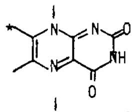
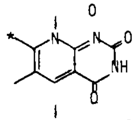
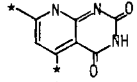
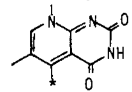
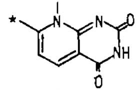
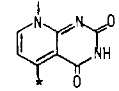
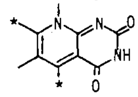
Table I. Rate Data for Proton Loss from Activated Methyl Groups[a] in Methyl Lumazines, 1-7, in Water at 35.7 °C

Compound	pK_{SH^+}	$10^7 k_{S + AcO^-}$ M^{-1} sec^{-1}	$10^5 k_{SH^+ + AcO^-}$ M^{-1} sec^{-1}
1 	0.93	142,000[b]	238,000[b]
2 	2.12	230	461
3 	2.26	9.92 (7-Me 7.0) (5-Me 2.9)	13.0 (7-Me 9.2) (5-Me 3.8)
4 	2.46	87.8	122
5 	1.81	95.8	130
6 	2.14	25.8	38.6
7 	2.57	39.2 (7-Me 28) (5-Me 11)	51.2 (7-Me 36) (5-Me 15)

[a] Reactive sites shown by asterisks; lumazine numbering system: the C-7 position in **5** and the C-5 position in **6** have the reactive groups. [b] Reference 6b, $t = 34.5$ °C.

of the iodination rate between the two methyl groups in **3** was made by following the reaction in D_2O for an extended period and measuring the relative degrees of exchange with a 270-MHz spectrometer. The upfield methyl group assigned above to the C-7 position exchanged 2.4 times as fast as that at C-5. The same partition ratio was assumed to hold for **7**. The pK_{SH^+} values were required to convert the catalytic coefficients to values of $k_{SH^+ + AcO^-}$, and these were determined spectrophotometrically.

The results given in Table I show a remarkable effect of methyl substitution. Introducing a methyl group at the next ring position but one (remote substitution) has the expected deactivating effect on kinetic acidity of the reacting methyl group, whether proton loss involves the neutral compound or the cation. Comparing **2** and **7** or **3** and **5** shows that C-5 CH_3 decreases the rate of proton loss from C-7 CH_3 by factors of 8.2–14. Comparing **3** and **6** or **4** and **7** shows that C-7 CH_3 has a comparable effect on C-5 CH_3 (factors of 8.0–10.2). These results can be ascribed to the operation of a large polar effect. (Compare the still greater effect, again presumably polar in origin, when CH replaces N at position 5, i.e., **1** and **2**.)

Substituting methyl for ring hydrogen at a position *adjacent* to a reactive methyl group, however, causes an increase in the rate of proton loss. For C-7 CH_3 dissociation, compare **2** and **5** or **3** and **7**. The rate constants for the general base reaction are 2.4–4.0 times greater and for the general acid reaction 3.5–3.9 times greater when another methyl group is adjacent to the reactive methyl site. For C-5 CH_3 dissociation, compare **3** and **7** or **4** and **6**, where the effect is 3.2–3.9 times. Although these rate increases are not large in themselves, they are remarkable when one considers that the electron-donating effect of an adjacent methyl group should be markedly greater than that of a remote methyl group, where a rate *decrease* of 8–14 times was observed. The special proximity effect of methyl, whatever its origin, is thus causing a rate increase of possibly two orders of magnitude for proton loss from methyl groups at either C-5 or C-7.

Might proton loss be causing the essentially aromatic system to change to a nonplanar arrangement, thus allowing relief of steric stain? This might explain the effect at either C-5 or C-7 but not at both, since **3** is the least reactive compound of all. Furthermore, the reaction in both the general acid route (reactions 1 and 3) and general base route (reaction 2) is bimolecular, and the transition state contains an extra species, acetate ion, at the reaction site. Additionally, there appears to be no buttressing effect;[7] the rates of the tetramethyl compound **7** are in agreement with a simple additive effect of adjacent and remote methyls.

The C-7 methyl group is an activated site in lumazines (and in flavins) and is an important center for chemical condensation in these compounds.[2,8,9] Our results point to a special proximity effect of neighboring methyl (at C-6) that is the reverse of the expected steric and electronic effects[10] and that facilitates proton loss from the C-7 methyl group in such compounds.

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(7) Westheimer, F. H. In "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.: Wiley: New York, 1956; p 552.

