Communications to the Editor

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PHOTOCHEMISTRY OF 1-ACETOXY-2-(PENT-4-ENOYL)CYCLOPENTENES: AN EFFICIENT SYNTHESIS OF 7-ACETOXY-5-METHYLTRICYCLO[5.3.0^{1,5}]DECAN-2-ONE, A POTENTIAL INTERMEDIATE TO PSEUDOGUAIANE RING

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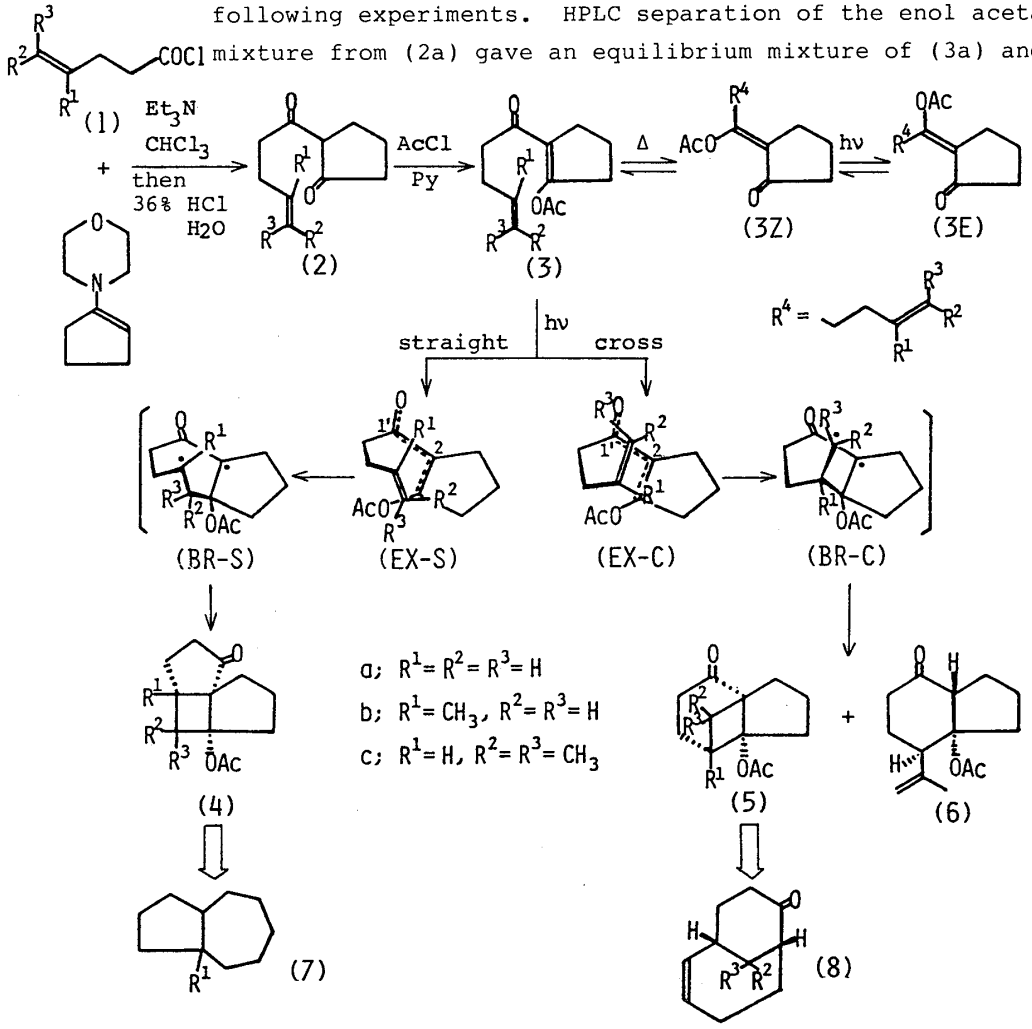
The intramolecular photocycloadditions of 1-acetoxy-2-(pent-4-enoyl)cyclopentene (3a) and its analogues have been investigated. The 4'-methyl analogue (3b) afforded a straight adduct (4b) in 82.5% yield as a sole product, in contrast to the case for (3a) resulting in a mixture of the straight and cross adducts, (4a) and (5a), in a 1:1 - 1:8 ratio. On the other hand, 5',5'-dimethyl analogue (3c) yielded the cross adduct (5c) together with a major product (6) due to a concurrent photo-ene reaction. The differences of regioselectivity due to the substitution pattern of the terminal double bond in (3) may be interpreted in terms of the preferential formation of corresponding exciplexes governed by non-bonding steric interactions.

