Novel Route to β-Lactam Systems

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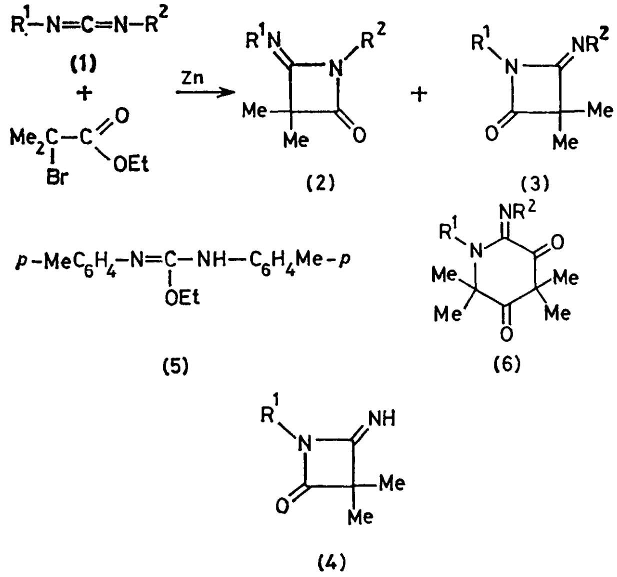
Summary The reactions of carbodiimides with a Reformatsky reagent give 4-iminoazetidin-2-ones in 51—88% yield.

4-IMINOAZETIDIN-2-ONES are mainly synthesized by the thermally induced cycloaddition of ketens to carbodiimides[1—3] or keten imines to isocyanates.[4] We have found that they can be obtained in a Reformatsky-type reaction, as shown in the Scheme. The reactions of a number of carbodiimides with ethyl α-bromoisobutyrate were performed in refluxing toluene in the presence of powdered Zn for several hours. After the usual work-up the mixtures were separated by column chromatography (flash chromatography).[5] The results are shown in the Table. The reactions of dialkyl (**1a**) or arylalkyl-substituted carbodiimides (**1b**—**d**) gave the β-lactam derivatives (**2**) and (**3**) in 77—88% total yield.



SCHEME

TABLE. Reactions of the carbodiimides (**1**) to give the azetidinones (**2**) and (**3**).

	R^1	R^2	% Yield (**2**)	% Yield (**3**)
a	c-C_6H_{11}[a]	c-C_6H_{11}[a]	81	—
b	Ph	Bu^n	54	23
c	Ph	Pr^i	69	19
d	Ph	Bu^t	78[b]	—
e	p-Tolyl	p-Tolyl	51	—

[a] Cyclohexyl. [b] Compound (**4**) was also formed.

The non-symmetrically substituted carbodiimides (**1b**—**d**) gave the 1-alkyl-4-aryliminoazetidin-2-ones (**2**) as the main products, but the 4-alkylimino-1-arylazetidinones (**3**) were also generated. We believe that compound (**4d**) obtained in the reaction of (**1d**) is a result of thermal elimination of isobutene from compound (**3d**).

Fully aromatic carbodiimides gave the desired β-lactams with more difficulty. Di-p-tolycarbodiimide (**1**, $R^1 = R^2 = p$-MeC_6H_4) gave the 1-p-tolyl-4-(p-tolylimino)azetidin-2-one in 51% yield accompanied by the isourea (**5**) in 11% yield but di-p-methoxyphenylcarbodiimide and di-p-nitrophenylcarbodiimide did not produce the respective azetidinones at all, the former giving compound (**6**) as the main product, and the latter giving only unchanged substrate and polymers.

All compounds synthesized were characterized by spectral (i.r., n.m.r., m.s.) and elemental analysis data. Thus, the i.r. spectra of the iminoazetidinones (**2**)—(**4**) showed carbonyl absorptions at 1800—1820 cm^{-1} and C=N absorptions at 1680—1700 cm^{-1} and their structures were confirmed by comparison of their n.m.r. spectra with spectra of known analogous compounds.[3] (Full details of structure assignments will be published elsewhere.)

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