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A NEW METHOD FOR THE SYNTHESIS OF THE 1,3-DIAZETIDIN-2-ONES BY THE OZONOLYSIS OF THE 2-OXO-1,3-DIAZABICYCLO[2.2.0]HEX-5-ENES

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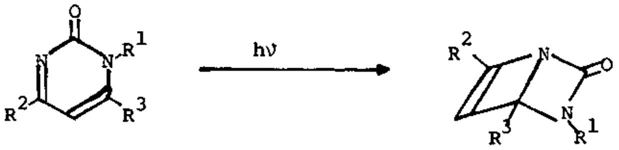
Abstract --- Ozonolysis of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-enes (2) in dichloromethane gave the 1,3-diazetidin-2-ones (3) in good yields, while ozonolysis of (2) in methanol gave the 1,3-diazetidin-2-ones (3), the cyclic acetals (4), and the unstable semi-acetals (5), which were identified as the acetate derivative (6).

It is well known that azomethines react isocyanates to give cyclic 1:1-adducts, 1,3-diazetidin-2-ones, via 1,4-dipolar intermediates, or react further with another molecule of the starting azomethine or isocyanate to produce 1:2- or 2:1-adducts, 1,3,5-triazines.[1-4] We recently reported the synthesis of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-enes (2) by the photochemical electrocyclization of the pyrimidin-2(1H)-ones (1)[5,6] (Scheme 1).

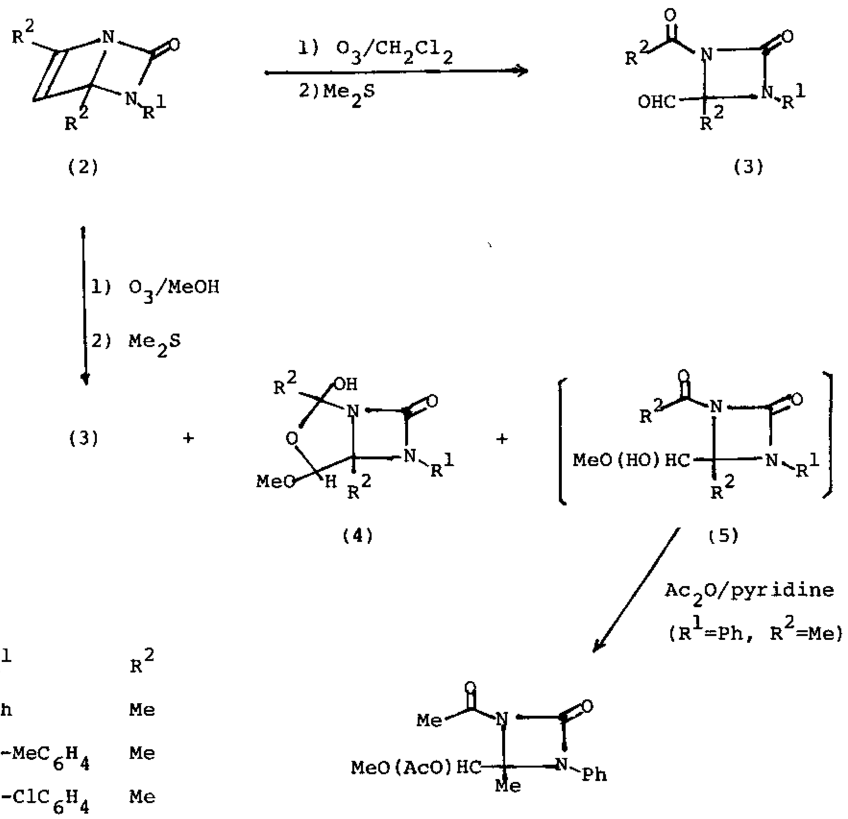


(1) (2) Scheme 1

We report herein a new method for the synthesis of 1,3-diazetidin-2-ones (3), which could be considered as aza analogues of β-lactam, by the ozonolysis of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-enes (2).

The ozonolysis[7] of 3-phenyl-4,6-dimethyl-2-oxo-1,3-diazabicyclo[2.2.0]hex-5-ene

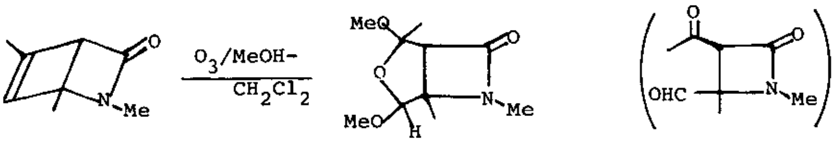
(2a) in dichloromethane at -78°C and then reduction with dimethyl sulfide gave 1-phenyl-3-acetyl-4-formyl-4-methyl-1,3-diazetidin-2-one (3a; m.p. 174-175°C) in 62% yield. The structure of (3a) was elucidated on the basis of spectral data and elemental analysis. Similarly, the 1,3-diazetidin-2-ones (3b-d) were obtained by the ozonolysis, followed by reduction of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-enes (2b-d) in 30-74% yields.



