than values we have observed in related Ir(III) derivatives.[13] The structure reported here for compound **4** closely resembles that suggested[7] for the rhodium–tin complex **1** on the basis of spectroscopic data.

It may be speculated that "anchoring" of the silyl group to Ir(III) in **3** results in reductive loss of H_2 or CH_4 (rather than a SiR_3-bound fragment) in a rate-determining step to give an extremely reactive square Ir(I) intermediate which is subsequently trapped as its CO adduct. Surprisingly, the same adduct is formed in photolysis experiments conducted in benzene or hexane in the absence of added CO, implicating compound **3** in an intermolecular CO transfer. We are continuing to examine potential routes to coordinatively unsaturated species where the electron-releasing character[1,14] of anchored silyl ligands may lead to novel reactivity.

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Supplementary Material Available: Fractional atomic coordinates and temperature parameters, anisotropic temperature parameters, and tables of bond distances and angles for compound **4** (4 pages). Ordering information is given on any current masthead page.

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Ammonolysis of Cephamycins: ^{13}C NMR Characterization of the Intermediates from β-Lactam Ring Cleavage Prior to Loss of the 3′-Group

E. J. J. Grabowski,* A. W. Douglas, and G. B. Smith

Merck Sharp & Dohme Research Laboratories
Merck & Co., Inc., Rahway, New Jersey 07065

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Recently Faraci and Pratt[1] provided the first evidence that loss of the 3′-group of a cephalosporin need not occur in concert with β-lactam opening. Such was accomplished via stopped-flow experiments on the reaction of TEM-2 β-lactamase with the cephalosporins PADAC and cephaloridine. We wish to report studies on the ammonolysis of cefoxitin and cephamycin C in which, for the first time, we have spectroscopically characterized the intermediates resulting from β-lactam cleavage prior to loss of the carbamic acid anion from position 3′. This was accomplished by examining the ammonolysis in liquid ammonia at −50 °C, using carbon-13 NMR spectroscopy.[2,3]

Experimental Section. Approximately 35–40% w/v solutions of cefoxitin[4] and cephamycin C[5] in anhydrous ammonia were prepared at −60 to −70 °C. These were placed in the spectrometer and warmed to −47 to −50 °C for the reaction studies. Carbon-13 NMR spectra were obtained at 25.16 MHz, using a Varian XL-100 spectrometer operated in the Fourier transform mode.

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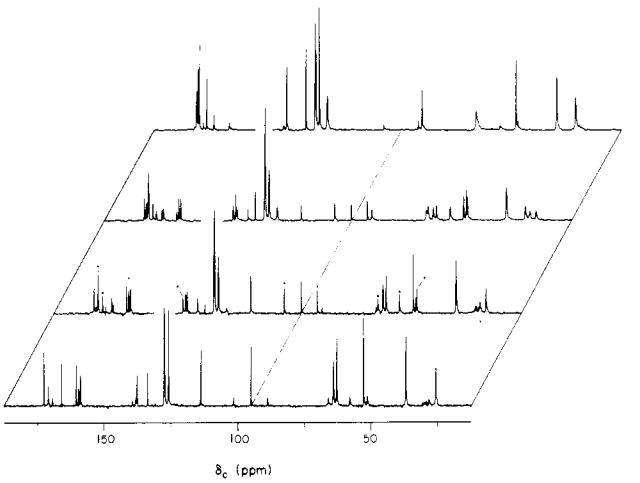
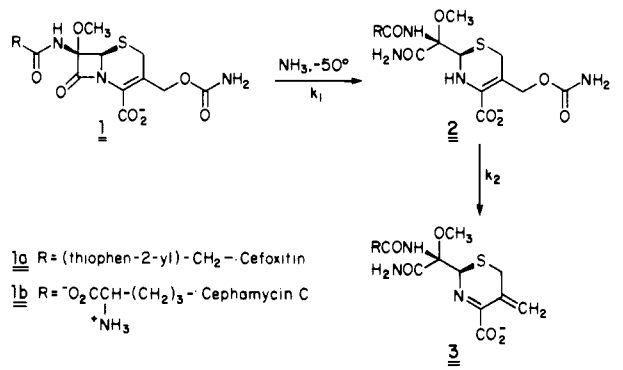


Figure 1. Elapsed reaction time plot for cefoxitin in liquid ammonia at approximately −50 °C. Reaction times are 11, 23.5, 45.5, and 185 min, respectively, from bottom to top. The accumulation interval is 10 min in each case, and absolute intensity presentations are shown at constant scale factor. Key carbon atoms in **2a** are starred; diagonals of constant chemical shift are shown.

