the high-temperature region, although the location of the emission maximum does not vary. The fluorescence intensities in water and in the CTAC micelle are much smaller and decrease gradually with temperature (20–35 °C); in the CTAC micelle I_F at 20 °C is ca. 2 times larger than that at 35 °C. The crystal-to-liquid crystal phase transition occurs at 31 °C (transition range 27–36 °C) for the aqueous bilayer of **1** (n = 4).[10] Therefore, the drastic spectral changes of Figure 1 are related to the phase transition of the membrane matrix. The I_F value is affected by the phase transition also when the cyanine dye is bound to the bilayer membrane of the simpler dialkylammonium salt **2** (transition temperature (T_c) 28 °C); however, the intensity enhancement is much smaller, I_F at 27 °C being only 20% larger than that at 30 °C.

On the other hand, the fluorescence spectrum of cyanine dye **4** is strongly influenced by the phase transition of both of bilayers **1** and **2**. The I_F value of dye **4** in the bilayer matrix of **1** (n = 4) drastically changes at T_c (I_F at 27 °C is 5 times larger than that at 30 °C), and I_F in the rigid membrane is 23 and 100 times larger than those in the CTAC micelle and in water, respectively. A similar, though less drastic, spectral change of dye **4** is observed at T_c in the bilayer matrix of **2**.

The fluorescence quantum yields (Φ_F) of dye **3**[15] in various media are summarized in Table I. The Φ_F is enhanced by more than 10 times in the CTAC micelle (0.035 at 20 °C) than in water; this increment coincides with that observed by Grätzel et al. for a cationic cyanine dye in the anionic micelle of sodium lauryl sulfate.[17] A much greater Φ_F enhancement is observed for the dye bound to the rigid (below T_c, 20 °C) bilayer membrane of **1** (n = 4, X = Cl). This value (0.64) is 20 times larger than that in the CTAC micelle and 250 times larger than those in water or in methanol. The enhancement is much reduced in the fluid membrane matrix, although Φ_F is still larger than that in the CTAC micelle.

The chemical structure of the membrane surface exerts significant influences on Φ_F. The Φ_F value of the membrane of **1**, n = 6 and 10, is close to that of **1**, n = 4, whereas that for **1**, n = 2, is reduced (0.40). The small difference in the spacer length can be crucial for obtaining high Φ_F values. The Φ_F value obtained in the matrix of the simple dialkylammonium bilayer of **2** is only 2 times larger than that in the CTAC micelle. It is clear that large fluorescence enhancement is rendered possible by dye binding to specific membrane surfaces.

The degree of fluorescence polarization (P)[18] is used as a measure of the rotational motion of the excited state. The P value (Table I) is relatively large even in water, and consequently, the increment in the membrane matrix is small. In general, Φ_F of cyanine dyes is enhanced by the prevention of internal conversion due to suppression of twisting of the polymethine chain, as confirmed by fluorescence measurements of rigidized dyes.[20,21] Our preliminary experiments indicate that the fluorescence lifetime (τ_F) of **3** is lengthened to approximately the same extent in bilayer membranes (**1** and **2**), CTAC micelle, and glycerol. The Φ_F value is still different among these media, and therefore, the Φ_F enhancement cannot be explained by the τ_F term alone. We reported recently that absorption spectra of methyl orange and cyanine dyes were extensively modified in the bilayer matrix, and discussed the results in terms of specific orientation and association of the dye molecules at the membrane surface.[11,14] The absorption spectrum of **3** changes also specifically with the physical state (Figure 1) or chemical structure[22] of the matrix membrane. This indicates that the ground-state electronic configuration is perturbed by the specific interaction and that the Φ_F variation may not be attributed solely to the excited-state characteristics. It is well-known that the fluorescence property changes drastically by dye aggregation.