	R^1	R^2
a;	Ph	Me
b;	p-MeC_6H_4	Me
c;	o-ClC_6H_4	Me
d;	Ph	Ph

Scheme 2

This procedure might be one of useful and convenient method for the synthesis of 1,3-diazetidin-2-ones (3). Furrer[8)] reported that the ozonolysis and subsequent reduction of the 3-oxo-2-azabicyclo[2.2.0]hex-5-ene (7), which was formed by the photochemical reaction of 1,4,6-trimethyl-2-pyridone, in dichloromethane-methanol gave the acetal (8), instead of β-lactam (9) (Scheme 3). Next, we carried out the



(7) (8) (9)

Scheme 3

ozonolysis of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-enes (2) in methanol. The treatment of (2a) with ozone, followed by dimethyl sulfide under similar conditions

Table 1. The IR and NMR spectra of the products (3, 4, and 6a) from (2).

Product	Yield (%)	IR (cm^{-1})	NMR (δ in $CDCl_3$)
(3a)	62	1805, 1745, 1690, 1670[c]	1.92(s, 3H), 2.44(s, 3H), 7.05-7.42(m, 5H), 9.42(s, 1H)
(3b)	74	1790, 1650[d]	1.89(s, 3H), 2.29(s, 3H), 2.43 (s, 3H), 7.10-7.20(m, 4H), 9.43(s, 1H)
(3c)	65	1810, 1740, 1690[e]	1.71(s, 3H), 2.42(s, 3H), 7.30-7.50(m, 4H), 9.54(s, 1H)
(3d)	30	1800, 1760, 1650[c]	7.20-8.35(m, 15H), 9.90(s, 1H)
(4a)	19 (29)[a]	3330, 1790, 1200, 1135, 1050[d]	1.68(s, 3H), 1.78(s, 3H), 3.37 (s, 3H), 4.07(br s, 1H), 5.43 (s, 1H), 6.95-7.45(m, 5H)
(4b)	12 (18)[a]	3300, 1780, 1140, 1110, 1030[c]	1.68(s, 3H), 1.81(s, 3H), 2.30 (s, 3H), 3.40(s, 3H), 4.3(br s, 1H), 5.42(s, 1H), 7.16(s, 4H)
(6a)	40[b]	1790, 1745, 1680, 1310, 1190, 1100, 1040[d]	1.85(s, 3H), 2.00(s, 3H), 2.30 (s, 3H), 3.51(s, 3H), 6.30(s, 1H), 7.20-7.60(m, 5H)

a) Yield of the 1,3-diazetidin-2-one (3). b) Yield from (5a). c) $CHCl_3$. d) KBr. e) film.

as described above afforded the 1,3-diazetidin-2-one (3a) (29%), the cyclic acetal (4a; m.p. 189-190°C) (19%), and the unstable semi-acetal [(5a) (40%); δ($CDCl_3$) 1.91, 2.41, 3.40, 4.6, 7.3-7.5 in the ratio of 3:3:3:1:5)]. The semi-acetal (5a) was also produced when the 1,3-diazetidin-2-one (3a) was stirred in methanol for several hours. Since the semi-acetal (5a) was unstable, it could not be isolated and was identified as the acetate derivative (6a). The semi-acetal (5a) was treated with acetic anhydride in pyridine to give the acetate derivative (6a) in 40% yield. Furthermore, (5a) was converted to the 1,3-diazetidin-2-one (3a) by treatment with silica gel. The similar results were obtained by the ozonolysis and reduction of (2b) in methanol. These results are summarized in Table 1 and Scheme 2.

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7) In a typical run, to a solution of the 2-oxo-1,3-diazabicyclo[2.2.0]hex-5-ene (2) (100 mg) in dichloromethane (20 ml) was passed a stream of ozone at -78°C for 0.5 h and the reaction mixture was kept at -78°C for 1 h. After flush with argon, dimethyl sulfide (4 eq. molar) was added dropwise to this reaction mixture at 0°C (ice-bath) and then stirred at room temperature for 1 h. The solvent was concentrated in vacuo and the residual oil was poured into water and extracted with dichloromethane. The extract was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene-ethyl acetate (4:1) to give the 1,3-diazetidin-2-one (3).
8) H. Furrer, *Chem. Ber.*, 1972, **105**, 2780: The similar conversion of Dewar pyridons to azetidin-2-ones was reported recently; T. Kametani, T. Mochizuki, and T. Honda, *Heterocycles*, 1982, **19**, 89; J. Brennan, *J. Chem. Soc. Chem. Comm.*, 1981, 890.

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