Reaction solutions were observed in 10-mm tubes placed inside 12-mm tubes with annular CD_3COCD_3 lock. Spectral widths, acquisition times (and exponential smoothing parameters), and pulse nutation angles were 10 kHz, 0.4 s, and 23°, respectively.

Results and Discussion. The ammonolyses of **1a** and **1b** were straightforward. Initially both compounds undergo β-lactam cleavage to intermediates **2a** and **2b** in accord with the reaction path proposed by Faraci and Pratt.[1] Both **2a** and **2b** retain their carbamate groups and have lifetimes sufficient for carbon-13 spectral characterization. Subsequent reactions yield **3a** and **3b**,



which are stable to the ammonolysis conditions, and readily characterized by carbon-13 spectroscopy. This is the first time that intermediates such as **2a** and **2b** have been observed, thus establishing the formation of **3a** and **3b** via two-step processes.

Identification of **2a** is based on the carbon-13 data presented in Figure 1. In the bottom trace the strongest signals are those of **1a**. The same signals persist in the center traces with decreasing intensities. They are virtually absent in the top trace, which is essentially the spectrum of **3a** and the anion of carbamic acid at δ_c 168.4. Comparison of the traces reveals an additional set of signals ascribed to **2a** (Table I). Off-resonance proton decoupling supported all assignments listed in Table I. Examination of traces corresponding to other reaction times establishes the gradual increase and subsequent decrease of the signals, as a group, ascribed to **2a**. Key carbon-13 shift effects identifying **2a** are the increased shielding of C_3 by 12.6 ppm, now conjugated to an amine rather than an amide nitrogen, and large changes in shielding of C_4, C_6, C_7, and C_8, the latter having been converted to a primary amide carbonyl. Conversion to **3a** produces some 30 ppm deshielding of C_3 and C_4 with smaller but significant effects at C_6 and the 4-carboxylate. The exo-methylene carbon becomes olefinic and appears downfield. Analogous spectral changes occur when

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Table I. ^{13}C Chemical Shifts of Cefoxitin (**1a**) and Its Ammonolysis Products

carbon atom	1a	2a[a]	3a[a]
C_2	26.05	28.39	30.04
C_3	114.30	101.74	131.33
C_4	134.05	139.60	172.09
C_6	63.42	58.36	67.21
C_7	95.43	89.38	87.73
C_8	160.72	171.32	171.50
3-CH_2	64.59	66.63	123.25
carbamate	159.16	159.93	168.39
4-CO_2^-	166.26	169.67	165.66
OCH_3	53.30	51.84	52.33
7-NHCOR	172.88	171.32	171.13
thienyl CH_2	37.24	37.24	37.05
thienyl C_2	138.04	138.62	138.62
thienyl C_3 / thienyl C_4	127.74, 127.91	not observed	127.55, 127.83
thienyl C_5	126.27	126.09	126.27

[a] Numbering for **2a** and **3a** follows that of cefoxitin.

Table II. ^{13}C Chemical Shifts of Cephamycin C (**1b**) and Its Ammonolysis Products

carbon atom	1b	2b[a]	3b[a]
C_2	~26.0		~30.0
C_3	113.90	101.43	131.31
C_4	134.04	139.64	172.37
C_6	63.31	58.34	67.29
C_7	95.30	88.88	87.34
C_8	160.90	171.31	171.49
3-CH_2	64.66	66.52	123.23
carbamate	159.13	159.82	168.37
4-CO_2^-	166.32	169.75	165.76
OCH_3	53.19	51.63	52.30
7-NHCOR	176.64	174.81	174.81
C_δ	36.2	36.2	36.2
C_γ	23.22	23.22	23.22
C_β	36.2	36.2	36.2
C_α	56.88	56.88	56.88
CO_2^-	181.51	181.51	181.51

[a] Numbering for **2b** and **3b** follows that of cephamycin C.

cephamycin C (**1b**) is treated similarly (Table II).

