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Short Communications

A New Rearrangement of Cephalosporins in the Presence of Mercury(II) Trifluoroacetate

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The functionalization of the allylic 3-Me group of deacetoxycephalosporins is of great importance for obtaining pharmacologically significant cephalosporins, A well-known procedure[1] is the allylic bromination of deacetoxycephalosporin sulfoxides with subsequent nucleophilic exchange of the bromine into, *e.g.*, –OAc. Another possibility could be the one-step acyloxylation of the 3-Me group by various Pb, Hg, Tl *etc.* salts.[2] Recently Massiot *et al.* have found that mercury(II) trifluoroacetate is an excellent reagent for introducing a hydroxy function into steroids.[3]

We have now found that when *1a* or *b* was allowed to react with two equiv. of mercury(II) trifluoroacetate (dry CH_2Cl_2, room temperature, 12 h, aq. $NaHCO_3$ work-up) an interesting rearrangement occurred leading to *2a* or *b* (m.p.'s: 170 and 167–168 °C, resp.).

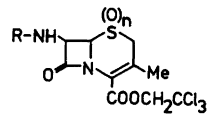
A similar compound, but having sulfur in lieu of oxygen (*3a*), was observed first by Morin *et al.*[4] when phenoxymethylpenicillin sulfoxide methyl ester was heated in the presence of acetic anhydride. The same rearrangement occurs if phenoxymethylpenicillin sulfoxide 4-nitrobenzyl ester is heated in dioxan in the presence of pyridine picrate, yielding *3b*, and also when the same sulfoxide 2,2,2-trichloroethyl ester is heated together with acetic anhydride in a toluene–dimethylacetamide mixture giving *3c* as the main product.[6,*]

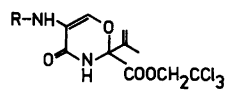
The IR spectra of *2a* and *b* show the presence of two amide NH groups (3365 and 3215 for *2a*; 3375 and 3180 for *2b*; 3360 and 3164 for *3c*[6]) and three C=O groups (1765, 1695 and 1660 cm^{-1} for *2a*; 1776 (*sic*!) and 1680 (br) cm^{-1} for *2b*; 1750, 1680 and 1660 cm^{-1} were reported for *3a*[4], similarly 1756, 1688 and 1651 cm^{-1} were observed for *3c*[6]). The mass spectrum of *2a* exhibits M^+ at 404 (four chlorine atoms according to isotopic clusters).

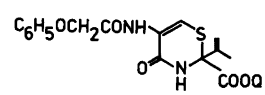
Both of the ^1H NMR spectra (*2a*: (60 MHz, DMSO-d_6) δ 1.88 (3 H, s) 4.27 (2 H, s), 5.04 (2 H, s), 5.3–5.4 (2 H, m), 8.17 (H, s), 9.35 (H, s) and 9.42 (H, s); *2b*: δ 1.89 (3 H, s), 4.68 (2 H, s) 5.05 (2 H, s), 5.35 (2 H, s), 6.7–7.5 (5 H, m), 8.14 (H, s), 8.97 (H, s) and 9.45 (H, s)) show the disappearance of of the β-lactam methine protons and of the 2-CH_2 group and the presence of two olefinic protons at ~5.4 (~5.3 for *3a*). In the case of *2a* they are weakly coupled to the methyl group. The olefinic proton of the other double bond is strongly shifted downfield to δ 8.1 (cf. *3a* δ 8.05).

The same conclusions can be drawn from the ^{13}C NMR spectra, where the 2-CH_2 and β-lactam CH signals are absent showing two more sp^2-carbons instead.

* *Note added in proof.* Wolfe *et al.* [*Can. J. Chem. 53* (1975) 497] reported a compound having the same ring system as in *2* obtained by exposing methyl 2-(2'R-phenylacetoxy-3'S-amino-4'-oxo)azetidinyl-3-bromomethyl-2-butenoate to NEt_3. In this case *4b*-like intermediary was assumed to form *via* an O→N acyl transfer.







1a	R = $ClCH_2CO$-	n = 0	*2a*	R = $ClCH_2CO$-	*3a*	Q = Me-
b	$C_6H_5OCH_2CO$-	n = 0	*b*	$C_6H_5OCH_2CO$-	*b*	4-$NO_2C_6H_4CH_2$-
c	$ClCH_2CO$-	n = 1			*c*	Cl_3CCH_2-

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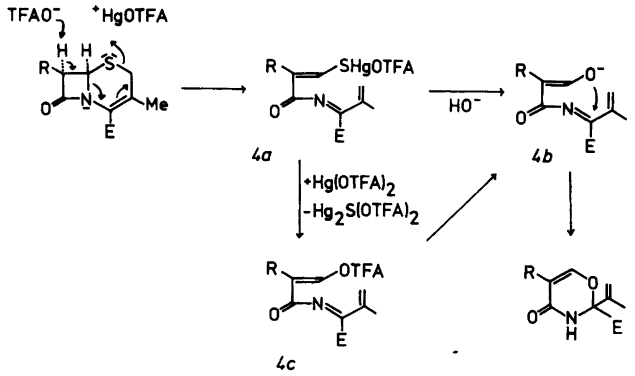

Under the same reaction conditions no similar reaction was observed in case of the sulfoxide *1c*.

The formation of *2a* and *b* may be understood by assuming that an initial Hg→S attack, assisted by the attack of base at 6-C, opens the dihydrothiazine ring, resulting in an intramolecular β-elimination leading to *4a*. This, in turn, is hydrolyzed directly or *via 4c* followed by a Michael-type addition to the acyl-imine system.

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1. Webber, J. A., Huffman, G. W., Koehler, R. E., Murphy, C. F., Ryan, C. W., Van Heyningen, E. M. and Vasileff, R. T. *J. Med. Chem. 14* (1971) 1136.
2. Rawlinson, D. J. and Sosnowsky, G. *Synthesis* (1973) 567.
3. Massiot, G., Husson, H. P. and Potier, P. *Synthesis* (1974) 723.
4. Morin, R. B., Jackson, B. G., Mueller, R. A., Lavagnino, E. R., Scanlon, W. B. and Andrews, S. L. *J. Am. Chem. Soc. 91* (1969) 1401.
5. Gunda, T. E. *Unpublished results.*
6. Enebäck, C. *Unpublished results.*

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