A Convenient Synthesis of β-Lactams

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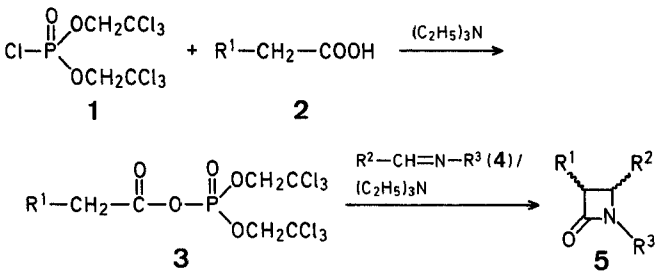
There have been many reports on the synthesis of β-lactams. Phosphorylating agents such as diethyl phosphorochloridate, diphenyl phosphorochloridate, or 2-chloro-2-oxo-P^V-1,3,2-benzodioxaphosphole have been found[1] to convert suitably substituted acetic acids and imines to β-lactams. Similarly, *N,N*-bis[2-oxo-3-oxazolidinyl)-phosphorodiamidic chloride has been used in the presence of triethylamine[2].

We report the use of bis[2,2,2-trichloroethyl] phosphorochloridate **(1)** and substituted acetic acids **(2)** instead of usually employed acid chlorides for the conversion of imines **(4)** to monocyclic β-lactam compounds **(5)**. A mixture of an imine **(4)** and a substituted acetic acid **(2)** in the presence of triethylamine is stirred with bis[2,2,2-trichloroethyl] phosphorochloridate **(1)** at room temperature for 48 h to give the corresponding substituted β-lactams **(5)** in a moderate yields (Table) under mild conditions.



The structures of the β-lactams **5** were confirmed by I.R. ($\nu_{C=O}$ = 1740–1760 cm^{-1}), ^{1}H-N.M.R. spectroscopy, and microanalyses. The stereochemistry at C-3 and C-4 of the lactam ring was deduced from the coupling constants of the protons attached to these carbon atoms in the ^{1}H-N.M.R. spectra. For compounds **5a, 5b, 5c, 5d,** and **5e,** the configuration was observed to be *cis*- (J = 5 Hz), whereas the phthalimide derivative **5f** was a *trans*-isomer (J = 2 Hz).

Bis[2,2,2-trichloroethyl] phosphorochloridate (**1**; m.p. 45–47 °C) was obtained from Aldrich Chemical Co. and used without further purification.

β-Lactams 5; General Procedure:

A mixture of an imine **4** (1 mmol), a substituted acetic acid **2** (1 mmol) and triethylamine (2 mmol) in dichloromethane (3 ml) is stirred at room temperature and bis[2,2,2-trichloroethyl] phosphorochloridate (**1**; 0.379 g, 1 mmol) is added dropwise. The resulting mixture is stirred at room temperature for 48 h, washed with water (3 ml) and dried with anhydrous sodium sulfate. Removal of the solvent followed by recrystallization from dichloromethane/ethanol gives the pure β-lactam **5** (Table).

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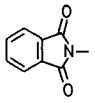
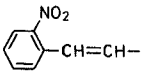
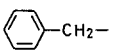
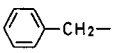
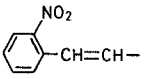
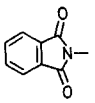
[1] M. S. Manhas, B. Lal, S. G. Amin, A. K. Bose, *Synth. Commun.* **6**, 435 (1976).
[2] D. R. Schridhar, B. Ram, V. L. Narayana, *Synthesis* **1982**, 63.
[3] A. K. Bose, G. Spielman, M. S. Manhas, *Tetrahedron Lett.* **1971**, 3167.
[4] J. C. Sheehan, J. J. Ryan, *J. Am. Chem. Soc.* **73**, 1204 (1951).

Table. β-Lactams **5a–f** prepared

Product No.	R^1	R^2	R^3	Yield [%]	m.p.[a] [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$)[c] δ [ppm]
5a				59	191.5–192.5°	192–195°[3]	1750	5.35 (d, J = 5 Hz); 5.55 (d, J = 5 Hz)
5b				44	160–161°	$C_{26}H_{19}N_3O_5$ (453.4)	1780, 1760, 1710	4.50[d]; 5.60 (d, J = 5 Hz)
5c	H_3CO–			43	130–131°	141–142°[3]	1740	4.82 (d, J = 5 Hz); 5.22 (d, J = 5 Hz)
5d				46	109–110°	$C_{22}H_{19}NO_2$ (329.4)	1740	4.75 (d, J = 5 Hz); 5.45 (d, J = 5 Hz)
5e				52	140–141°	$C_{23}H_{18}N_2O_4$ (386.4)	1760	4.97, 5.10 (dd, J = 5 Hz, 9 Hz); 5.49 (d, J = 5 Hz)
5f				58	230–231°	227–230°[4]	1780, 1760, 1710	5.27 (d, J = 2 Hz); 5.39 (d, J = 2 Hz)

[a] Not corrected.
[b] Satisfactory microanalyses obtained: C ±0.30, H ±0.12, N ±0.29.
[c] Data for 3-H and 4-H only.
[d] Overlap with signal for the benzyl methylene group.

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