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ADDITIONS TO CYCLOBUTENES: SYNTHESIS OF 5-AZABICYCLO[2.1.0]PENTANES, 2-AZABICYCLO[2.2.0]HEXANES, AND 1-AZASPIRO[3.3]HEPTANES[1]

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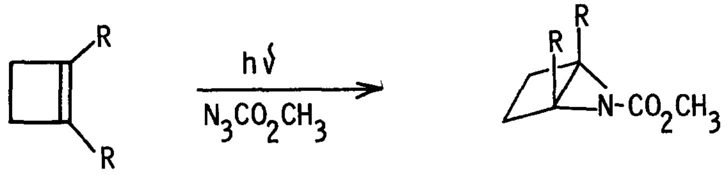
As part of a study on additions to strained olefins and synthesis of strained nitrogen heterocycles, we have found that addition of methoxycarbonylnitrene to 1,2-dimethylcyclobutene, **1a**, and 1-methylcyclobutene, **1b**, provides a convenient synthesis of the corresponding 5-azabicyclo[2.1.0]pentanes **2a** and **2b**.[3] Irradiation of a solution of methylazidoformate in **1a** with a medium pressure mercury lamp gives **2a** (*ca.* 50%), b.p. 40° (1.5 mm); ir (CCl_4) 1730, 1450, 1272, 1224, 1199, 1132, 1090, 897 cm^{-1}; nmr (CCl_4) δ 1.32 (s, 6H), 1.84 (AA′BB′, 4H), 3.66 (s, 3H); *m/e* 155.0953. The monomethylderivative

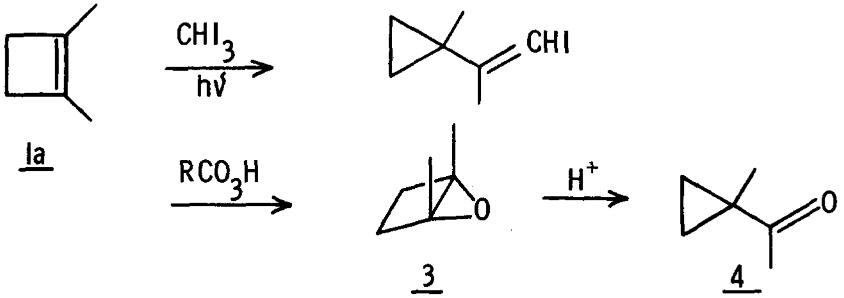


1a: $R=R'=CH_3$
1b: $R=CH_3, R'=H$

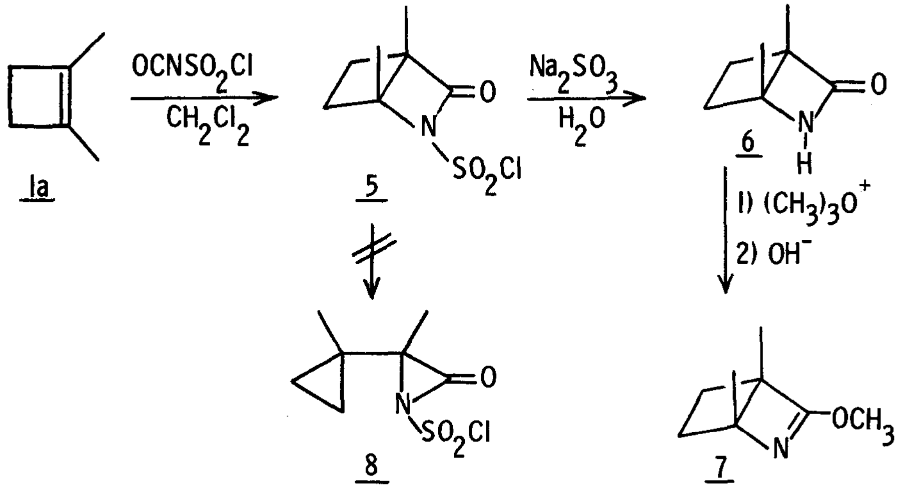
2a
2b

2b is formed in similar fashion; ir (CCl_4) 1730, 1445, 1291, 1282, 1238, 1206, 1128, 888 cm^{-1}; nmr (CCl_4) δ 1.34 (s, 3H), 1.54-2.28 (ABCD mult., 4H), 2.96 (t, J=2.1 Hz, 1H), 3.71 (s, 3H); *m/e* 141.0788. This route is a potentially general one for this little known 5-azabicyclo[2.1.0]pentane ring system.[3] In contrast to bicyclo[2.1.0]pentane[4] and some other aziridines,[5] **2a** is remarkably unreactive toward dimethylacetylenedicarboxylate at temperatures up to 150°C. The reluctance of **2a** to add to dimethylacetylenedicarboxylate *via* an ylid intermediate appears not simply the result of structural constraints on conrotatory opening to the ylid, however, since 1-methoxycarbonyl-2,2,3-trimethylaziridine and 1-methoxycarbonyl-1-azaspiro[2.2]pentane[6] also fail to react with dimethylacetylenedicarboxylate at elevated temperatures.