(8) Weimar, W. R.; Neims, A. H. In "Riboflavin": Rivlin, R. S., Ed.; Plenum Press: New York, 1975; Chapter 1.

(9) The lumazine that is the precursor of riboflavin in nature carries at N-8 not a methyl group as in **1** but a ribityl group, and this unit is known to have an important influence on the condensation process. See: Plaut, G. W. E.; Beach, R. L. In "Chemistry and Biology of Pteridines"; Pfleiderer, W., Ed.; de Gruyter: Berlin, 1975.

(10) For an account of the steric and electronic effects of methyl on the rate of proton loss from other compounds, see: Bordwell, F. G.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3116. Zoltewicz, J. A.; Helmick, L. S. *Ibid.* **1978**, *43*, 1718.

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Mercury(I)/(II): A Novel Trap for Harvesting Excited-State Energies

Sir:

Reversible excited-state electron transfer in solution, like photochemical production of hydrogen and valence isomerization, has been widely studied in connection with solar energy conversion.[1-5] Most of the studies to date have utilized systems based on eq 1-3, where a number of organic and inorganic donors (D)

$$D \xrightarrow{h\nu} {}^*D \qquad \phi' \tag{1}$$

$$^*D + Q \xrightarrow{k_2} D^{\mp} + Q^{\pm} \tag{2}$$

$$D^{\mp} + Q^{\pm} \xrightarrow{k_b} D + Q \tag{3}$$

have been employed. Most of these systems suffer from the fact that the back thermal reaction (eq 3) is too rapid to allow efficient harvesting of the redox energy. ϕ' is the efficiency of population of the sensitizing state following excitation. An example of this

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(1) (a) Jonak, G. D.; Matheson, M. S.; Meisel, D. *J. Am. Chem. Soc.* **1978**, *100*, 1449. (b) Hoselton, M. A.; Lin, C-T; Schwarz, H. A.; Sutin, N. *Ibid.* **1978**, *100*, 2383. (c) Winterle, J. S.; Kliger, D. S.; Hammond, G. S. *Ibid.* *98*, 3719.

(2) (a) Sprintschnik, G.; Sprintschnik, H. W.; Kirsch, R. P.; Whitten, D. G. *J. Am. Chem. Soc.* **1976**, *98*, 2337; **1977**, *99*, 4947. (b) Lehn, J. M.; Sauvage, J. P. *Nouv J. Chim.* **1978**, *1*, 449.

(3) (a) Lin, C-T; Bottcher, W.; Chou, M.; Creutz, C.; Sutin, N. *J. Am. Chem. Soc.* **1976**, *98*, 6536-6544. (b) Clark, W. D. K.; Sutin, N. *Ibid.* **1977**, *99*, 4676-4682. (c) Lin, C-T; Sutin, N. *J. Phys. Chem.* **1976**, *80*, 97.

(4) (a) Sutin, N.; Creutz, C. *Adv. Chem. Ser.* **1978**, *No. 168*, 1. (b) Delaive, P. J.; Lee, J. T.; Abruna, H.; Sprintschnik, H; Meyer, T. J.; Whitten, D. G. *Ibid.* **1978**, *No. 168*, 1. (c) Balzani, V.; Bolletta, F.; Gandolfi, M. T.; Maestri, M. *Top. Curr. Chem.* **1978**, *75*, 1.

(5) (a) Whitten, D. G.; DeLaive, P. J.; Foreman, T. K.; Mercer-Smith, J. A.; Schmehl, R. H.; Gianotti, C. *Sol. Energy: Chem. Convers. Storage, Symp.* **1979**, 117. (b) Thomas, J. K. *Ibid.* **1979**, 141. (c) Hoffman, M. Z.; Lichtin, N. N. *Ibid.* **1979**, 153. (d) DeGraff, B. A.; Demas, J. N.; Taylor, D. G. *Ibid.* **1979**, 189. (e) Tien, H. T.; Higgins, J.; Mountz, J. *Ibid* **1979**, 203. (f) Huatala, R. R.; King, R. Bruce; Kutal, C. *Ibid.* **1979**, 333.