We have observed similar fluorescence enhancements for other anionic cyanine dyes. In addition, cationic cyanine dyes show enhanced fluorescence in the presence of the anionic bilayer membrane.[23] Therefore, the fluorescence enhancement in the rigid bilayer matrix appears to be a widely observable phenomenon. Recent data by Whitten and co-workers for a stilbene surfactant point to the same conclusion.[24] We are currently examining the effect of the bilayer matrix on the fluorescence property of a large variety of cyanine and merocyanine dyes. These studies would provide unique means to control the flow of the excitation energy of cyanine and related dyes at the membrane surface. Practical applications of this technique in various fields can be readily envisaged.

Acknowledgment. We thank H. Fukushima for his capable experimental assistance and Dr. K. Kano for the lifetime measurement.

Registry No. 1 (n = 2; X = Br), 82135-66-8; **1** (n = 4; X = Cl), 82135-67-9; **1** (n = 6; X = Br), 82135-68-0; **1** (n = 10; X = Br), 82135-69-1; **2**, 70755-47-4; **3**, 82135-70-4; **4**, 82135-71-5; CTAC, 112-02-7; water, 7732-18-5; methanol, 67-56-1; glycerol, 56-81-5.

(15) The quantum yield of Rhodamine B (recyrstallized twice from ethanol; absorption spectrum, λ_{max} 542 nm; fluorescence spectrum (corrected), λ_{max} 570 nm) in ethanol at 20 °C is assumed to be 0.5[16] and is used as reference.

(16) Karsten, T.; Kobs, K. *J. Phys. Chem.* **1980**, *84*, 1871–1872.

(17) Humphry-Baker, R.; Grätzel, M.; Steiger, R. *J. Am. Chem. Soc.* **1980**, *102*, 847–848.

(18)

$$P = \frac{I_{\parallel\parallel} - I_{\parallel\perp}(I_{\perp\parallel}/I_{\perp\perp})}{I_{\parallel\parallel} + I_{\parallel\perp}(I_{\perp\parallel}/I_{\perp\perp})}$$

where $I_{\parallel\parallel}$ and $I_{\perp\perp}$ are emission intensities measured with parallel polarizers (veritical and horizontal) and $I_{\parallel\perp}$ and $I_{\perp\parallel}$ are those measured with crossed polarizers.[19]

(19) Kano, K.; Fendler, J. H. *Chem. Phys. Lipids* **1977**, *23*, 189–200.

(20) Tredwell, C. J.; Keary, C. M. *J. Chem. Phys.* **1979**, *43*, 307–316.

(21) O'Brien, D. F.; Kelly, T. M.; Costa, L.-F. *Photogr. Sci. Eng.* **1974**, *18*, 76–83.

(22) λ_{max} (ϵ_{max}) of absorption spectra of dye **3** at 20 °C are as follows: 562 nm (240 000) in **1**, n = 2; 565 nm (240 000) in **1**, n = 4; 566 nm (264 000) in **1**, n = 6; 569 nm (310 000) in **1**, n = 10; 563 nm (130 000) in **2**; 563 nm (148 000) in CTAC; 540 nm (124 000) in methanol; 540 nm (110 000) in H_2O; 545 nm (140 000) in glycerol.

(23) Nakashima, N., unpublished results in these laboratories.

(24) Russell, J. C.; Costa, S. B.; Seiders, R. P.; Whitten, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 5678–5679.

Photochemical Transformation of Cephalosporins into Carbapenems

Robert L. Rosati,* Leilani V. Kapili, and Peter Morrissey

Pfizer Central Research, Groton, Connecticut 06340

Jon Bordner* and E. Subramanian

North Carolina State University
Raleigh, North Carolina 27650

Received December 21, 1981

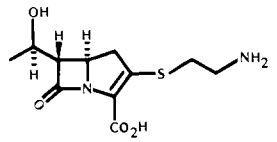
Thienamycin **1** is the first reported member of a series of recently discovered antibiotics possessing the novel carbapen-2-em ring system.[1,2] Its remarkable antibacterial activity[3] has prompted

(1) Albers-Schönberg, G.; Arison, B. H.; Hensens, O. D.; Hirshfield, J.; Hoogsteen, K.; Kaczka, E. A.; Rhodes, R. E.; Kahan, J. S.; Kahan, F. M.; Ratcliffe, R. W.; Walton, E.; Ruswinkle, L. J.; Morin, R. B.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 6491.

