TOTAL SYNTHESES OF 1-CARBACEPHEM DERIVATIVES

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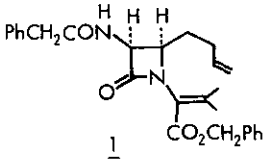
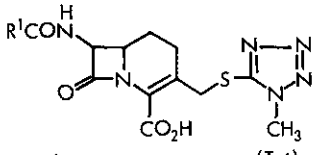
1-Carbacephem derivatives, in which sulfur atom of cephalosporins is replaced by carbon (methylene), have been demonstrated to retain antibacterial activity of the corresponding cephems (R. N. Guthikonda et al., J. Amer. Chem. Soc., 96, 7584 (1974); R. A. Firestone et al., J. Med. Chem., 20, 551 (1977)). In connection with studies on β-lactam antibiotics carried out extensively in our laboratories, we have independently prepared various kinds of 1-carbacephems 2-13 shown below using an azetidinone (racemic) 1 as a common intermediate and sequence of reactions which were developed for 1-oxacephem syntheses involving intramolecular Wittig reaction (M. Narisada et al., J. Med. Chem., 22, 757 (1979)). Preliminary biological evaluation suggested that none of these 1-carbacephems exceeded both 1-oxa and 1-thia congeners in antibacterial activity.

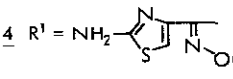


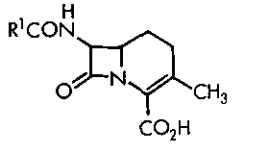
1



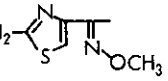
2 R^1 = PhCH(NH$_2$)-

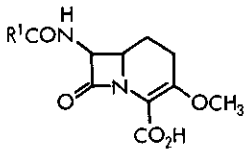
3 R^1 = PhCH(NHCON(C$_2$H$_5$)CO$_2$)-

4 R^1 = 



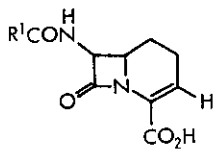
5 R^1 = $PhCH_2$-

6 R^1 = 



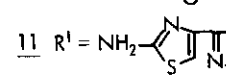
7 R^1 = PhCH(NH$_2$)-

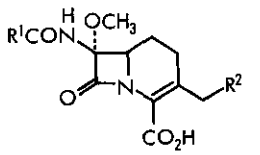
8 R^1 = PhCH(NHCON(C$_2$H$_5$)CO$_2$)-

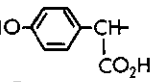


9 R^1 = PhCH(NH$_2$)-

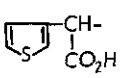
10 R^1 = PhCH(NHCON(C$_2$H$_5$)CO$_2$)-

11 R^1 = 



12 R^1 = 

R^2 = S-Tet

13 R^1 = 

R^2 = $OCONH_2$