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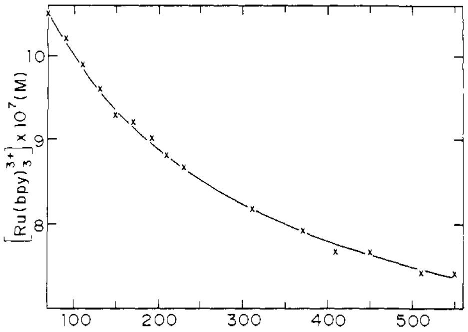

Figure 1. Calculated (—) and observed (X) concentrations of $Ru(bpy)_3^{3+}$, following flash photolysis of $Ru(bpy)_3^{2+}$ and Hg^{2+}.

type of system is the $[Ru(bpy)_3]^{2+}/Fe^{3+}$ photogalvanic cell described by Lin and Sutin,[3c] where $k_b \sim 10^5$ M^{-1} s^{-1} limits its usefulness. We describe here a novel inorganic trap system which slows the back reaction by $\sim 10^5$ times over the Lin–Sutin system and shows promise as a photogalvanic energy conversion cell.

While studying the oxidative quenching of $*[Ru(bpy)_3]^{2+}$ by Cu(II) complexes and by Fe^{3+} with luminescence and flash photolysis methods,[5d] we examined Hg^{2+} as a potential electron-transfer quencher. As with the Cu(II) and Fe^{3+} systems, flash photolysis resulted in efficient transient bleaching of $[Ru(bpy)_3]^{2+}$ to $[Ru(bpy)_3]^{3+}$. Unlike the Cu(II) and Fe^{3+} systems, however, fast (ms) and complete regeneration of the initial reactants by the thermal back reaction (eq 3) was not observed. Some of the $[Ru(bpy)_3]^{3+}$ was rapidly depleted, but restoration leveled off at 50% completion of the initial system as shown in Figure 1. A very slow thermal reaction, lasting for many minutes, then completely restored the starting materials.

The reactions in the Hg^{2+} system are described in eq 4–7, where D and D $^+$ are $[Ru(bpy)_3]^{2+}$ and $[Ru(bpy)_3]^{3+}$, respectively.

$$*D + Hg^{2+} \xrightarrow{k_2} D^+ + Hg^+ \text{ or } D + Hg^{2+} \tag{4}$$

$$D^+ + Hg^+ \xrightarrow{k_b} D + Hg^{2+} \tag{5}$$

$$Hg^+ + Hg^+ \xrightarrow{k_d} Hg_2^{2+} \tag{6}$$

$$D^+ + {}^1/_2Hg_2^{2+} \xrightarrow{k_{th}} D + Hg^{2+} \tag{7}$$

The spectral distribution of the bleaching on flash photolysis was consistent with production of $[Ru(bpy)_3]^{3+}$ but inconsistent with production of $[Ru(bpy)_3]^+$.[6] Reduction of $[Ru(bpy)_3]^{3+}$ by the reactive Hg^+ free radical (eq 5) accounts for the fast regeneration of the sensitizer. An additional process must be invoked to account for the incomplete fast regeneration of $[Ru(bpy)_3]^{2+}$. We attribute this to the dimerization reaction of the Hg^+ free radical to form normal Hg_2^{2+} (eq 6), which is in accordance with the fast dimerization of Hg^+ at low pHs.[7] The oxidation of Hg^+ by $[Ru(bpy)_3]^{3+}$ and the dimerization proceed at similar rates, which permits simultaneous measurements of both k_b and k_d. For initially equal concentrations of Hg^+ and D^+, the differential equations of reactions 5 and 6 were solved numerically for different k_b and k_d values. These parameters were adjusted by a grid-search method to give the best least-squares agreement between the calculated and observed data. The fits were always within experimental error; a typical result is shown in Figure 1. Because of the dissymmetry in the products of reactions 5 and 6, there was no ambiguity in the assignment of k_b and k_d.

The fast reduction of $[Ru(bpy)_3]^{3+}$ cannot be by Hg_2^{2+}. Flash photolysis experiments with added Hg_2^{2+} yield the same k_b and k_d values as do those without excess Hg_2^{2+}. The very slow regeneration of $[Ru(bpy)_3]^{2+}$ is, however, accelerated by the addition of Hg_2^{2+}. Most (>90%) of the rate of disappearance of $[Ru(bpy)_3]^{3+}$ in our photolysis experiments is due to the slow oxidation of water by $[Ru(bpy)_3]^{3+}$. Using added Hg_2^{2+}, we measure $k_{th} = 1.65 \pm 0.07$ M^{-1} s^{-1} (extrapolated to infinite acid concentration where oxidation of water by $[Ru(bpy)_3]^{3+}$ is negligible). The k_b and k_d values for Hg^+ and $[Ru(bpy)_3]^{3+}$ are given in Table I.