The lack of rearrangement in the nitrene addition is interesting in view of the observation of a rearranged product on addition of iodocarbene to 1,2-dimethylcyclobutene, 1a.[7] This rearrangement was postulated to occur from a dipolar intermediate from stepwise addition of the iodocarbene. Epoxidation of 1a gives only unrearranged product 3, although 3 rearranges on treatment with acids to 4.[8,9] Trifluoroacetic and formic acid additions to 1a fail to give any rearranged addition products.[10]



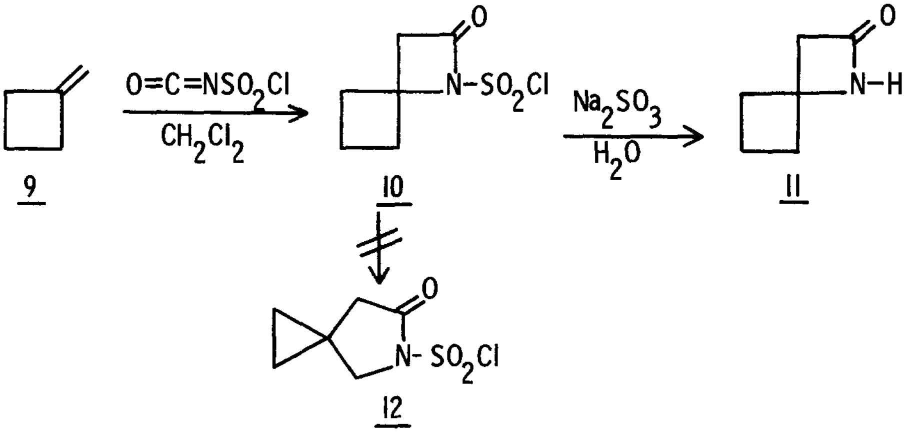
Since chlorosulfonylisocyanate additions often proceed through dipolar intermediates,[11,12] chlorosulfonylisocyanate addition was examined as a further test of the possibility of rearrangement in electrophilic additions to 1a. In this case also, the addition gave only the unrearranged β-lactam 5 which was converted to 6, (39%) b.p. 70° (0.1 mm), m.p. 70-72°, ir (CCl_4) 1750, 1760 cm^{-1}; nmr (CCl_4) δ 1.16 (s, 3H), 1.29 (s, 3H), 1.6-2.4 (m, 4H), 7.6 (brd. 1H); *m/e* 125.0834. This reaction provides a convenient synthetic route to the



2-azabicyclo[2.2.0]hexane ring system.[13] The corresponding 2-azabicyclo[2.2.0]hex-2-ene 7 is readily prepared by treatment with trimethyloxonium fluoroborate followed by aqueous base.

The β-lactam 5 does not rearrange to 8 on heating in chlorosulfonylisocyanate solvent at 80°. Since rearrangement of 5 to the α-lactam 9 might be thermodynamically unfavorable,[1 the addition of chlorosulfonylisocyanate to methylenecyclobutane, 9, was investigated. In this case the rearranged γ-lactam 12 should be thermodynamically favored over the β-lactam 10.[14] However, 10 is the only product observed in the reaction mixture. The β-lactam 10 does not rearrange to 12, even on heating to 80° in chlorosulfonylisocyanate, in marked contrast to several other β-lactams known to rearrange under mild conditions.[11,12]

Reductive workup[15] of the reaction mixture from 9 and chlorosulfonylisocyanate gives 11; ir ($CHCl_3$) 1760 cm^{-1}; nmr ($CDCl_3$) δ 1.44-2.00 (mult., 2H), 2.18-2.60 (mult., 4H), 2.99 (d, J = 1.5 Hz, 2H), 6.8-7.8 (brd. s, 1H); m/e 111.06890.



These reactions indicate that rearrangement to cyclopropane containing products is not generally favorable in a variety of electrophilic additions to 1,2-dimethylcyclobutene and methylenecyclobutane. The reactions provide convenient methods, however, for the synthesis of 5-azabicyclo[2.1.0]pentanes, 2-azabicyclo[2.2.0]hexanes, and 1-azaspiro-[3.3]heptanes.

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References

1) Presented in part at the Sixth Western Regional Meeting of the American Chemical Society, San Francisco, California, October 1970.

2) NSF-URP program participant, Summer 1969.

3) Another derivative of this ring system has been reported by A. G. Anderson, Jr. and D. R. Fagerburg, *J. Het. Chem.*, **6**, 987 (1969). While this work was in progress. we learned of a similar study by J. N. Labows, Jr. and D. Swern, *Tetrahedron Lett*. 4523 (1972). We thank Dr. Swern for correspondence before publication.

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9) Compound *2a* also rearranges with acid catalysis to a cyclopropane derivative and other products.

10) D. H. Aue, H. Iwahashi, and R. B. Lorens, to be published.

11) We have evidence suggesting that dipolar intermediates are involved in the formation of rearrangement products from methylenecyclopropanes and CSI without the intervention of β-lactams, D. H. Aue and D. F. Shellhamer, unpublished results.

12) Rearrangements proceeding through dipolar intermediates from cleavage of β-lactams are known. E. J. Moriconi and W. C. Meyer, *J. Org. Chem.*, **36**, 2841 (1971), T. J. Barton and R. J. Rogido, *Tetrahedron Lett.*, 3901 (1972), T. J. Barton and R. J. Rogido, *J. Chem. Soc. Chem. Commun.*, 878 (1972), J. R. Malpass, *ibid.*, 1246 (1972), J. R. Malpass and N. J. Tweddle, *ibid.*, 1247 (1972), H. J. Friedrich, *Tetrahedron Lett.*, 2981 (1971).

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14) For strain energies see, P.v.R. Schleyer, J. E. Williams and K. R. Blanchard, *J. Amer. Chem. Soc.*, **92**, 2377 (1970).

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