Thiazepine Photochemistry. The Photoaddition of Methanol Involving Participation by Sulphur

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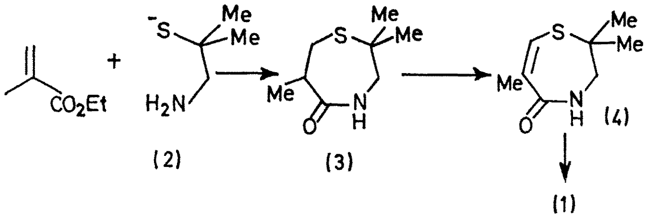
Summary Irradiation of 5-ethoxy-2,3-dihydro-2,2,6-trimethyl-1,4-thiazepine (**1**) leads to dimerization in aprotic media and solvent addition in methanol, with ring contraction *via* participation of sulphur; under the same conditions, the hydrochloride of (**1**) adds methanol without rearrangement.

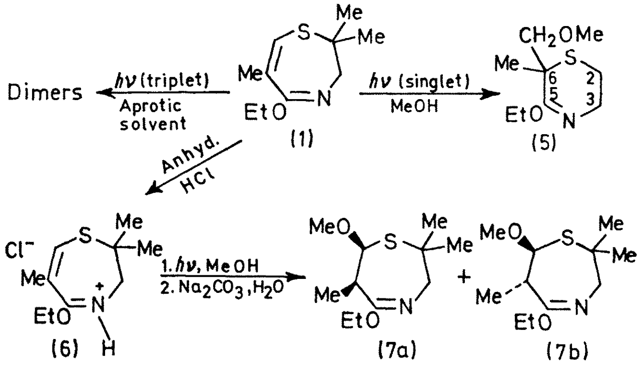
THE possibility of rearrangement of dihydrothiazepines [*e.g.*, (**1**)] to the thiazabicyclo[3,2,0]hept-6-ene-system, potential precursors of penicillin analogues, and our interest in the effect of heteroatoms on excited-state reactivity led us to study the photochemistry of (**1**) and related molecules. In contrast to many hetero-substituted derivatives of cyclohepta-1,3-diene,[1] (**1**) does not give the bicyclo[3,2,0]-isomer under a variety of irradiation conditions, but dimerizes *via* a triplet excited state in aprotic solvents, and in methanol rearranges with addition of solvent; addition without rearrangement is observed with the hydrochloride of (**1**).

The thiazepine (**1**) was prepared from the 1-amino-2-methylpropane-2-thiolate (**2**) and ethyl methacrylate[2,3] giving the perhydrothiazepinone (**3**), m.p. 107—108°.† Chlorination of (**3**) with sulphuryl chloride in dichloromethane at −30° followed by warming to 25° and then spontaneous loss of HCl gave tetrahydrothiazepinone (**4**) (94%), m.p. 134—135°, which was then converted by triethyloxonium tetrafluoroborate in dichloromethane into (**1**) (80%), b.p. 58—60°/0·35 Torr.



Irradiation of (**1**) [λ_{max} (hexane) 284 nm (ϵ 4500)] in a variety of aprotic solvents (ether, dichloromethane, or hexane) over the temperature range −50 to +35° and concentrations greater than 10^{-4} M, with a medium-pressure (Hanovia 450 W) or low-pressure (Rayonet 253·7 nm) lamp (Vycor or Pyrex filters) gave in every case a mixture of dimers of (**1**).‡ That the dimerization arises *via* the triplet excited state of (**1**) is indicated by the mixtures (i.r., n.m.r., and t.l.c.) resulting from direct irradiation in ether (Pyrex filter) compared to photosensitization with thioxanthone (E_T 65·5 kcal mol^{-1})[4] and a uranium glass filter (50% transmission at 350 nm).[5] No reaction of (**1**) occurs on prolonged irradiation (uranium glass filter) in the absence of sensitizer.