Table I. Photochemical Properties of $*[Ru(bpy)_3]^{2+}$, Hg(II) Species

quencher[a]	K_{SV}[φ]	ϕ_{et}	$k_2 \times 10^{-8}$,[b] M^{-1} s^{-1}	$k_b \times 10^{-9}$,[c] M^{-1} s^{-1}	$k_d \times 10^{-9}$,[c] M^{-1} s^{-1}
Hg^{2+}[d]	90 ± 10	>0.6	1.5	2.0	2.9
$HgCl_2$[d]	227 ± 5	$<10^{-2}$	3.8		

[a] Deoxygenated aqueous solutions at 21 °C with ionic strength of 1.0. [b] Accuracy ±10–15%. [c] Accuracy ±25%. [d] 0.1 M $HClO_4$.

We do not have direct chemical evidence for the production of Hg_2^{2+}. Reactions 4–6 are, however, supported by the production of $[Ru(bpy)_3]^{3+}$, the successful kinetic modeling, and the absence of chemically realistic alternatives. For example, production of Hg^0 would be expected to result in formation of a precipitate or a mirror, but even on protracted irradiation or cycling neither of these was observed.

The yield of detectible electron transfer to Hg^{2+}, ϕ_{et}, was determined by a relative flash photolysis method by using the $[Ru(bpy)_3]^{2+}/Fe^{3+}$ reaction as a chemical actinometer[5d] with an electron-transfer efficiency of unity.[8] We estimate that this method yields ϕ_{et} values accurate to ~30%. The principal error is the finite flash width. The ϕ_{et}'s determined are included in Table I.

In the case of Hg^{2+} quenching, only electron-transfer quenching can be important. Hg^{2+} has no low-lying excited states which can quench by energy transfer, and heavy atom quenching of $[Ru(bpy)_3]^{2+}$ has been shown to be an unimportant process.[9] The apparent subunity yield for Hg^+ production from Hg^{2+} would then arise from reverse electron transfer in the encounter pair (eq 8).

$$D^+|M(I) \rightarrow D + M(II) \tag{8}$$

The failure to see Hg^+ with $HgCl_2$ probably arises from very efficient back electron transfer in the electrostatically stabilized encounter pair ($[Ru(bpy)_3]^{3+}|HgCl_2^-$). This phenomenon seems well documented in the case of oxidative quenching of $*[Ru(bpy)_3]^{2+}$ by neutral organic electron-transfer quenchers where no Ru(III) or reduced quencher is observed in spite of efficient electron-transfer quenching.[10]

The remarkable slowness of the $[Ru(bpy)_3]^{3+}/Hg_2^{2+}$ back reaction bears comment. The driving force for the reaction is relatively small (~330 mV). Also, since the one-electron oxidizer, $[Ru(bpy)_3]^{3+}$, is attacking a two-electron reducer, a high-energy Hg_2^{3+} intermediate species may well be involved.

To demonstrate the potential utility of the Hg^{2+}/Hg_2^{2+} pair as an efficient energy trap for harvesting excited-state energies, we have constructed a $[Ru(bpy)_3]^2/Hg^{2+}$-based photogalvanic cell.[11] When irradiated with a $CuSO_4$-filtered 500-W tungsten lamp, the cell rapidly (<15 s) produced potentials ranging from 130 to 230 mV. The potential developed increased with increasing initial $[Ru(bpy)_3]^{2+}$ concentration in the range (1–4) × 10^{-5} M. After the illumination was terminated, the potential decayed only

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[6] Meisel, D.; Matheson, M. S.; Mulac, W. A.; Rabini, J. *J. Phys. Chem.* **1977** *81*, 1449.

[7] Fujita, S.; Horii, H.; Tanigucki, S. *J. Phys. Chem.* **1973**, *77*, 2868.

[8] (a) Demas, J. N.; Taylor, D. G., *Inorg. Chem.* **1979**, *18*, 3177. (b) Taylor, D. G.; Demas, J. N. *J. Chem. Phys.* **1979**, *71*, 1032. (c) Mandal, K; Pearson, T. D. L.; Demas, J. N. *Ibid.*, in press.

[9] Demas, J. N.; Addington, J. W. *J. Am. Chem. Soc.* **1976**, *98*, 5800.