(2) Since the discovery of thienamycin, additional antibiotics possessing the carbapen-2-em ring system have been discovered: (a) Cassidy, P. J.; Stapley, E. O.; Geogelman, R.; Miller, T. W.; Arison, B.; Albers-Schönberg, G.; Zimmerman, S. B.; Birnbaum, J. Abstract 81, 17th Interscience Conference Antimicr. Agents and Chemother.; New York, 1977. (b) Brown, A. G.; Corbett, D. F.; Eglington, A. J.; Howarth, T. T. *J. Chem. Soc., Chem. Commun.* **1977**, 523. (c) Corbett, D. F.; Eglington, A. J.; Howarth, T. T. *Ibid.* **1977**, 953. (d) Okamura, K.; Hirata, S.; Okumura, Y.; Fukagawa, Y.; Shimauchi, Y.; Kouno, K.; Ishikura, T.; Lein, J. *J. Antibiot.* **1978**, *31*, 480. (e) Brown, A. G.; Corbett, D. F.; Eglington, A. J.; Howarth, T. T. *J. Antibiot.* **1979**, *32*, 961. (f) Nakayama, M.; Iwasaki, A.; Kimura, S.; Mizoguchi, T.; Tanabe, S.; Murakami, A.; Okuchi, M.; Itoh, H.; Saino, Y.; Kobayashi, F.; Mori, T. *J. Antibiot.* **1980**, *33*, 1388. (g) Shibamoto, N.; Koki, A.; Nishino, M.; Nakamura, K.; Kiyohima, K.; Okamura, K.; Okabe, M.; Okamoto, R.; Fukagawa, Y.; Shimauchi, Y.; Ihikura, T. *J. Antibiot.* **1980**, *33*, 1128. (h) Tsuji, N.; Kondo, E.; Mayama, M.; Kawamura, Y.; Hattori, T.; Matsumoto, K.; Yoshido, T. *J. Antibiot.* **1981**, *34*, 909.

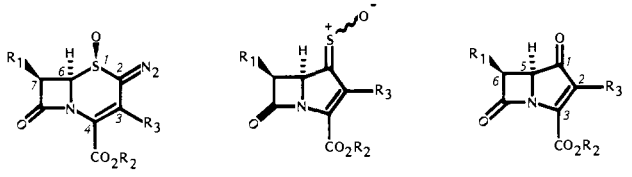
0002-7863/82/1504-4262$01.25/0

considerable synthetic interest; the total synthesis of **1** has been reported,[4] as have the syntheses of simpler analogues.[5]



1

We now report the unprecedented conversion of cephalosporinates to structures having the carbapenem skeleton. It occcurred to us that a direct and economical entry into this ring system might be achieved through a photolytic rearrangement of readily available[6] 2-diazoceph 3-em 1-oxides **2** to sulfines **3**. On the basis



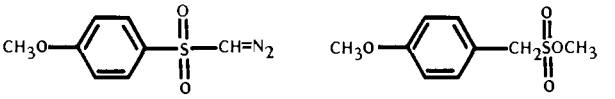
2 3 4

a, R_1=H, R_2=$CH(C_6H_5)_2$, R_3=CH_3
b, R_1=H, R_2=$CH_2OCOC(CH_3)_3$, R_3=CH_3
c, R_1=$C_6H_5OCH_2CONH$, R_2=$CH(C_6H_5)_2$, R_3=CH_3

of the chemistry of less complex sulfines,[7] we projected that initially formed **3** on further photolysis could be induced to extrude sulfur to afford carbapen-2-ems **4**.

