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PHOTOCHEMICAL CYCLOADDITION OF 5-METHYL-2,3-DIHYDRO-3-FURANONE TO OLEFINS

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Photochemical reactions of 5-methyl-2,3-dihydro-3-furanone 1 with methyl acrylate, vinyl acetate, and cyclopentene have been examined and found to give adducts having 4-oxa-bicyclo[3.2.0]heptanone structure in all the cases. Orientation and stereochemistry of the adducts were deduced on the basis of NMR studies using shift reagent. Stereospecificity was observed with the head-to-head adducts of the acyclic olefins. The cyclopentene adducts were transformed to a bicyclic enonealdehyde 22 by subsequent modification.

Photochemical cycloaddition reaction of cyclenone to olefin has found substantial use in synthesis in recent years2), but there have been only few studies for the photoannelation reaction of 4-oxa-cyclenone with olefin3). We wish to describe the photochemical reactions of 5-methyl-2,3-dihydro-3-furanone 14) with olefins leading to 4-oxa-bicyclo[3.2.0]heptanones.

A solution of 1 and large excess of methyl acrylate in benzene was irradiated with a 500 W high pressure mercury lamp through a pyrex filter for 24 hours under nitrogen atmosphere. After evaporation of the solvent and excess olefin, the product was extracted with ether from the polymeric residue formed during irradiation and distilled at 95-105°(bath temp.)/6 mm. From the VPC analysis, this product, obtained in 65 % yield, was found to consist of three isomeric 1:1 adducts 2, 3, and 4 in the ratio of 6:3:1, no other products being detectable.

The head-to-head orientation of the major adduct 25), which was isolated by preparative VPC, was deduced on the basis of the spin-spin splitting of the signals due to the protons on the cyclobutane ring in the NMR spectrum taken with Eu(dpm)$_3$ [δ (CCl$_4$+ Eu(dpm)$_3$) 3.27(2H, d, J=8 Hz), 4.01(2H, m)]6). The higher signals are attributable to the methylene protons at C-6 since irradiation at this region leads the lower signals to an AB type quartet(J=4 Hz) attributable to the methine protons at C-1 and C-7.

The configuration of the methoxycarbonyl group in 2 was established to be exo from the following experiments. 2 was reduced with NaBH$_4$ to give selectively an endo-alcohol 5 [ν (film) 3420, 1725 cm^{-1}; δ (CCl$_4$) 1.31(3H, s), 2.26(2H, d, J=8 Hz), 2.72(dd, J=8, 4.5 Hz), 3.07(td, J=8, 4.5 Hz), 3.55(dd, J=9, 8 Hz), 3.66(3H, s), 4.01(dd, J=9, 7 Hz), 4.37(td, J=8, 7 Hz)]. 5 was recovered when this was subjected to alkaline hydrolysis in aqueous methanol and the solution of resulting carboxylate was subsequently acidified with conc. sulfuric acid. On the other hand, after heating with NaOMe in methanol, a γ-lactone 6 [ν (film) 1770 cm^{-1}; δ (CCl$_4$) 1.32(3H, s), 2.12(dd, J=13, 3.5 Hz), 2.47(ddd, J=13, 9.5, 1.5 Hz), 2.88(ddd, J=9.5, 7.5, 3.5 Hz), 3.17(br.t, J=7.5 Hz), 3.72(dd, J=11, 3 Hz), 4.02(d, J=11 Hz), 5.02(dd, J=7, 3 Hz)] was obtained by the same procedure with 5.