[10] Bock, C. R.; Meyer, T. J.; Whitten, D. G. *J. Am. Chem. Soc.* **1974**, *96*, 4710.

[11] A symmetrical "H"-shaped cell with a fritted glass divider in the arm was used. The approximate cell volume was 100 mL. The area of the platinum electrodes was 31 cm^2 each. The solutions were initially identical, but one solution was irradiated, and the other was shielded from the light. Solutions were deoxygenated before and during irradiation. The solutions were in perchloric acid, 0.05 M in mercury(II) perchlorate, and with $[Ru(bpy)_3]^{2+}$ concentration = (1–4) × 10^{-5} M.

slowly, typically less than 5 mV/min. This is consistent with the slow rate of reaction 7.

The steady-state short-circuit current (lamp on) ranged from 20 to 70 μA, depending on the $[\mathrm{Ru(bpy)_3}]^{2+}$ concentration. The cell could be recycled repeatedly over a period of days with no deterioration of performance. These figures represent the greatest potentials reported to date for a cell of this type.[3c]

The Hg^{2+}-quenched system represents a unique system in the area of storage of reversible excited-state electron-transfer energy. With no attempt at optimization, at $[\mathrm{H}^+] = 0.1$ M the products $\mathrm{Hg_2}^{2+}$ and $[\mathrm{Ru(bpy)_3}]^{3+}$ will coexist for >20 min, which represents ~5 orders of magnitude improvement over the $[\mathrm{Ru(bpy)_3}]^{3+}/\mathrm{Fe}^{2+}$ system.[3c] The energy stored in the $[\mathrm{Ru(bpy)_3}]^{3+}/\mathrm{Hg_2}^{2+}$ couple is ~7.7 kcal/mol of $[\mathrm{Ru(bpy)_3}]^{3+}$, which could represent a maximum ~15% efficient utilization of the 51 kcal zero-point excited-state energy of $^*[\mathrm{Ru(bpy)_3}]^{2+}$.[9] This calculation assumes no losses through reaction 5. For transition-metal photosensitizers with CT excited states, the available evidence points to ϕ' being unity,[8] and losses through this pathway do not need to be considered. While the efficiency per photon is not high, the trap system does not absorb the UV-vis component of the solar spectrum which allows considerable flexibility in sensitizer selection. In contrast to organic energy traps (e.g., thionine), the completely inorganic $\mathrm{Hg}^{2+}/\mathrm{Hg_2}^{2+}$ system should be free of the instabilities of large organic molecules. Chemical modifications of the sensitizer to extend the absorption cutoff wavelength and thus the fraction of the solar spectrum absorbed and modifications of the $\mathrm{Hg}^{2+}/\mathrm{Hg_2}^{2+}$ couple to improve per photon efficiency are presently under investigation.

Acknowledgment. We gratefully acknowledge the assistance of James Madison University and the National Science Foundation (CHE-77-20379).

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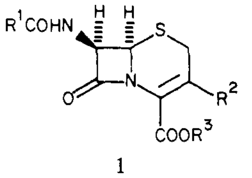
Received December 17, 1979

Synthesis of 3-Azacephalosporins

Sir:

The biological activity of the β-lactam antibiotics is generally believed to be associated with the chemical reactivity of their β-lactam rings. For the high reactivity of the β-lactam system in cephalosporins (**1**), a rationalization has been given in terms of an electronic activation by a conjugation of the lone-pair electrons on nitrogen with the C-3 double bond, in competition with the β-lactamamide resonance.[1] We thought that replacement of the C-3 carbon atom of the cephalosporin nucleus with the electron-withdrawing nitrogen atom would enhance the reactivity of the azetidinone carbonyl and consequently modify the antibacterial activity. In this communication, we report a successful approach for preparing this novel bicyclic ring system, 3-azacephem **2**, and the related 3-azacepham nucleus from which the former was derived.



