3), 1.43 (s, 23-H_3), 1.18 (d, J = 6.8 Hz, 24-H_3), 0.99 (d, J = 7.1 Hz, 25-H_3), 2.07 (s, 27-H_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.5 (C-1), 40.0 (C-2), 70.9 (C-3), 55.1 (C-4), 221.4 (C-5), 40.7 (C-6), 72.5 (C-7), 37.3 (C-8), 31.5 (C-9), 22.0 (C-10), 33.3 (C-11), 62.3(C-12), 63.0 (C-13), 33.4 (C-14), 75.6(C-15), 144.3 (C-16), 111.1 (C-17), 143.3 (C-18), 110.3 (C-19), 144.7 (C-20), 13.4 (C-21), 15.3 (C-22), 23.2 (C-23), 12.5 (C-24), 16.5 (C-25), 22.2 (C-26), 18.2 (C-27); HR-EI-MS (70 eV): m/z (%): 509.2483 (45, M^+), calcd ($C_{26}H_{39}NO_7S$): 509.2447; EI-MS (70 eV): m/z (%): 494 (4), 493 (4), 492 (4), 410 (48), 322 (50), 304 (18), 194 (15), 182 (52), 154 (100), 126 (44).

Preparation of **3a**, **3b**, and **4a**: a) Compound **2a** (102 mg, 0.2 mmol) was dissolved in acetic anhydride (2 mL) and heated at 75 °C for 5 min. The solution was subsequently concentrated at 30 °C/1 mbar to a viscous oil, which was separated on silica gel (Si60; hexanes/methyl *tert*-butyl ether/methanol, 66/33/1), during which first 65 mg (41%) of **4a**, then 17 mg (11%) each of **3a** and **3b** were eluted. b) Compound **2a** (102 mg, 0.2 mmol) was dissolved in acetic anhydride (1 mL) and heated at 75 °C for 5 min. Acetic acid (0.2 mL) was added, and the mixture was maintained at 75 °C for an additional 80 min. Workup and separation as in a) provided 81 mg (74%) **4a**.

3a: Colorless oil; TLC: $R_f = 0.66$ (for conditions see **2a**); UV (MeOH): λ_{max} (ε) = 203 (13800), 267 (13200), 315 nm (5000); $[\alpha]_D^{21} = -185.1$ ($c = 0.94$ in $CHCl_3$/MeOH 1:1); IR (KBr): $\tilde{\nu} = 3446, 2965, 2936, 2877, 1742, 1691$ cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 2.43 (dd, J = 14.8, 3.7 Hz, H 2_a), 2.53 (dd, J = 14.8, 10.2 Hz, H 2_b), 4.13 (m, 3-H), 3.33 (d, J = 6.4 Hz, 3-OH), 1.86 (dt, J = 15.0, 7.8 Hz, 14-H_a), 2.08 (m, 14-H_b), 5.39 (dd, J = 7.8, 2.2 Hz, 15-H), 6.23 (br s, 17-H), 6.95 (s, 19-H), 5.18 (s, 21-H_a), 5.71 (br s, 21-H_b), 2.26 (br s, 27-H_3), 2.12 (s, CH_3CO); ^{13}C NMR ($CDCl_3$): δ = 73.4 (C-3), 52.8 (C-4), 151.5 (C-16), 116.0 (C-17), 158.0 (C-18), 88.7 (C-19), 166.9 (C-20), 107.2 (C-21), 20.7 (C-22), 170.2, 21.2 (acetyl); positive-ion HPLC/ESI-MS (acetonitrile/0.02 M ammonium actate buffer (pH 7)): m/z: 569 $[M+NH_4^+]$. **3b**: Colorless oil; TLC: $R_f = 0.69$ (for conditions see **2a**); $[\alpha]_D^{21} = 119.6$ ($c = 1.1$ in $CHCl_3$/MeOH, 1/1); ^{1}H NMR ($CDCl_3$): 1.90 (m, 14-H_a), 2.09 (m, 14-H_b), 5.42 (dd, J = 7.8, 2.2 Hz, 15-H), 6.92 (s, 19-H), 2.23 (s, 27-H_3), 2.10 (s, CH_3CO); ^{13}C NMR ($CDCl_3$): 150.8 (C-16), 116.5 (C-17), 17.2 (C-27), 170.3, 21.0 (acetyl).