KEYWORDS —— photochemical synthesis; intramolecular [2+2] photocycloaddition; 1-acetoxy-2-(pent-4-enoyl)cyclopentene; 6-acetoxytricyclo[4.3.1^{1,5}]decan-2-one; 7-acetoxytricyclo[5.3.0^{1,5}]decan-2-one

Recently, attention has been focused on the intramolecular [2+2] photocycloadditions of cyclic α,β-enones with remote double bonds as a powerful tool for natural products synthesis, particularly for the construction of complex polycyclic carbon skeletons.[1] Previously, we described a new five step synthesis of bicyclo[4.3.1]dec-2-en-7-one (8a) from 1-acetoxy-2-(pent-4-enoyl)cyclopentene (3a) using photocycloaddition as a key reaction.[2] In this connection, Pattenden *et al.* briefly reported a similar result dealing with the photocycloaddition of (3a) with low regioselectivity.[3] In order to view the scope of this synthetic pathway leading to the bicyclo[4.3.1]decane ring system, we further explored the photochemistry of 1-acetoxy-2-(pent-4-enoyl)cyclopentenes (3a-c), and now found that the photocycloaddition was primarily controlled by the substituents attached to the double bond in a side chain and also dependent on solvent and temperature to a certain extent. As a result, we could obtain as cross adducts 6-acetoxytricyclo[4.3.1^{1,5}]-decan-2-ones (5a,c) which were successfully converted to bicyclo[4.3.1]decane system (8), and as straight adducts 7-acetoxytricyclo[5.3.0^{1,5}]decan-2-ones (4a,b), the potential intermediates leading to bicyclo[5.3.0]decane system (7)[4] which is an important carbon skeleton of widely occurring guaiane and pseudoguaiane type sesquiterpenoids.[5] We now wish to summarize the results.

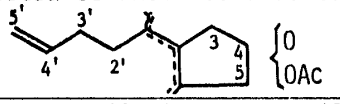
Enol acetates, (3a)[2], (3b)[11] [a colorless oil, bp 63.5-65 °C/0.005mmHg], and (3c)[11] [a colorless oil, bp 62-64.5 °C/0.005mmHg], were prepared from acid chlorides (1a-c)[11] and 1-morpholinocyclopentene in 60-65% overall yields [i, Et_3N, $CHCl_3$, r.t., overnight, then 36% HCl, H_2O, reflux, 5 h; ii, 1.5 eq of AcCl, Py, 0 °C, 4 h]. The enol acetates prepared in this manner consist of the *endo*-enol form (3) and the *exo*-enol forms (3Z and 3E) due to non-regioselective O-acetylation of the 1,3-diketones (2)[11]. However, we found that the light induced *cis-trans* isomerization of *exo*-enol acetates and subsequent 1,5-acyl migration of (3Z) and (3) constituted a ready equilibrium [(3)⇄(3Z)⇄(3E)], where the enol ester mixture underwent photocycloaddition *via* the *endo*-enol esters (3), while the excited *exo*-enol esters, (3Z) and (3E), only recycled in equilibrium with *cis-trans* isomerization.[6]