Analysis of the carbon-13 intensities of the methoxyl groups of species **1–3** affords approximate rates of β-lactam opening and side-chain expulsion. Although proton-decoupled carbon-13 FTNMR spectra may exhibit systematic departures from quantitative accuracy due to differences in relaxation rates and Overhauser enhancements,[3] use of the methoxyl signals as measures of relative concentrations minimizes such factors.

Intensity data for each cephamycin were analyzed by standard kinetics techniques[6] and were found consistent with a reaction having two consecutive, first-order steps. The following rate constant values were calculated: $k_{1a} = 0.000\,36 \pm 0.000\,04\ s^{-1}$, $k_{1b} = 0.000\,18 \pm 0.000\,02\ s^{-1}$, and $k_{2a} = k_{2b} = k_{1a}$. A weak effect of the 7-acyl group on the rate of β-lactam cleavage was noted in that k_{1a} was twice k_{1b}.

In summary, we have characterized the intermediates of cephamycin ammonolysis and confirmed that such can occur via a two-step process. Although anhydrous ammonia is unlike physiological media, it does represent solvolysis in a dipolar, protic medium in which all species can be observed. This provides a unique means for gaining insight into β-lactam chemistry not possible or recognized previously.[7,8]

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On the Antarafacial Stereochemistry of the Thermal [1,7]-Sigmatropic Hydrogen Shift

Carl A. Hoeger and William H. Okamura*

Department of Chemistry, University of California Riverside, California 92521

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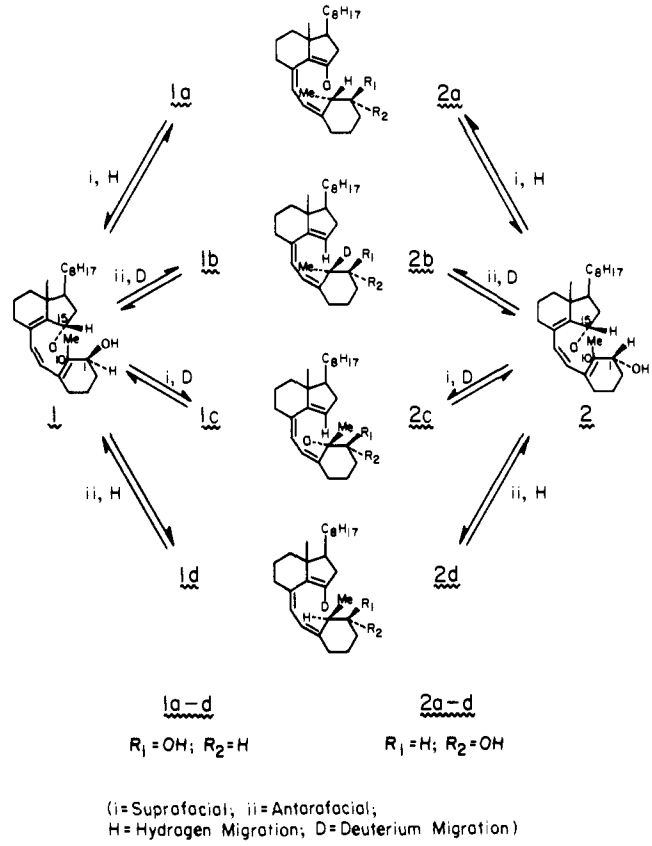
The classical thermal [1,7]-sigmatropic hydrogen migration[1] is considered to be a pivotal event in the metabolic production of vitamin D.[2] Although the intramolecular nature of this thermal process has been established,[3,4] and the stereochemistry of the corresponding [1,5] migration has been demonstrated to be suprafacial,[1,5] no direct evidence has yet been obtained for the antarafacial nature of the [1,7] process.[1] Our interest in the chemistry of vitamin D prompted us to prepare the labeled *cis*-isotachysterols **1** and **2** and to study their thermal behavior.[6] We herein wish to report the first example of the antarafacial nature of this rearrangement (Scheme I).

The labeled *cis*-isotachysterols **1** and **2** were synthesized as outlined in Scheme II (steroid numbering). Treatment of Grundmann's ketone **3**[6b] with trimethylsilyl iodide (generated in

Scheme I



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