The formation of sulfines **3** would be mechanistically analogous to the formation of ketenes during the Wolff rearrangement[8] of α-diazo ketones. Although there were no reports in the literature of such a rearrangement with α-diazo sulfoxides, there was a report on the photolysis in methanol of α-diazo sulfone **5**, which was shown to afford sulfonate **6** in low yield.[9]

When a dilute solution of diazo cephalosporinate **2a**[6b] in methylene chloride at −55 °C was photolyzed in a Pyrex vessel

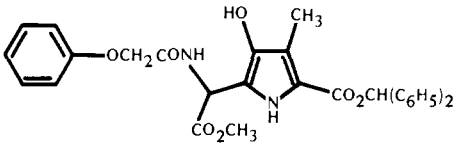


5 6

with a commercial 275-W sun lamp (0.5–1.0 h, rapid stream of nitrogen), a new substance was formed along with elemental sulfur. This new substance exhibited not only limited solution stability but also extreme instability on silica gel, which precluded chromatographic isolation. Nevertheless by working quickly, we were able to obtain good spectral data on the crude photoproduct which led to the assignment of its structure as **4a**: IR (CH_2Cl_2) 1810 (β-lactam), 1715 cm^{-1} (ketone, ester); ^1H NMR ($CDCl_3$) δ 2.05 (s, 3 H), 2.70–3.80 (m, 2 H), 4.05 (dd, 1 H, J = 5, 8 Hz), 7.00 (s, 1 H), 7.40 (s, 10 H); UV (CH_2Cl_2) λ_{max} 309 nm. The ^{13}C NMR of **4a** possessed signals for the carbonyl carbons at 159.9, 171.9, and 203.2 ppm; the signal at 203.2 ppm is assigned the ketone carbonyl. Disappointingly, the mass spectrum of **4a** exhibited fragmentation ions only; however, close analogue **4b** (derived by photolysis of **2b**[6c]) did in fact possess a molecular ion (high-resolution confirmation for $C_{14}H_{17}NO_6$). The surprising, direct isolation of enone **4a** implied that the presumed intermediate sulfine **3a** was unstable to the photolysis conditions and spontaneously extruded sulfur.[10]

The assignment of the absolute configuration of **4a** (as drawn) was based on an NMR analysis of related enone **4c** (produced by the photolysis of diazocephalosporinate **2c**[6c]). Since the chiral center at C-7 of **2c** is unlikely to change during photorearrangement, an inspection of the coupling constant between the protons at C-5 and C-6 in product **4c** should permit assignment of the configuration of the migrating carbon center. The observed 8-Hz coupling constant for **4c** reveals[11] a cis relationship between the protons at C-5 and C-6 and thus suggests that the photorearrangement proceeded in a stereospecific sense with retention of configuration. Retention[12] translates to the natural[1] configuration at C-5 in **4c** and by analogy to the natural configuration in **4a** also.

For further confirmation of structure **4**, a sample of freshly prepared **4c** was treated with methanol at 25 °C for 2 h to afford a non-β-lactam-containing substance (as a foam) after silica gel chromatography (53% yield from **2c**): IR (CH_2Cl_2) 1740, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.30 (s, 3 H), 3.65 (s, 3 H), 4.40 (s, 2 H), 5.70 (d, 1 H, J = 7 Hz), 6.60–7.40 (m, 15 H), 7.90 (d, 1 H, J = 7 Hz); UV (CH_2Cl_2) λ_{max} 286 nm; MS, M^+ ($C_{30}H_{28}N_2O_7$). These data are consistent with pyrrole structure **7**, presumably formed by ring opening of the β-lactam moiety of **4c** by methanol, followed by tautomerization of the ketone function.



7

(3) Kropp, H.; Kahan, J. S.; Kahan, F. M.; Sundelof, J.; Darland, G.; Birnbaum, J. Abstract 228, 16th Interscience Conference Antimicr. Agents and Chemother.; Chicago, 1976.

