Simple N-Substituted Δ^2-Azetines; Their Preparation and Reactivity

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Summary A photochemical route to *N*-methoxycarbonyl- and *N*-tosyl-Δ^2-azetine is described, photochemical hydration of which is shown to lead to ring-opened products.

Of the unsubstituted 4-membered unsaturated heterocycle series (**1**—**3a**), only thiet (**2**)[1] and its 1,1 dioxide[2] have been reported. The Δ^2-azetine ring has been produced as part of a bicyclic system by irradiation of diazepines which contain the azabutadiene chromophore, but this approach has limitations if other 4π-electrocyclic routes are available.[3] Open-chain azabutadienes are even more reluctant to form small-ring products. *N*-Phenylbenzazetine is perhaps the simplest ring-fused azetine yet reported.[4] Intermolecular $[_{\pi}2_{s} + {}_{\pi}2_{s}]$ cycloadditions, which have been used to prepare azetidines and β-lactams, have similarly not provided worthwhile routes to azetines. While some reactions have produced products presumed to arise from azetine intermediates, only heavily or specifically substituted cases have yielded isolable products.[5]

We report here the preparation and chemical reactivity of two simple azetines, unsubstituted on carbon, by application of a 1,2-photoaromatisation reaction.[6] This work shows that only strongly electron-withdrawing groups attached to nitrogen stabilise the ring sufficiently to yield stable products.

Reaction of 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone with *N*-methoxycarbonyl-2-azabicyclo[2.2.0]hex-5-ene[7] in refluxing benzene yielded a mixture of two stereoisomeric 1:1 adducts (**4d**, ratio 2·5:1).[†] The major isomer, m.p. 165—166 °C (from methanol), was used for the subsequent photochemical experiments. The ^{1}H n.m.r. spectra of the adducts (**4d**) were solvent and temperature dependent, owing to configurational changes about the nitrogen atom or conformational changes of the methoxycarbonyl group. Mass spectral analysis (*m/e* 399), the general features of the ^{1}H n.m.r. spectrum, and subsequent

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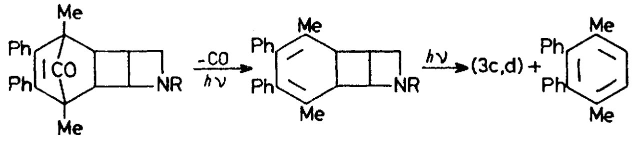
[†] On the basis of reactions between this dienone and other cyclobutenes, we presume these isomers are the *exo,anti*- and *endo,anti*-cyclobutyl adducts.

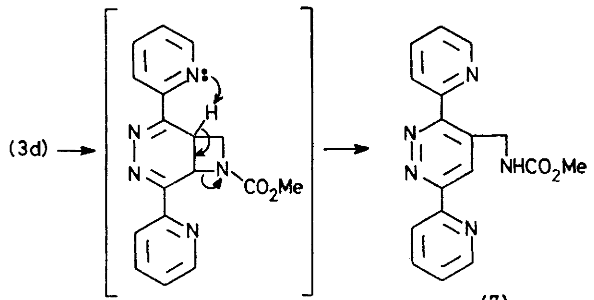
reactions, supported the gross structural assignment (**4d**) for the adducts.

The *N*-methyl adduct (**4b**) was formed, as above, from *N*-methyl-2-azabicyclo[2.2.0]hex-5-ene. The unsubstituted analogue (**4a**) was prepared by hydrolysis (methanolic KOH) of the major isomer of the *N*-methoxycarbonyl compound (**4d**). Compounds (**4a**) and (**4b**) were unstable, and were prepared immediately prior to irradiation studies. The *N*-tosyl compound (**4c**), m.p. 174—175 °C (*m/e* 497), was prepared from the secondary amine (**4a**) by reaction with toluenesulphonyl chloride in pyridine.

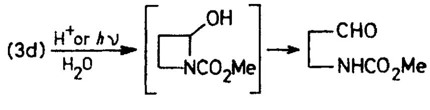
(1) X = O
(2) X = S
(3) X = NR



(4) (5)



(6) (7)



(8) (9)

a; R = H
b; R = Me
c; R = *p*-MeC$_6$H$_4$SO$_2$
d; R = CO$_2$Me

Irradiation (dilute solution, CHCl$_3$, −20 °C, quartz, dry N$_2$) of the *N*-methoxycarbonyl adduct (**4d**) effected smooth decarbonylation to the diene (**5**) which fragmented to give 1,4-dimethyl-2,3-diphenylbenzene and *N*-methoxycarbonyl-Δ^2-azetine (**3d**) which was isolated by short path distillation as a colourless liquid [*m/e* 113; ^{1}H n.m.r. (CDCl$_3$) δ 3·72 (s, OMe), 4·47 (br s, $w_{\frac{1}{2}}$ 2·8 Hz, 4-H), 5·65 (br s, $w_{\frac{1}{2}}$ 3·8 Hz, 3-H), and 6·64 (br s, $w_{\frac{1}{2}}$ 3·1 Hz, 2-H). The *N*-tosyl azetine (**3c**) [*m/e* 209; ^{1}H n.m.r. (Me$_2$SO) δ 2·44 (s, CMe), 4·08 (s, 4-H), 5·70 (br s, $w_{\frac{1}{2}}$ 3·1 Hz, 3-H), 6·74 (br s, $w_{\frac{1}{2}}$ 3·2 Hz, 2-H), and 7·50 and 7·80 (dd, *J* 8 Hz, ArH)] was prepared (33% isolated yield) from irradiation of (**4c**). Similar attempts to produce the parent azetine (**3a**) or its *N*-methyl derivative (**3b**) were unsuccessful, even at temperature as low as −50 °C.

The azetine (**3d**) is thermally stable below 50 °C, but undergoes rapid polymerisation above this temperature. The enamine character of this compound is suppressed since an adduct was not obtained on reaction with tetracyanoethylene or with 1,3-diphenylisobenzofuran.‡ Compound (**3d**) did react with 3,6-di(2-pyridyl)-*s*-tetrazine, however, at room temperature to yield, predominantly, the pyridazine (**7**), m.p. 124 °C, which is presumed to arise *via* aromatisation of the intermediate dihydropyridazine (**6**), involving scission of the azetidine ring. Treatment of (**3d**) with acid (5% aq. HCl) slowly gave ($t_{\frac{1}{2}}$ 18 h, room temp.) the ring-opened aldehyde (**9**).§ This reaction is dramatically accelerated ($t_{\frac{1}{2}}$ 30 min at 0 °C) by irradiation. This is best explained by photochemical hydration of the $\Delta^{2,3}$-double bond to form (**8**), followed by ring-opening. This photohydration has precedent in other systems.[8]

The methylene protons appear as a singlet in the ^{1}H n.m.r. spectra of the azetines (**3c**) and (**3d**), which could be ascribed either to planarity of the compounds or to rapid inversion at the nitrogen atom. Our results of INDO MO calculations indicate a non-planar geometry for the azetine (**3a**) in which the NH bond makes an angle of 48° with the molecular plane. However rapid inversion is expected as the barrier is calculated to be only *ca.* 4·2 kcal mol^{-1}.

The tosyl compound (**3c**) is a potential precursor to azete, but treatment with t-butoxide or attempts to induce photoelimination have so far yielded no products immediately associated with azete.

(*Received*, 22*nd June* 1977; *Com.* 625.)

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‡ *Cf.* cycloadducts readily formed from thiet 1,1-dioxide (ref. 2).

§ Thiete has been observed to behave similarly (ref. 1).

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