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REGIOSELECTIVITY IN $[_{\pi}2 + _{\pi}2]$ PHOTOCYCLOADDITION REACTIONS BETWEEN CYCLOPENT-2-ENONES AND β-OXYSUBSTITUTED ACRYLATES

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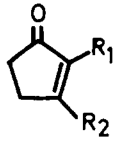
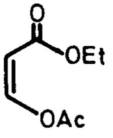
Our continuous interest in the $(_{\pi}2 + _{\pi}2)$ photocycloaddition reactions between cyclopent-2-enones and various alkenes for the synthesis of natural products[1,2,3], prompted us to study the regioselectivity of the reaction of the substrates 1, 2, 3 with the easily available acrylates 4[4] and 5[5]. It is clear that cleavage of the C_6-C_7-bond in the bicyclo[3,2,0]heptane derivatives 6 to 11 (the head-to-tail adducts; h-t)[6] would lead to prostanoid synthons with suitable substituted one- and two-carbon units for the elaboration of the PG side chains. During the course of the present study, Ogino and co-workers[7] described the reaction between compound 1 and methyl β-acetoxyacrylate in benzene.

Selective irradiation in the region of the n → π* band of the cyclopent-2-enones was achieved at 366 nm in a Rayonet photoreactor with a 10-fold excess of the alkene in pentane at 25°C or at -40°C. The reactions were monitored by TLC. The ratio's of the regio- and stereoisomers obtained were determined by GC after removal of the excess alkene (yields 65 to 75 %). Structure identification was performed by combined GC-CIMS or -CEMS techniques[8].

Irradiation of 1 with 4 gave a mixture consisting of six isomers; CIMS-data showed the presence of the useful regioisomers 6 (MH^+ at m/z 241) for 65 % (at 25°C) and for 78 % (at -40°C)[9]. Substrate 2 gave with 4 a mixture of seven isomers (GC); the ratio h-t(7)/h-h at 25°C and -40°C are 24/76 and 38/62, respectively. GC-CIMS analysis of the cycloaddition reaction of 3 with 4 revealed that the GC peaks were not homogeneous. Indeed, in addition to the expected regio- and stereoisomers of 8, products occurring from the loss (for about 20 %) of the methyl group at C_3 of substrate 3 were discovered[10]. It is obvious that these discouraging results do not call for further transformations.



1,2,3



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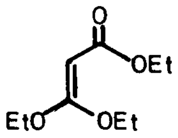

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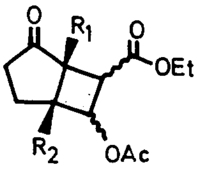
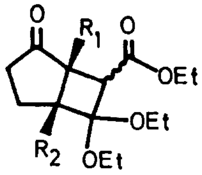
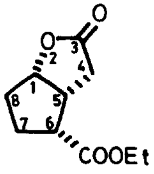


6,7,8

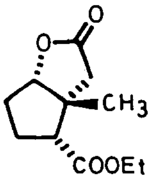


9,10,11

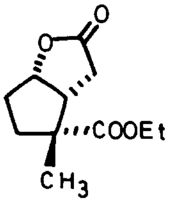
1,6,9 $R_1 = R_2 = H$
2,7,10 $R_1 = CH_3$, $R_2 = H$
3,8,11 $R_1 = H$, $R_2 = CH_3$



12



13



14

We therefore concentrated our attention on the photocycloadditions with ethyl β,β-diethoxyacrylate 5, which, due to the larger electron donating power of two β-ethoxy groups, are expected to be more regiospecific[2]. The results are summarized in the table. The regioselectivity is excellent, especially when irradation was performed at -40°C; the temperature effect is most pronounced with 3, indicating a substantial steric influence of the methyl group at C_3. The h-t structural assignment for the major components followed from CEMS data[11]. No loss of the methyl substituent in the reaction between 3 and 6 could be detected by GC-CIMS analysis (mass fragmentographic scanning at m/z 229, the base peak of 9)

Table : GC analysis of the cycloadditions with ethyl β,β-diethoxyacrylate[11]
(isomers given in order of increasing GC retention time)

substrate	t°	h-t %	h-h %	h-t %	h-h %	Σh-t % 9,10,11
1	25°C	52.5	13	30	4.5	82.5
	-40°C	59.5	6	34.5	-	94
2	25°C	39.5	-	44	16.5	83.5
	-40°C	39.5	-	52	8.5	91.5
3	25°C	46.5	-	24.5	29	71
	-40°C	61	-	39	-	100