(4) (a) Johnston, D. B. R.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313. (b) Schmitt, S. M.; Johnston, D. B. R.; Christensen, B. G. *J. Org. Chem.* **1980**, *45*, 1142. (c) Melillo, D. G.; Shinkai, I.; Liu, T.; Ryan, K.; Sletzinger, M. *Tetrahedron Lett.* **1980**, 2783. (d) Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bouffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161.

(5) (a) Cama, L. D.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 8006. (b) Baxter, A. J. G.; Dickinson, K. H.; Roberts, P. M.; Smale, T. C.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1979**, 236. (c) Onoue, H.; Narisada, M.; Uyeo, S.; Matsumura, H.; Okada, K.; Yano, T.; Nagata, W. *Tetrahedron Lett.* **1979**, 3867. (d) Ponsford, R. J.; Roberts, P. M.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1979**, 847. (e) Ratcliffe, R. W.; Salzmann, T. N.; Christensen, B. G. *Tetrahedron Lett.* **1980**, 31. (f) Kametani, T.; Huang, S.; Yokohama, S.; Suzuki, Y.; Ihara, M. *J. Am. Chem. Soc.* **1980**, *102*, 2060. (g) Schmitt, S. M.; Johnston, D. B. R.; Christensen, B. G. *J. Org. Chem.* **1980**, *45*, 1135. (h) Cama, L.; Christensen, B. G. *Tetrahedron Lett.* **1980**, 2013. (i) Baxter, A. J. G.; Ponsford, R. J.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1980**, 429. (j) Shibuya, M.; Kubota, S. *Tetrahedron Lett.* **1980**, 4009. (k) Bateson, J. H.; Hickling, R. I.; Roberts, P. M.; Smale, T. C.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1980**, 1084. (l) Ponsford, R. J.; Southgate, R. *Ibid.* **1980**, 1085. (m) Baxter, A. J. G.; Davis, P.; Ponsford, R. J.; Southgate, R. *Tetrahedron Lett.* **1980**, 5071. (n) Foxton, M. W.; Mearman, R. C.; Newall, C. E.; Ward, P. *Ibid.* **1981**, 2497.

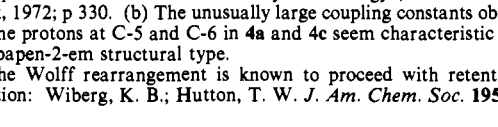
(6) (a) Bremner, D. H.; Campbell, M. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2298. (b) Ebbinghaus, C. F.; Morrissey, P.; Rosati, R. L. *J. Org. Chem.* **1979**, *44*, 4697. The procedure published in this reference describes the use of picryl azide/diisopropylethylamine for diazo transfer. The authors have since discovered that picryl azide/diisopropylethylamine/potassium *tert*-butoxide affords far shorter reaction times (unpublished results). (c) Prepared by the general method described in ref 6b.

(7) Sulfines are known to extrude sulfur on photolysis to afford the corresponding carbonyl compound: (a) Strating, J.; Thijs, L.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1964**, *83*, 631. (b) Zwanenburg, B.; Strating, J. *Q. Rep. Sulfur Chem.* **1970**, *5*, 79.

(8) Meier, H.; Zeller, K. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.

(9) Mulder, R. J.; van Leusen, A. M.; Strating, J. *Tetrahedron Lett.* **1967**, 3057. The authors proposed a Wolff-like mechanism.

(10) After this work was completed, a report appeared on the photorearrangement of sulfinyl pyrazolenines to enones; the authors proposed a Wolff-like mechanism involving the intermediacy of a sulfine. Franck-Neumann, M.; Lohmann, J. J. *Tetrahedron Lett.* **1979**, 2397.



(11) (a) In β-lactam ring systems, cis coupling constants (4–5 Hz) are larger than trans coupling constants (1.5–2 Hz): Flynn, E. H., Ed. "Cephalosporins and Pencillins: Chemistry and Biology"; Academic Press: New York, 1972; p 330. (b) The unusually large coupling constants observed between the protons at C-5 and C-6 in **4a** and **4c** seem characteristic of the 1-oxo-carbapen-2-em structural type.