4a: Colorless oil; TLC: $R_f = 0.45$ (for conditions see **2a**); UV (MeOH): λ_{max} (ε) = 213 (15800), 246 (13500), 257 sh (9800) 275 sh (2900); $[\alpha]_D^{21} = -34.4$ ($c = 0.6$ in methanol); IR (KBr): $\tilde{\nu} = 3470, 2965, 2936, 2877, 1741, 1690$ cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 2.43 (dd, J = 14.7 Hz, 3.4, 2-H_a), 2.53 (dd, J = 14.7, 10.3 Hz, 2-H_b), 4.13 (m, 3-H), 3.26 (d, J = 6.6 Hz, 3-OH), 1.89 (dt, J = 15.1, 8.0 Hz, 14-H_a), 2.10 (ddd, J = 15.1, 4.6, 2.7 Hz, 14-H_b), 5.43 (dd, J = 8.0, 2.7 Hz, 15-H), 6.60 (br s, 17-H), 7.14 (s, 19-H), 5.34 (s, 21-H_2), 1.09 (s, 22-H_3), 1.35 (s, 23-H_3), 2.10 (s, 27-H_3), 2.14 (s, Acetyl); ^{13}C NMR ($CDCl_3$): δ = 38.8 (C-2), 73.5 (C-3), 52.7 (C-4), 43.6 (C-6), 74.8 (C-7), 137.8 (C-16), 119.6 (C-17), 152.5 (C-18), 118 (C-19), 167.7 (C-20), 62.5 (C-21), 20.7 (C-22), 21.3 (C-23), 14.3 (C-24), 15.5 (C-27), 170.2, 20.9 (acetyl); HR-EI-MS (70 eV): m/z (%): 551.2519 (26, M^+), calc ($C_{28}H_{41}NO_8S$): 551.2553; EI-MS (70 eV): m/z (%): 364 (65), 224 (100), 222 (56), 209 (35), 164 (36).

4g: a) Compound **4b** (40 mg, 70 µmol) was dissolved in methanol (1 mL), and a 25% ammonia solution (60 µL, 8 mmol) was added. After 3 min at 40 °C the solution was concentrated to dryness in vacuo, and the residue was separated by preparative HPLC using Nucleosil C-18 with acetonitrile/water (3/7). Yield 25 mg (68%). b) Compound **2b** (40 mg, 77 µmol) was dissolved in dichloromethane (1 mL), and 2,6-lutidine (80 µL, 690 µmol) and trifluoroacetic acid anhydride (80 µL, 570 µmol) were added with stirring. After heating at 75 °C for 10 min, the solution was concentrated to dryness in vacuo. The residue was treated with 25% ammonia (0.5 mL) in THF (2 mL) and heated at 45 °C for 10 min, then concentrated to dryness in vacuo and separated by chromatography as above. Yield 31 mg (78%) colorless oil; TLC: $R_f = 0.15$; HPLC: $R_t = 2.2$ min (for conditions see **2a**); UV (MeOH): λ_{max} (ε) = 212 (19000), 247 nm (13800); $[\alpha]_D^{21} = -27.4$ ($c = 0.5$ in methanol); IR (KBr): $\tilde{\nu} = 3437, 2959, 2930, 2874, 1735, 1690$ cm^{-1};

1433-7851/99/3813-1973 $ 17.50+.50/0

^1H NMR ($CDCl_3$): $\delta = 2.80$ (dd, $J = 7.4$, 5.0 Hz, 13-H), 4.92 (s, 21-H_2), 1.27 (s, 23-H_3), 1.35 (s, 26-H_3); ^{13}C NMR ($CDCl_3$): $\delta = 32.2$ (C-11), 61.3 (C-12), 61.5 (C-13), 170.0 (C-20), 62.2 (C-21).

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[17] An *S*-oxide proposed in a report of a total synthesis of epothilone A (K. C. Nicolaou, Y. He, D. Vourloumis, H. Vallberg, F. Roschanger, F. Sarabia, S. Ninkovic, Z. Yang, J. I. Frujillo, *J. Am. Chem. Soc.* **1997**, *119*, 7960–7973) was presumably the *N*-oxide **2a**.

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[21] Also without precedent is the isomeric structure of the *N*-acetyl-*S*-oxide **II**. For structural proof, the reaction is to be applied to model compounds to possibly obtain crystalline compounds of type **II** or **III**.

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Molecular Beside Ionic: Crystal Structures of a 1/1 and a 1/4 Adduct of Pyridine and Formic Acid[**]

Dirk Wiechert and Dietrich Mootz[*]

*Dedicated to Professor Heinz Dieter Lutz
on the occasion of his 65th birthday*

In the context of longstanding work in this laboratory on binary adducts composed of a neutral (uncharged) selected Brønsted base and acid, two such phases have recently been identified in the system pyridine/formic acid and their crystal structures determined. With rare reported precedence in analogous systems, one is molecular and the other ionic. Phase analysis of the system has been done by differential thermal analysis (DTA) and differential scanning calorimetry (DSC) as well as temperature-dependent X-ray powder diffraction. The adducts have stoichiometries $C_5H_5N \cdot HCOOH$ and $C_5H_5N \cdot 4\,HCOOH$ and melt at 219 and 233 K, respectively. The structures have been determined at 173 and 183 K.[1]

The results are visualized in Figure 1. In the 1/1 compound, a neutral molecule of the base and one of the acid form an $O{-}H \cdots N$ hydrogen-bonded heterodimer. The 1/4 compound is a pyridinium salt, $[C_5H_5NH][HCOO(HCOOH)_3]$. In the complex anion, reported here in a crystal for the first time, a central formate ion is coordinated, through rather strong $O{-}H \cdots O$ hydrogen bonds, by the three extra molecules of the acid. In these, the conformation of the carboxylic group is twice synplanar and once antiplanar. A hydrogen bond

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