HETEROCYCLES, Vol 20, No. 7, 1983

PHOTOCHEMICAL REACTIONS OF CONDENSED AZOLES WITH DIMETHYL ACETYLENEDICARBOXYLATE IV[1)]

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Abstract ---- Adducts of azole derivatives and dimethyl acetylenedicarboxylate on irradiation are described.

Previously, it was reported from our laboratory that the reaction of dimethyl acetylenedicarboxylate(DMAD) with benzothiazole[2)](1) in MeOH afforded tetramethyl 1H-pyrido[2,1-b]benzothiazole-1,2,3,4-tetracarboxylate and dimethyl 4-formyl-2,3-dihydro-1,4-benzothiazine-2,3-dicarboxylate in 5 and 8% yield, respectively.
A similar reaction in DMF, however, gave 4aH-pyrido[2,1-b]benzothiazole-2,3,4,4a-tetracarboxylate in 10% yield. Recently, the formation of the tricyclic system, [1,4]benzoxazine[2,3-b]pyran, was observed[3a)] in the reaction between 2-unsubstituted benzoxazole (2) and DMAD in water.
Reaction of a 2-alkylbenzoxazole (5) with DMAD in EtOH or t-BuOH afforded[3b)] a tricyclic product with the acepino[2,1-b]benzoxazole system, together with the hydration, solvation and ring-opened products. The latter reaction under irradiation, however, did not give the azepinobenzoxazole product but mainly the ring-opened aminophenol derivative. Apparently, the reactions with azoles and DMAD under photochemical conditions proceed rather differently than those without irradiation giving rise to different results. We thus investigated the reactions of DMAD with benzo(or naphtho)thiazoles and benzo(or naphtho)oxazoles under irradiation.

I. With 2-Unsubstituted Benzothiazole (1) and Benzoxazole (2).

In a typical experiment, a mixture of 1 (1.63g, 10 mmoles) and DMAD (4.26g, 30mmoles) in acetone (or MeCN, 350ml) was irradiated for 7-8 hours under N_2 with a 400 W high pressure mercury arc lamp through a pyrex filter. The only product detected in the reaction mixture was the known2) tetramethyl 4aH-pyrido[2,1-b]-thiazole-2,3,4,4a-tetracarboxylate (3) which was isolated in 27-32% yield. When benzoxazole (2) instead of 1 was employed in a similar reaction, only the known4) oxazine 4 was obtained in 27% yield.

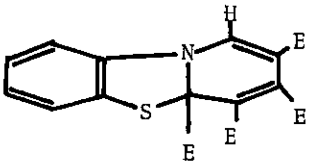
II. With 2-Methyl(or ethyl)benzothiazoles (5a-c) and 2-Methylbenzoxazole(5d).

When 2-substituted benzothiazoles (5a-c) were irradiated with DMAD in acetone (or MeCN), the corresponding tricyclic adducts with the azepino[2,1-b]-benzothiazole system, 6a (mp 213°C, 31%)4a), 6b (mp 176°C, 28%) and 6c (mp 185°C, 32%4a)) were obtained, respectively, after chromatographic purification on a silica gel column using $CHCl_3$ as the eluent. Compound 6b has the following mass and ^1H nmr spectral data which are consistent with the corresponding structure shown in Chart 1. 6b ; m/e 447(M^+), ^1H nmr($CDCl_3$) δ ; 2.42(3H, s, CH_3), 3.60 3.73, 3.80, 3.83 (each 3H, s, $COOCH_3$x4), 5.15 (1H, s, $\supset$C=CH-), 5.45 (1H, d, J=6.0 Hz, =NCHE-C$\underline{H}$E-), 5.97(1H, d, J=6.0 Hz, =NC$\underline{H}$E-CHE-), 6.80-7.18(3H, m, aromatic protons).

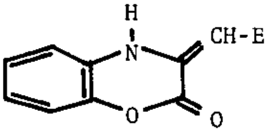
2-Methylbenzoxazole (5d), on the other hand, afforded only the known3b) aminophenol derivative 7 in 38% yield. In the presence of a small amount of water (3.5 ml H_2O in 350 ml acetone), the yield of 7 increased to 60-70%. No azepinobenzoxazole was obtained from the reaction mixture.