(12) The Wolff rearrangement is known to proceed with retention of configuration: Wiberg, K. B.; Hutton, T. W. *J. Am. Chem. Soc.* **1956**, *78*, 1640.

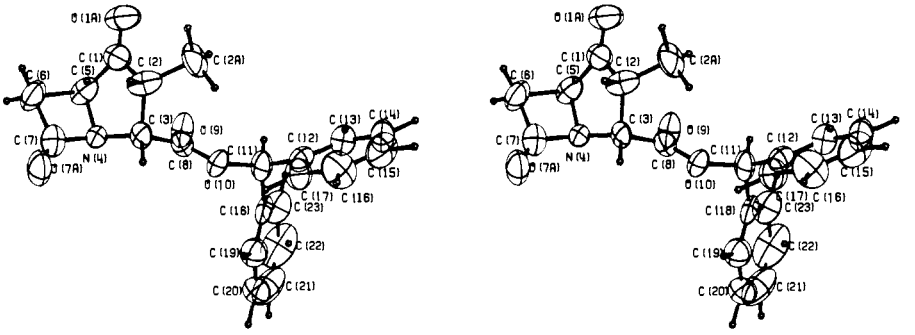
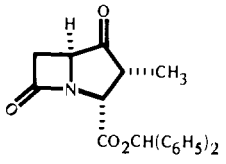


Figure 1. Stereoview of **8** and its numbering system.

A stable β-lactam-containing derivative was needed to provide additional proof for structure **4**. To that end, the crude photoreaction mixture containing **4a** was subjected to a dissolving metal reduction employing zinc[13]/acetic acid/tetrahydrofuran at 0 °C for 1 h. After filtration and evaporation, the result was a mixture consisting of elemental sulfur and a new β-lactam. Although this new substance proved to be unstable on silica gel chromatography, fortunately a pure sample could be obtained by crystallization of the crude reaction mixture using methylene chloride/hexane (mp 132–133 °C); spectral data were consistent with 1-oxocarbapenam structure **8**: IR (CH_2Cl_2) 1785, 1750 cm^{-1}; ^1H NMR ($CDCl_3$)



8

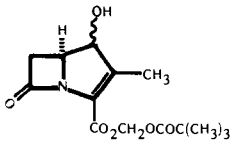
0.90 (d, 3 H, J = 7 Hz), 2.60–3.80 (m, 3 H), 3.90 (dd, 1 H, J = 3, 6 Hz), 5.00 (d, 1 H, J = 9 Hz), 6.90 (s, 1 H), 7.30 (s, 10 H); $[\alpha]^{22}_D$ −27° (CH_2Cl_2); MS, M^+ ($C_{21}H_{19}NO_4$). The ^{13}C NMR possessed signals for the carbonyl carbon atoms at 167.2, 175.4, and 212.0 ppm. Subsequent investigations revealed that **8** could be isolated from the crude reaction mixture by chromatography on Sephadex LH-20 (35% yield from **2a**).

The overall structure and relative stereochemistry of carbapenam **8** was unequivocally determined in a routine single-crystal X-ray diffraction study. Crystals of this compound belonged to the monoclinic space group $P2_1$ with a = 8.275 (2) Å, b = 5.796 (1) Å, c = 19.409 (5) Å, β = 102.36 (2)°, and Z = 2. A 1-Å data set (maximum $\sin\theta/\lambda$ = 0.5) was collected on a Syntex $P\bar{1}$ diffractometer using copper radiation (λ = 1.5418 Å) at room temperature.