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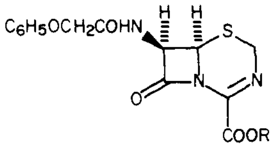
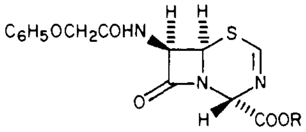
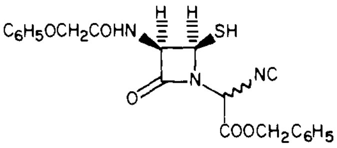


2, R = $\mathrm{CH_2C_6H_5}$
20, R = $\mathrm{CH_2OCOC(CH_3)_3}$



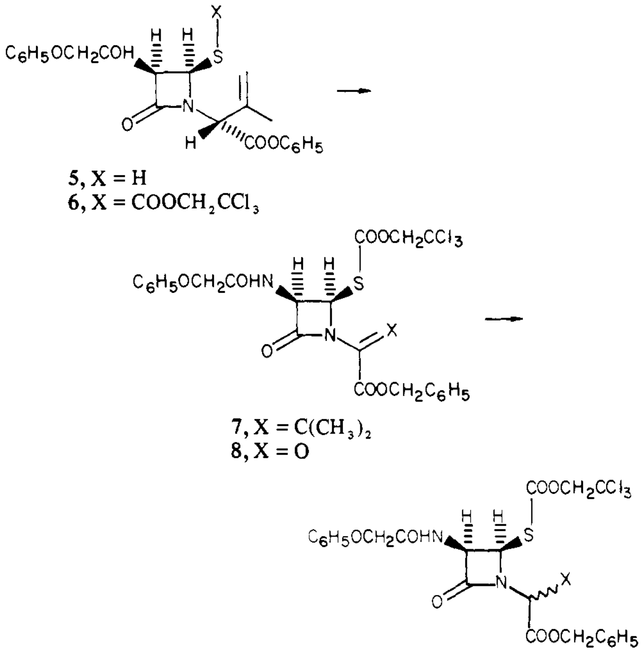
3, R = $\mathrm{CH_2C_6H_5}$
21, R = H



4

Our approach was based on the anticipation that the dihydrothiadiazine ring of **2** could be constructed by a route involving, as a key step, the intramolecular cyclization of the mercapto isocyanide **4** to the Δ^2-azacephem **3**, followed by the conversion of **3** into **2**. Thus, our initial goal was to prepare the isocyanide **4** in which the mercapto group is appropriately protected so as to be readily regenerated by a mild deprotection.

The requisite intermediate, isocyanide **14**, was prepared in a straightforward manner from the 4-mercaptoazetidinone **5**,[2] readily accessible from penicillin V. The mercapto group of **5** was first protected by acylation with (trichloroethoxy)carbonyl chloride (pyridine/$\mathrm{CH_2Cl_2}$), and the product **6** was then treated with $\mathrm{Et_3N}$ in benzene, giving the α,β-unsaturated ester **7** (100%). Ozonolysis of **7** (AcOEt, -78 °C), followed by workup with an aqueous solution of $\mathrm{NaHSO_3}$ and $\mathrm{Na_2SO_3}$, gave the crystalline oxalyl derivative **8** [mp 152 °C (dec), 77%], which was then subjected to reduction with $\mathrm{NaBH_4}$ (AcOH/THF, 0 °C) to give the epimeric alcohol **9** (presumably 1:1). Chlorination of **9** with $\mathrm{SOCl_2}$ (2,6-lutidine/$\mathrm{CH_2Cl_2}$, $-35 \rightarrow 0$ °C) and subsequent treatment of the resulting chloride **10** with $\mathrm{NaN_3}$ in DMF at 0 °C produced, after purification by silica gel chromatography, the azide **11** [IR ($\mathrm{CH_2Cl_2}$) 2120 cm^{-1}; a ratio of 1:1 on high-pressure liquid chromatography (high-pressure LC)] in 55% yield from **8**. Catalytic reduction of **11** (10% Pd/C, $\mathrm{HCO_2H}$), followed by formylation ($\mathrm{HCO_2H/Ac_2O}$, 0 °C), gave a 77% yield of the formamide **13**, which was finally treated with $\mathrm{POCl_3}$ (2,6-



5, X = H
6, X = $\mathrm{COOCH_2CCl_3}$

7, X = $\mathrm{C(CH_3)_2}$
8, X = O

9, X = OH
10, X = Cl
11, X = $\mathrm{N_3}$
12, X = $\mathrm{NH_2}$
13, X = NHCHO
14, X = NC

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(1) See, e.g.: R. M. Sweet, "Cephalosporins and Penicillins: Chemistry and Biology", E. H. Flynn, Ed., Academic Press, New York, 1972, pp 305-306.

(2) J. E. Baldwin and M. A. Christie, *J. Chem. Soc., Chem. Commun.*, 239 (1978).