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Photocycloaddition of Uracils with Dimethyl Acetylenedicarboxylate

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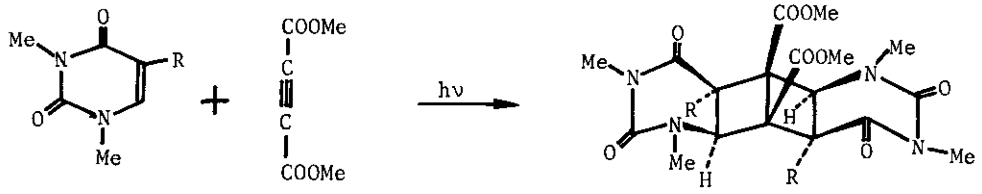
Abstract — Photocycloaddition of dimethyl acetylenedicarboxylate (DMAD) with 1,3-dimethyl uracils gave new 2 + 2 + 2 cycloaddition products which contain a bicyclo[2.2.0] hexane system in the molecule.

Acetylenic esters are useful reagents for the synthesis of heterocyclic compounds.[1] Photochemical cycloaddition of an acetylenic ester with nucleic acid bases, however, has not been described. This report deals with the first photochemical cycloaddition of an acetylenic ester with nucleic acid bases.

A mixture of 1,3-dimethyl uracil (Ia, 426 mg, 3 mmol) and dimethyl acetylenedicarboxylate (DMAD, 420 mg) in acetone (350 ml) was irradiated for 12 hours under nitrogen at 20°C (400W high pressure mercury arc lamp in a pyrex cell). From the reaction mixture, in addition to the known tetramer of DMAD, bicyclo[2.2.2]octa-2,5,7-triene-1,2,3,4,5,6,7,8-octacarboxylic acid octamethyl ester[2] (62 mg, m.p. 161-162°C), a nitrogen containing product (76 mg, m.p. 283-285°C) was obtained. The structure of the latter was assigned to the trans-trans-anti derivative IIa on the basis of the following data: High resolution mass spectrum showed m/e 422,1455 (M^+) (calcd. for $C_{18}H_{22}N_4O_8$: 422, 1437). In the ^1H n.m.r. ($CDCl_3$) spectrum of this product, only three methyl signals appeared at δ 2.79 (NMe), 3.10(NMe) and 3.80(COOMe) and two vicinal proton signals were found at δ 4.17 and 4.74 as AB quartets (J_{AB} 14 Hz). The integration was 3:3:3:1:1. These data indicate that there are pairs of equivalent NMe, CO_2Me and vicinal protons in the molecule. The ^{13}C n.m.r. ($CDCl_3$, Me_4Si) showed only eight signals at δ28.4, 34.8 (NMe), 51.4, 53.5, 53.9 ($CO_2\underline{Me}$ ≡CH ≡C-), 151.5, 164.8 and 168.9 (C=O), indicating each of the all carbon atoms in the molecule is paired with an equivalent counterpart. These data exclude the isomeric trans-trans-syn structure (III) in which the methyl esters should be non-equivalent in both the ^1H and ^{13}C n.m.r. spectra. In addition, the

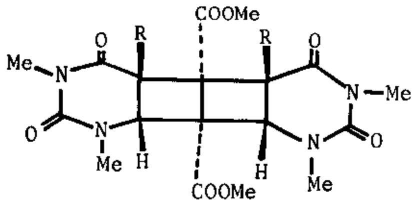


I

a ; R=H
b ; R=CH_3

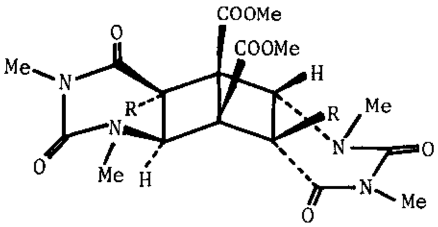
II

trans–trans–anti



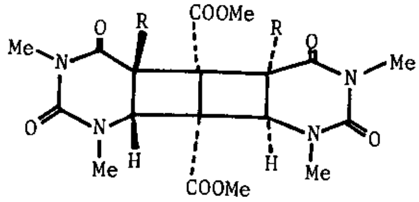
III

trans–trans–syn



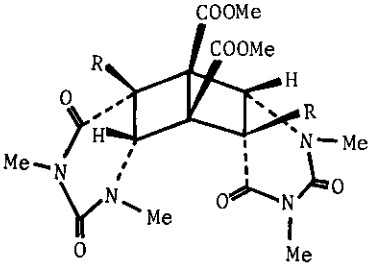
V

trans–cis–anti



IV

trans–cis–syn



VI

cis–cis–anti

ring carbons attached to carboxylic esters should also be non-equivalent. The trans-cis-syn (IV) and trans-cis-anti (V) isomers are also ruled out since in these structures all the protons and carbons are nonequivalent. The cis-cis-anti structure VI can also be eliminated, since studies with molecular model showed that such an endo structure is unstable. Furthermore the close spatial proximity of the two NMe groups and the carbonyl oxygens in such an endo structure would cause the NMe hydrogens to resonate at low field in the ^{1}H n.m.r.[3]; however, a lower field chemical shift was not observed.

Photochemical cycloaddition of 1,3-dimethylthymine (Ib, 462 mg, 3 mmol) with DMAD under similar conditions was also studied. The 2:1 addition product (IIb) was obtained in 18.8% yield as colorless crystals (127 mg, m.p. 300°C). The ^{1}H n.m.r. ($CDCl_3$) spectrum showed five singlets at δ 1.60 (CMe), 3.08, 3.15 (NMe), 3.72 (OMe) and 3.90 ($\equiv$CH) with an intensity ratio of 3:3:3:3:1. In the ^{13}C n.m.r. ($CDCl_3$, Me_4Si) spectrum ten signals were observed at δ18.5 (CMe), 28.3, 35.6 (NMe), 50.3, 52.2, 60.2, 60.5 (OMe and ring C), 151.5, 166.2 and 169.7 (C=O). The high resolution mass spectrum showed m/e 450.1737 (M^+) (calcd. for $C_{20}H_{26}N_4O_8$: 450.1753). All these data are consistent with the trans-trans-anti structure IIb.

Thus, photocyclization of dimethyluracil (Ia) or dimethylthymine (Ib) with DMAD led to a new 2 + 2 + 2 cycloaddition product which contains a bicyclo[2.2.0]hexane system.

Acknowledgement and References

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