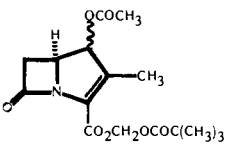
All crystallographic calculations were facilitated by the CRYM crystallographic computer system.[14] A trial structure was obtained with the aid of the Multan program.[15] This trial structure routinely refined to a final R index of 0.065 ($R = \sum||F_o| - |F_c||/\sum|F_o|$). The final cycles of full-matrix least-squares refinement contained the scale factor, secondary extinction coefficient, non-hydrogen coordinates, and anisotropic temperature factors in a single matrix. While the hydrogens were located and added to the structure factor calculations during the later stages of refinement, their parameters were not refined. A final difference Fourier revealed no missing or misplaced electron density. A stereoview of the molecule is given in Figure 1. Other pertinent crystallographic data appears as supplementary material.

Assignment of the absolute configuration of **8** (as drawn) rests on the assignment given precursor enone **4a**, with the reasonable assumption that the configuration at C-5 in **4a** did not change in the course of zinc reduction.

Since (as was mentioned previously) oxocarbapenems **4** are unstable substances, an important goal for us has been the utilization of such materials as intermediates for the preparation of carbapenems of increased stability. To that end the reduction of the 1-oxo moiety of **4** was investigated. Treatment of **4b** with tetrabutylammonium borohydride (methylene chloride, −78 °C) for 1 h followed by sequential treatment with acetic acid and pH 7.0 buffer afforded clean conversion to a new substance presumed to be allylic alcohol **9**.[16] This substance was too unstable to fully



9



10

characterize but fortunately could be converted (acetic anhydride, 4-(dimethylamino)pyridine, −78 °C) to the stable acetate **10**, which was isolated as a foam after silica gel chromatography (21% overall yield from **2b**): IR (CH_2Cl_2) 1785, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) 1.20 (s, 9 H), 2.10 (d, 3 H, J = 1 Hz), 2.15 (s, 3 H), 3.00–3.50 (m, 2 H), 3.80 (m, 1 H), 5.70 (br d, 1 H, J = 7 Hz), 5.85 and 5.95 (AB q, 2 H, J = 5 Hz); UV (CH_2Cl_2) λ_{max} 275 nm; MS, M^+ ($C_{16}H_{21}NO_7$).

In summary, a facile synthesis of 1-oxo-carbapen-2-ems from readily available cephalosporinates has been discovered; furthermore, these carbapen-2-ems, which are selectively reducible, providing entry into novel carbapenam and 1-hydroxycarbapenem derivatives. The scope of the photorearrangement is being studied as is the subsequent chemistry of enones such as **4** and carbapenams such as **8**.

Acknowledgment. We express our gratitude to colleagues at Pfizer, especially to Dr. M. S. Kellogg for helpful suggestions and C. F. Ebbinghaus for expert technical assistance. We also thank Professor E. J. Corey for helpful discussions.

Registry No. 2a, 71786-02-2; **2b**, 80903-57-7; **2c**, 80903-78-2; **4a**, 82113-57-3; **4b**, 82113-58-4; **4c**, 82113-59-5; **7**, 82113-60-8; **8**, 80903-64-6; **9**, 80903-61-3; **10**, 80903-62-4.

Supplementary Material Available: Listings of coordinates and anisotropic temperature factors for non-hydrogen atoms, hydrogen coordinates, distances, and angles (2 pages). Ordering information is given on any current masthead page.

(13) Rieke, R.; Uhm, S. J. *Synthesis* **1975**, 452. The use of such highly reactive zinc was crucial for the success of the reduction.

(14) Duchamp, D. J., American Crystallographic Association Meeting, Bozeman, MT, 1964; Paper B-14, p 29.

(15) Germain, G.; Main, P.; Woolfson, M. M. *Acta. Crystallogr., Sect. A* **1971**, *A27*, 368.

(16) The stereochemistry of the hydroxyl at C-1 is not known with certainty but is believed to be of the β configuration, which is consistent with hydride attack from the less hindered α direction. This stereochemical course would then be similar to that seen with the borohydride reduction of 2-oxo-Δ-3-carbacephems: Martel, A.; Doyle, T. W.; Luh, B. *Can. J. Chem.* **1979**, *57*, 614.