Reduction of the adduct mixture 9 with $NaBH_4$ in ethanol at -40°C gave the alcohol (endo-hydroxyl; see ref. 2 and 5 for similar reductions), which was isolated by addition of NH_4Cl, evaporation of EtOH and extraction with ether. (IR : 3360, 1730 cm^{-1}). Cleavage of the C_6-C_7 bond and lactonisation occurred upon treatment of the intermediate alcohol with $TsOH.H_2O$ in benzene for 10 hrs. Usual work-up and column chromatography (silicagel; ethylacetate) affords 12 in 59 % yield (overall from 1). MH^+ at m/z 199 (base peak); IR : 1780, 1730 cm^{-1}; ^1H-NMR : $\delta(CCl_4)$: 5.06 (H-1, m, $^3J(1-5)$ = 7.0 Hz); 2.39 and 2.68 (H-4, m, ^2J = |18.8|Hz), 3.27 (H-5, m, $^3J(4-5)$ = 10.8 Hz, $^3J(4-5)$ = 4.8 Hz), 2.90 (H-6, m, $^3J(6-5)$ = 8.6 Hz), 1.78, ∿ 1.92, ∿ 1.92 and 2.14 (H-7 and H-8, m), 1.27 (CH_3-, t, ^3J = 7.2 Hz), 4.17 (-CH_2-, q, ^3J = 7.2 Hz).

The lactones 13 and 14 are obtained from 10 and 11, respectively, as described for the preparation of 12.

13 : yield : 53 %; MH^+ at m/z 213 (base peak); IR : 1780, 1735 cm^{-1}; ^1H-NMR : $\delta(CCl_4)$: 4.56 (H-1, t), 2.32 and 2.56 (H-4, 2xd, ^2J = |19.0|Hz), 2.58 (H-6, t), ∿ 2.00 (H-7 and H-8, broad), 1.27 (CH_3-, t, ^3J = 7.8 Hz), 1.44 (CH_3-, s), 4.20 (-CH_2-, q, ^3J = 7.8 Hz).

14 : yield : 45 %; MH^+ at m/z 213 (base peak); IR : 1780, 1735 cm^{-1}; ^1H-NMR : $\delta(CCl_4)$: 5.04 (H-1, m, $^3J(1-5)$ = 6.4 Hz), 2.24 and 2.70 (H-4, m, ^2J =|18.2|Hz), 2.84 (H-5, m, $^3J(4A-5)$ = 10.6 Hz, $^3J(4B-5)$ = 4.8 Hz), 1.66, ∿ 2.09, ∿ 2.09 and 2.28 (H-7 and H-8, m), 1.28 (CH_3-, s), 1.28 (CH_3-, t, ^3J = 7.2 Hz), 4.17 (CH_2-, q, ^3J = 7.2 Hz).

ACKNOWLEDGMENTS

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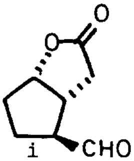
6. The structures of the for prostaglandin synthesis useless head-to-head isomers are not given. The h-t and h-h designations are based on the sequence rule priority of the substituents.
7. T. Ogino, K. Yamada and K. Isogai; Tetrahdron Letters, 28, 2445 (1977).
8. The mass spectral behaviour will be the subject of a separate paper.
9. From the crude mixture of the cycloadducts the 11-deoxyprostaglandin synthon i was obtained in a total yield (from 1) of 26 % by essentially identical conditions as described in reference 7. The poor yield is primarely due to the low regioselectivity of the cycloadditon reaction.



i

10. The mechanism of this unexpected and unprecedented expulsion of a β-substituent during photocycloaddition reactions is presently being studied.
11. The mass spectra of all major compounds (h-t) of the three reactions are identical when peak shifts due to the methyl substituents are taken into account (mass mapping) and differ largely from the minor components (reactions with 1 and 2). As the cycloadducts 11 from 3 lead exclusively to the lactone 14, both must be h-t regioisomers; this allows structure assignments in the two other series.