The minor adducts, 3 and 4, were only isolated in the form of corresponding endo-alcohols, 7 [mp 54-5°; ν (KBr) 3430, 1725 cm^{-1}; δ (CCl$_4$) 1.19(3H, s), 2.03(Hb, dd, J=8.5, 6 Hz), 2.03(Hc, dd, J=9.5, 6 Hz), 2.50(Hd, br.q, J=6.5 Hz), 3.06(Ha, td, J=9, 1 Hz), 3.62(dd, J=9.5, 7.5 Hz), 3.66(3H, s), 4.07(dd, J=9.5, 6.5 Hz), 4.38(ddd, J=8, 7.5, 6.5 Hz)] and 8 [ν (film) 3450, 1730 cm^{-1}; δ (CCl$_4$) 1.34(3H, s), 1.87(Hc, ddd, J=13, 9.5, 9 Hz), 2.40(Hb, ddd, J=13, 7.5, 6 Hz), 2.62(Hd, br.q, J=7 Hz), 3.01(Ha, ddd, J=9.5, 7.5, 1 Hz), 3.66(3H, s), 3.68(dd, J=9, 7 Hz), 3.88(dd, J=9, 6 Hz), 4.29(td, J=7, 6 Hz)] through NaBH$_4$ reduction of the mixture and chromatographic separation. These were found to be diastereomeric isomers at the carbon bearing methoxycarbonyl group, since 1:1 equilibrium mixture was obtained starting from one isomer on heating with NaOMe in methanol. From the NMR spectral data, the head-to-tail structures for these compounds are evident.

In order to establish the stereochemistry at C-6, $\Delta\delta$ values of protons on the cyclobutane ring were compared in the NMR spectra of 7 and 8 measured with same amount of Eu(dpm)$_3$ as the shift reagent (TABLE).$^{7)}$ The larger paramagnetic shift observed for Ha of 7, compared with that of 8, could be rationalized in terms of the strong affinity of the shift reagent for the endo-hydroxy group at C-2 having same orientation with Ha of 7. The marked difference between $\Delta\delta$ value of Hb of 7 and that of 8 is explainable on the assumption that the latter would suffer from larger shift than the former because of having the methoxycarbonyl group, a Lewis base, in same direction. Thus, the stereochemistry of methoxycarbonyl group was assigned to be exo for 7 and endo for 8.

With similar procedure, the irradiation of 1 with vinyl acetate afforded three isomeric 1:1 adducts, 9 [ν (film) 1745, 1240 cm^{-1}; δ (CCl$_4$) 1.51(3H, s), 1.98(3H, s), 2.50(d, J=8 Hz), 2.52 (dd, J=8, 3 Hz), 3.00(dd, J=8,3 Hz), 4.27(2H, s), 4.92(q, J=8 Hz)], 10 [ν (film) 1745, 1240 cm^{-1}; δ (CCl$_4$) 1.40(3H, s), 2.03(3H, s), 2.1–2.7(3H, m), 4.13(d, J=18 Hz), 4.23(d, J=18 Hz), 5.08(td, J=8, 1 Hz)], and 11 [ν (film) 1745, 1240 cm^{-1}; δ (CCl$_4$) 1.47(3H,s), 2.05(3H, s), 2.1–3.0(3H, m), 4.06(d, J=17 Hz), 4.23(d, J=17 Hz), 4.85(m)], in the ratio of 4:7:18 (80 % total yield). Also, no other products were detectable.

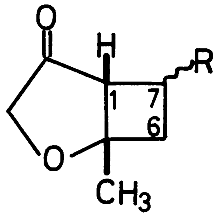
TABLE: $\Delta\delta$ Values (ppm)

Compound	7	8	19	20
Ha	0.62	0.41	0.61	0.33
Hb	0.71	1.24	1.41	0.60
Hc	0.56	0.52	1.02	0.78
Hd	0.61	0.65	—	>1.1

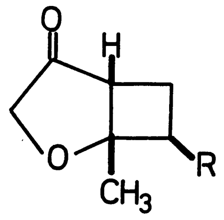
From the NMR spectral analysis, the head-to-head orientation of 9 was evident especially on the basis of the quartet signal at δ 4.92 due to the proton on the carbon bearing acetoxy group.

