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PHOTOCYCLOADDITIONS TO 3-PHENYL-1,2-BENZISOTHIAZOLE

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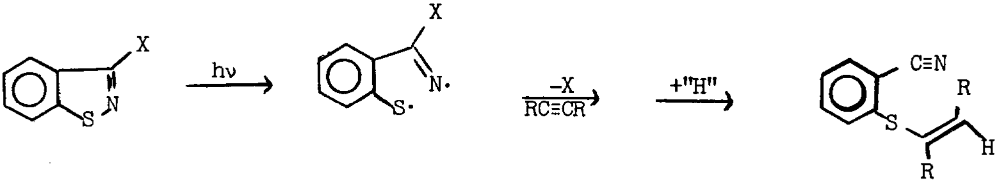
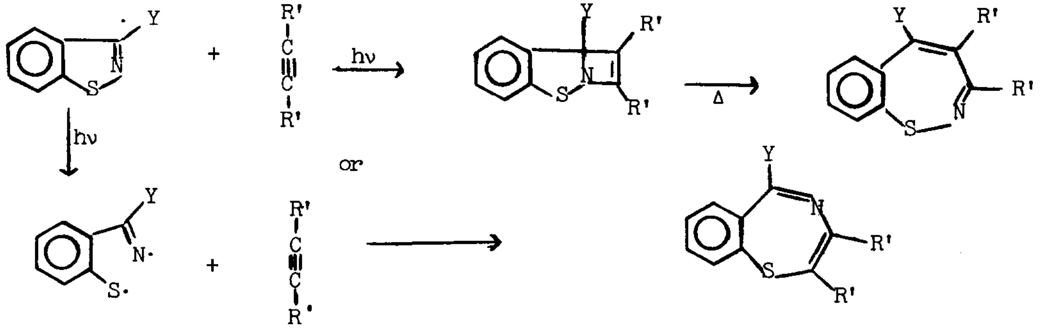
Summary: 3-Phenyl-1,2-benzisothiazole (1) gave upon irradiation in the presence of ethyl vinyl ether 3-ethoxy-5-phenyl-2,3-dihydro-1,4-benzosothiazepine (II) in high yield (80%).

In the previous communication[1] we reported that π [2+2] photocycloadditions between deactivated alkynes and benzisothiazole lead to linear addition products as well as benzo(b)-thiophenes. These products resulted, we suggested, from homolytic cleavage of the S-N bond of the benzisothiazole followed by atom transfer of the labile H or Cl originally located at the 3-position (1). As we have previously indicated, these results are in direct contrast with the proposed model systems, benzo(b)thiophene and indole.[2,3]

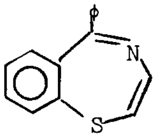


(1)

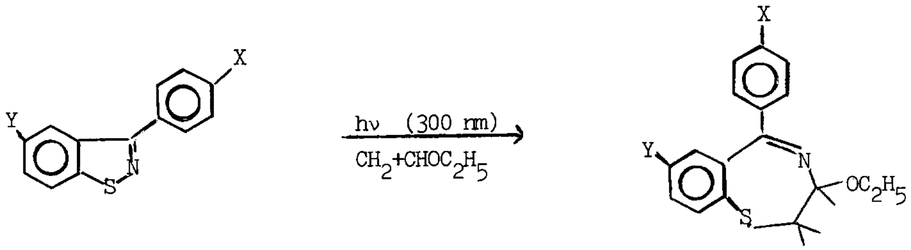
In view of the potential synthetic route to benzothiazepines afforded either by π[2+2] cycloaddition and thermal ring opening (2) or by concerted addition of the biradical to alkynes (3) benzisothiazoles with the 3-position blocked with non-dissociable functional



groups have now been examined. As per our expectation, 3-phenylbenzoisothiazole and its derivatives give direct cycloaddition and afford one step high yield [>80%] inlets to 1,4 benzothiazepine derivatives. We believe this the first one step route to these important, potentially pharmacologically active, systems.



3-Phenylbenzisothiazole[4] gave no photochemical reaction with acetylene dicarboxylate. However, ethyl vinyl ether, when irradiated with 3-phenylbenzisothiazole, produced 3-ethoxy-5-phenyl-2,3-dihydro-1,4-benzothiazepine (IIa) in 80% yield, this being the first example of 2+2 cycloaddition to an isothiazole which gave a benzothiazepine.

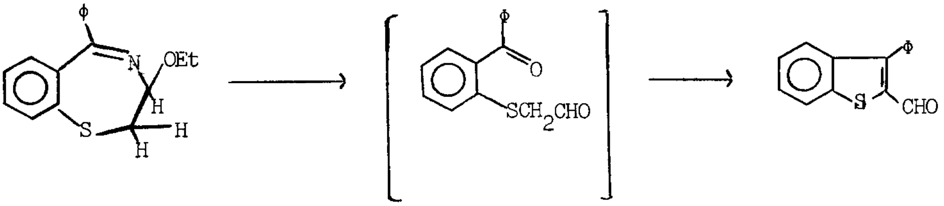


I a) X=H; Y=H
b) X=CH_3; Y=H
c) X=H; Y=Cl

II a)
b)
c)

Substituted 1,2-benzisothiazoles[5] were irradiated in the presence of ethyl vinyl ether (2×10^{-2}M) purged with nitrogen at 300 nm for 90 to 150 hrs. After the evaporation of ethyl vinyl ether the photomixture was chromatographed on silica gel column. The yield on isolated product was, in all cases, between 70 and 80%.