III. With 2-Methylnaphtho[1,2-d]thiazole (8a), 2-Methylnaphtho[2,1-d]-thiazole (8b) and 2-Methylnaphtho[1,2-d]oxazole (8c).

Compound 8a and its[2,1-d]isomer (8b), when treated with DMAD under irradiation, afforded 11,12-dihydro-9,10,11,12-tetramethoxycarbonylnaphtho[1',2':4,5]thiazolo-[3,2-a]azepine (9a), mp 243-245°C, 32%, m/e 483 (M^+), ^1H nmr ($CDCl_3$) δ ; 3.62, 3.63, 3.75, 3.80 (each 3H, s, $COOCH_3$x4), 5.24 (1H, s, $\supset$C=C$\underline{H}$-), 5.45 (1H, d, J=6.0, =NCHE-C$\underline{H}$E-), 6.90(1H, d, J=6.0 Hz, =NC$\underline{H}$E-CHE-), 7.24-8.48 (6H, m, aromatic protons), and its isomer 9b, mp 173-175°C, 28%, m/e 483 (M^+), ^1H nmr ($CDCl_3$) δ ; 3.53, 3.56, 3.75, 3.80 (each 3H, s, $COOCH_3$x4), 5.25(1H, s, $\supset$C=C$\underline{H}$-), 5.46(1H, d, J=6.0 Hz, =HCHE-C$\underline{H}$E-), 6.06(1H, d, J=6.0 Hz, =NC$\underline{H}$E-CHE-), 7.30-7.90 (6H, m, aromatic protons), respectively.



E=$COOCH_3$ 3



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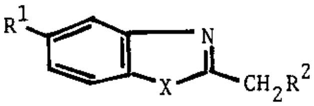
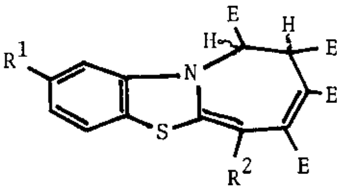
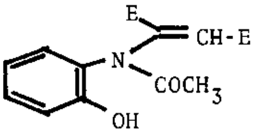


5a X=S, R^1=H, R^2=H
b X=S, R^1=CH_3, R^2=H
c X=S, R^1=CH_3, R^2=CH_3
d X=O, R^1=H, R^2=H



6a R^1=H, R^2=H
b R^1=CH_3, R^2=H
c R^1=H, R^2=CH_3



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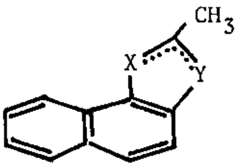
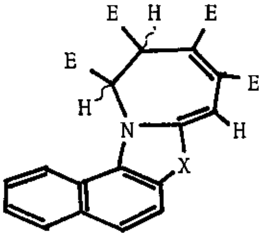
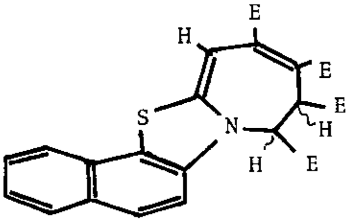


8a X=N, Y=S
b X=S, Y=N
c X=N, Y=O



9a X=S
c X=O



9b

Chart I

2-Methylnaphtho[1,2-d]oxazole (8c), in a similar manner, was converted into the cyclic product 9c in 31% yield ; mp 206-208°C, m/e 467 (M^+) ^1H nmr ($CDCl_3$) δ ; 3.56, 3.73, 3.80, 3.86 (each 3H, s, $COOCH_3$x4), 5.05 (1H, s, ≥C=CH-), 5.55 (1H, d, J=6.0 Hz, =NCHE-CHE-), 6.63 (1H, d, J=6.0 Hz, =NCHE-CHE-), 7.33-8.30 (6H, m, aromatic protons). The structures 9a and 9c were assigned on the basis of the low field shift of one of the aliphatic protons (9a, δ, 6.90; 9c, δ, 6.63) compared with the one of 9b (δ, 6.06) in the ^1H nmr spectrum. This paramagnetic shift is apparently caused by an anisotropic effect of the naphthalene ring due to close proximity of the proton on the azepine moiety.

It should be noted that unlike 2-methylbenzoxazole(5d) 2-methylnaphthoxazole (8c) gave only the cyclic product 9c, and no product corresponding to 7 was obtained. Note also that the reaction of azoles with DMAD under irradiation gave only single product.

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Received, 28th February, 1983