The structures of 10 and 11 were unambiguously revealed to be head-to-tail by NMDR spectral analyses of the corresponding alcohols, 12 [ν (CHCl$_3$) 3540, 1730 cm^{-1}; δ (CCl$_4$) 1.22(3H,s), 1.60 (ddd,J=11, 7, 4 Hz), 2.02(3H, s), 2.4(2H, m), 3.62(dd, J=9, 6 Hz), 4.00(dd, J=9, 6 Hz), 4.37(br.q, J=7 Hz), 4.88(br.t, J=8 Hz)] and 13 [ν (CHCl$_3$) 3600, 3450, 1730 cm^{-1}; δ (CCl$_4$) 1.31(3H, s), 2.03 (3H, s), 2.12(2H, br.t, J=7.5 Hz), 2.39(qd, J=7, 2 Hz), 3.64(t, J=8.5 Hz), 4.01(dd, J=8.5, 6.5 Hz), 4.34(dt, J=8.5, 7 Hz), 4.72(td, J=7.5, 2 Hz)], which were obtained by selective reduction of the ketones with NaBH$_4$, respectively. Furthermore, the endo-nature of the acetoxy group in 13 was suggested by the spin-spin splitting (J=2 Hz) observed with signals at δ 2.39 and 4.72, assignable to the protons in a cis-relatioship on C-1 and C-6.

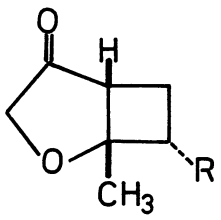
The assignment of the stereochemistry of 13 was also confirmed by the observation of an absorption band, ν (CCl$_4$, 0.007 M) 3540 cm^{-1}, due to the intramolecular hydrogen bonded hydroxy groups in the IR spectrum of the diol 15, derived from 13 by alkaline hydrolysis. In contrast, only an absorption band, ν (CCl$_4$, 0.007 M) 3625 cm^{-1}, of the free hydroxy groups was observed in the IR spectrum of the diol 14, derived from 12, supporting the exo-configuration of the acetoxy group in 12. Also, the configuration of the acetoxy group in 9 was revealed to be endo by the



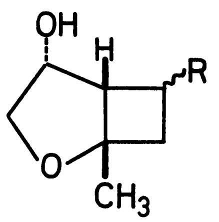
2: R=CO_2Me (exo)
9: R=OAc (endo)



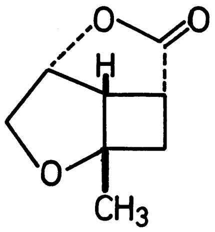
3: R=CO_2Me
10: R=OAc



4: R=CO_2Me
11: R=OAc



5: R=CO_2Me (exo)
16: R=OH (endo)



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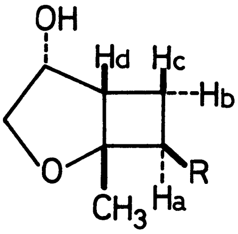
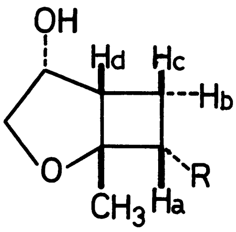
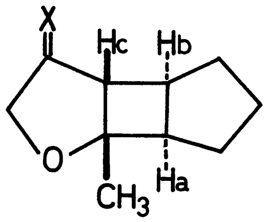


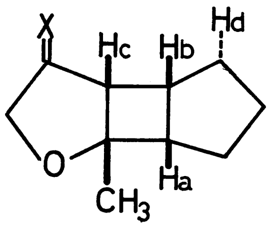
7: R=CO_2Me
12: R=OAc



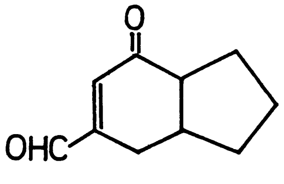
8: R=CO_2Me
13: R= OAc



17: X=O
19: $X=\,<^{OH}_{H}$



18: X=O
20: $X=\,<^{OH}_{H}$



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presence of an absorption band, ν (CCl_4, 0.007 M) 3530 cm^{-1}, due to the bonded hydroxy groups in the IR spectrum of the diol 16, obtained from 9 by $NaBH_4$ reduction and subsequent hydrolysis.