In methanol, the singlet excited state of (**1**) is trapped by the solvent[6] and rearranges to the six-membered heterocycle, (**5**), which is isolated by short-path distillation and preparative g.l.c. (30% yield). The lowest triplet state is clearly not involved because photosensitization with thioxanthone in methanol produces neither (**5**) nor any other products incorporating the solvent but only the mixture of dimers that is observed in aprotic media. The mass spectrum of (**5**) shows the molecular ion at *m/e* 231·1297 (calc. for $C_{11}H_{21}NO_2S$ is 231·1292) and the base peak at *m/e* 186·0952 due to loss of the side chain $-CH_2\cdot$OMe [loss of C_2H_5O from (**1**) is not observed]. In addition to the ethyl ether pattern and the *gem*-dimethyl singlet, the ^{1}H n.m.r. spectrum of (**5**) shows signals at δ 3·60 (2H, s, $CH_2\cdot$OMe), 3·49 and 3·23 (2H, AB quartet, *J* 12 Hz, $CH_2\cdot$N), 3·32 (3H, s, MeO), and 1·50 p.p.m. (6H, s, Me at C-6). A simple degradation *via* reduction with lithium aluminium hydride,[7] acetylation, and desulphurization converted (**5**) into *N*-isobutyl-*N*-(2-methyl-3-methoxypropyl)acetamide which was identical with an authentic sample prepared by unambiguous synthesis.



A different and more efficient addition of methanol occurs upon irradiation of the hydrochloride (**6**). Direct irradiation of (**6**) [λ_{max} (MeOH) 305 nm (ϵ 4000)] in methanol followed by treatment with aqueous sodium carbonate produces a mixture of epimers, (**7a**) (40%) and (**7b**) (60%) in 96% combined yield. Tentative structure assignments of *trans*-configuration for (**7b**) and *cis*- for (**7a**) are based on coupling constants for the doublets due to S–CH–O [δ 4·01 (*J* 7 Hz) in (**7b**); 4·10 (*J* 2 Hz) in (**7a**)] using the Karplus rule[8] and inspection of Dreiding models. The epimeric relationship of (**7a**) and (**7b**) is verified by the formation of one product, the dihydrothiazepine (**1**), from both isomers by base-induced elimination of methanol. Finally, the carbon skeleton in isomers (**7**) was determined by degradation to *N*-isobutyl-*N*-(2-methyl-3-methoxypropyl)acetamide as for (**5**).

A detailed understanding of the mechanisms of these

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† All new compounds were satisfactorily characterized by analyses and by i.r. and n.m.r. spectroscopy.

‡ The mixture is non-crystalline, inseparable by t.l.c., and decomposes on attempted high-vacuum distillation or g.l.c.; the mass spectrum of a fraction obtained by preparative t.l.c. showed peaks consistent with dimers of (**1**) (M^+, *m/e* 398) and indicated the absence of monomers (*m/e* 199) and higher oligomers.

photoadditions will require more information about the excited states available for (**1**) and (**6**), or closely related molecules. Clearly, the fact that methanol is added during irradiation suggests that the excited state involves a polarized π-system. The striking difference in products from irradiation of (**1**) compared to those from (**6**) can be explained by opposite polarizations in the excited state. For example, the $n \rightarrow \pi^*$ excited state of (**1**) can be represented by classical valence bond structure (**8**). Participation by the non-bonding electrons on sulphur would lead to the sulphonium ion (**9**), then protonation and attack by methanol would afford the ring-contracted product, (**5**). Irradiation of the iminium salt (**6**) appears to polarize the molecule so as to increase electron density at the nitrogen cation, with corresponding electron deficiency at the carbon atoms in the π-system, as in (**10**). A possible intermediate in the ionic addition of methanol to (**10**) is the protonated enamine (**11**) (not detected) which could lead to the observed products, (**7a**) and (**7b**) by a simple prototropic shift.

The study of (**1**) and related heterocycles is continuing in order to delineate the perturbations on normal hydrocarbon photoreactions due to the presence of heteroatoms.

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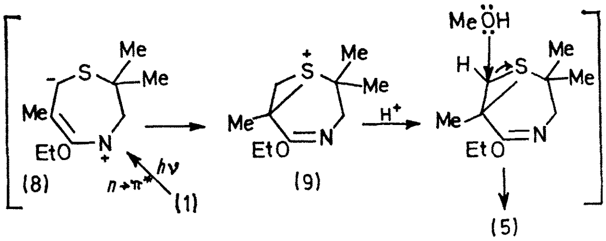

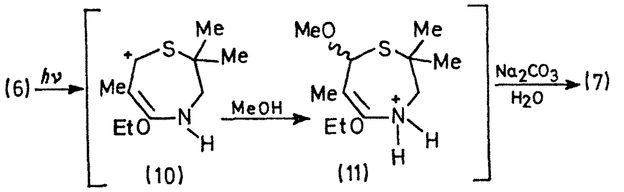

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