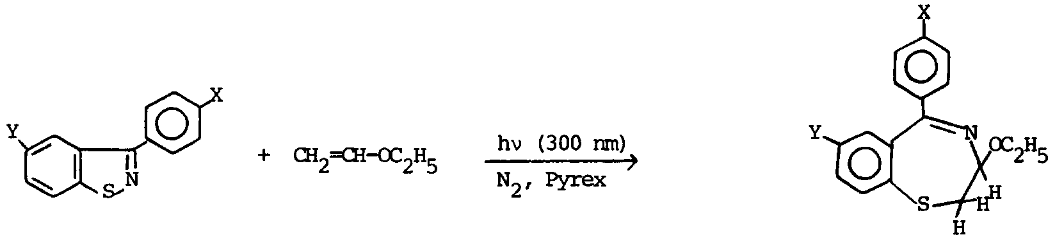
Structures (IIa-c) were suggested by spectroscopic and analytical evidence, Table I, and the structure of the adduct IIa was confirmed by a crystal structure.[6] Chemical evidence for IIa was as follows: IIa was stable to dilute HCl, and to concentrated HCl at room temperature, but when heated to reflux with 3N HCl it produced 3-phenylbenzo(b)thiophene-2-carboxaldehyde in virtually quantitative yield[7] (4), we presume by hydrolysis of the animal followed by acid catalyzed ring closure.



(4)

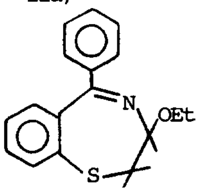
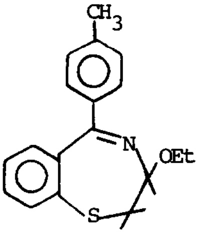
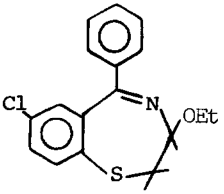
Table I

Photoadditions to 3-Arylbenzisothiazoles



I a) X=H; Y=H
b) $X=CH_3$; Y=H
c) X=H; Y=Cl

II a)
b)
c)

Dihydrobenzo-thiazepine	M.P. (°C)	NMR, δ ($CDCl_3$)
IIa)* 	134-5	4.50 (dd, 1H, J=6, 13Hz) 3.20-4.05 (m, 4H) 1.24 (t, 3H, J=8.5Hz) 7.06-7.73 (m, 9H)
IIb)* 	94.5-95	4.48 (dd, 1H, J=6, 13Hz) 3.19-4.03 (m, 4H) 2.38 (s, 3H); 1.23 (t, 3H, J=8.5Hz) 7.06-7.70 (m, 8H)
IIc)* 	126.5-127	4.47 (dd, 1H, J=6, 13Hz) 3.20-4.04 (m, 4H) 1.25 (t, 3H, J=9Hz) 7.11-7.72 (m, 8H)

* All new compounds gave satisfactory elemental analyses.

The mechanism of these cycloadditions is unclear at this juncture. On the one hand the reactions parallel those of biradicals. Yet electron transfer producing 3-phenylbenzisothiazole radical anion may occur with electron rich olefins such as ethyl vinyl ether. However, electron poor alkenes also give cycloaddition products. Thus competitive processes the rates of which are controlled by the ionization potential of the olefin or the alkyne seem worthy of consideration. The reactions appear not to be triplet reactions since they are not sensitized by either benzophenone (E_t=69 kcal/mole) or thioxanthone (E_t=59 kcal/mole)[8].

Unlike 3-phenylbenzisoxazole which rearranges photochemically to 3-phenylbenzoxasole,[9] there is no evidence for such a rearrangement of 3-phenylbenzisothiazole when irradiated in ether. More experiments are in progress to ascertain the mechanism of these cycloaddition processes.

Acknowledgement

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References

1. M. Sindler-Kulyk and D. C. Neckers, Tet Letters, previous communication
2. A. H. A. Tinnemans and D. C. Neckers, J. Org. Chem., 43, 2493 (1978)
3. P. D. Davis and D. C. Neckers, J. Org. Chem., 45, 456 (1980)
4. A. Ricci and A. Martani, Ann. Chim. (Roma) 53, 577 (1963)
5. Ib prepared as Ia; Ic prepared by the method of K. Fries, K. Eishold, B. Vahlberg, Ann. Chem., 454, 264 (1927)
6. To be published in detail later. M. Sindler-Kulyk, D. C. Neckers, and J. R. Blount, unpublished.
7. Identical in every respect with the authentic synthesized product (R. P. Dickinson, B. Iddon, R. G. Sommerville, Int. J. Sulfur Chem., 8(2), 233 (1973)
8. Measured from its phosphorescence spectrum in frozen ethanol glass.
9. K. H. Grellmann and E. Tauer, J. Photochem., 6, 365 (1977)

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