It should be noted that the only one isomer of two possible head-to-head adducts was actually formed in the photochemical reactions of 1 with the unsymmetrical olefins, *i.e.*, *exo* with methyl acrylate and *endo* with vinyl acetate, in contrast with the formation of both *exo* and *endo* isomers of the head-to-tail adducts. This might be related to the initial carbon-carbon bond formation at α-position of the enone 1 and to the dipolar nature of resulting diradicals[8]. Details are being investigated in this regard.

Two isomeric 1:1 adducts, 17 [ν (film) 1750 cm^{-1}; δ (CCl_4) 1.17(3H, s), 1.3-2.3(6H), 2.4-3.1 (3H), 3.98(d, J=16 Hz), 4.18(d, J=16 Hz)], and 18 [ν (film) 1750 cm^{-1}; δ(CCl_4) 1.39(3H, s), 1.1-2.1(6H), 2.2-3.0(3H), 3.99(2H, s)], were obtained by the photochemical reaction of 1 with cyclopentene in the ratio of 5:1 (78 %). The assignment of the stereochemistry was established on the basis of Δδ values (TABLE)[9] of the protons on the cyclobutane rings of the crresponding *endo*-alcohols, 19 and 20, derived from 17 and 18 by $NaBH_4$ reduction, respectively. An extraordinary shift (>1.1 ppm) was observed for a methylene proton of 20 assignable to *endo*-one on C-9 (Hd).

Treatment of the mixture of 17 and 18 with equimolar N-bromosuccinimide in refluxing CCl_4 for 1 hour followed by the addition of excess sodium acetate and a small amount of acetic anhydride at room temperature gave a mixture of 3-acetoxy derivatives of the adducts, 21 [ν (film) 1760, 1730, 1215 cm^{-1}]. This unstable acetates mixture was converted to a bicyclic enonealdehyde 22 [λ_{max}(EtOH)238 nm (11,300); ν ($CHCl_3$) 2720, 1695, 1680 cm^{-1}; δ (CCl_4) 6.45(s), 9.75(s)], a potential synthetic intermediate, in 40 % yield (from 17 and 18) by hydrolysis with sodium carbonate in aqueous dioxane and by subsequent treatment with methanolic sodium hydroxide at room temperature10).

The general scope and synthetic applicability of this reaction of the photoadducts of 1 are being investigated.

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References and Notes

1) A part of this work had been done during T. O.'s stay at the Department of Chemistry, University of Western Ontario (London, Canada), 1970-72. The authors wish to thank Prof. P. de Mayo, University of Western Ontario, for generous advices and supports.

2) For reviews, see P. E. Eaton, Accounts Chem. Res., 1, 50 (1968); P. de Mayo, ibid., 4, 41 (1971); P. G. Bauslaugh, Synthesis, 287 (1970).

3) H. Takeshita, R. Kikuchi, and Y. Shoji, Bull. Chem. Soc. Japan, 46, 690 (1973).

4) G. Casnati and A. Ricca, Tetrahedron Letters, 327 (1967).

5) Satisfactory analytical and/or mass spectral data are obtained for all the adducts.

6) $Eu(dpm)_3$ (25 mg) was added to a solution of 37 mg of 2 in 0.3 ml of CCl_4.

7) $Eu(dpm)_3$ (13 mg) was added to each solution of 7 and 8 in 0.3 ml of CCl_4 containing 30 mg of an isomer, respectively.

8) According to the "diradical reversion theory", the dipolar nature of the diradical has an important effect on the stereoselectivity and regioselectivity of the photochemical cycloaddition reaction. See Bauslaugh's review.

9) $Eu(dpm)_3$ (14 mg) was added to each solution of 19 and 20 in 0.3 ml of CCl_4 containing 30 mg of an isomer, respectively.

10) The direct treatment of the acetates with methanolic alkali gave the lower yield of 22, accompanied by the substitution of the acetoxy group with methanol.

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