This characteristic feature of these enol esters (3a-c) was evidenced by the following experiments. HPLC separation of the enol acetates mixture from (2a) gave an equilibrium mixture of (3a) and (3Za),



and pure (3Ea) in a ratio of 39:49:12 which was determined by ^{1}H-NMR spectra in $CDCl_3$ (Table. 1),[7] and the equilibrium constant K=[(3a)]/[(3Za)] in CD_2Cl_2 was found to be temperature dependent [°C, K; 20.3, 0.818; -19.9, 0.796 ; -60.5, 0.671; -80.5, 0.643. ΔH=295cal/mol]. Moreover, acetonitrile solutions of (3a+3Za+3Ea), (3a+3Za) and (3Ea) were separately irradiated [*ca.* 2.0 x 10^{-2}M solution, 300 W medium-pressure Hg lamp, Pyrex filter, in Ar]. After 4h the NMR analysis of each reaction mixture indicated that the ratio of isomeric enol esters was [(3a):(3Za):(3Ea)=4:5:11] and was unchanged throughout the reaction, and the enol acetates could

Table 1. ^{1}H-NMR Spectra of Enol Acetates of β-Diketone (2a)[a]



Compound	(3a)	(3Za)	(3Ea)
OAc	2.25(s)	2.26(s)	2.20(s)
H_2-4	1.93(quintet, 7.5)		1.87(quintet, 7.6)
H_2-5	2.61(tt, 7.5, 2.3)	b)	2.38(t, 7.6)
H_2-3	2.74(tt, 7.5, 2.3)	2.71(t, 7.5)	2.53(tt, 7.6, 1.3)
H_2-2'	b)	2.70(t, 7.5)	2.93(tt, 7.6, 1.3)
H_2-3'	b)		2.18 - 2.25
H_1-4'	5.77 - 5.90		5.80(ddt, 17.1, 10.3, 6.6)
H_2-5'	4.95 - 5.11		4.97(ddt, 10.3, 1.7, 1.2) 5.04(ddt, 17.1, 1.7, 1.7)

a) See ref. 11. Assignments were made by means of proton decoupling techniques. b) These protons appeared in 2.24 -2.38 ppm region.

not be detected after 40 h affording photoproducts (4a)[2,3] and (5a)[2,3] which resulted obviously from (3a). Thus the *endo*-enol forms (3a-c) can represent the enol ester mixture in the photolysis.

As described above, irradiation of (3a) led to the concurrent formation of the straight adduct (4a) and the cross adduct (5a). Product distributions in various conditions are summarized in Table 2. The formation of (5a) was markedly dominant over (4a) at -70 °C, suggesting that (5a) was a kinetically controlled product, while the solvent effect was not apparent.

Table 2. Effects of Reaction Temperature and Solvents on the Product Ratios of (4a):(5a)[a]

Solvent	Temp.; °C		
	-70±3	5-10	65±5
CH_3CN		43:57	48:52 (44.4:48.3)[b]
EtOH	26:74	49:51	51:49 (40.7:39.2)[b]
Acetone	20:80	44:56	
CH_2Cl_2	23:77	44:56	
AcOEt	20:80	43:57	
Et_2O	11:89 (7.8:74.8)[b]	40:60	
Benzene		43:57	47:53
Cyclohexane		42:58	45:55
Hexane	26:74	42:58	

a) The solutions (1.5 ml) were irradiated for 15 h, and the ratios were determined by ^{1}H-NMR spectrum. b) The solutions (700 ml) were irradiated for 40-50 h until starting materials were completely consumed. The numbers in parentheses are isolated yields by column chromatography on silica gel.

As a probable interpretation for the regioselectivity, we assume that it reflects the ratio of the corresponding isomeric exciplexes [as portrayed in formulas (EX-S) and (ES-C)], which are generally accepted as transient intermediate of the photocycloadditions between α,β-enones and alkenes.[8] The π-electron overlap between the α,β-double bond of enone and the double bond in the side chain should become sterically preferred in (EX-C) rather than in (EX-S) owing to the nature of the C_2-C_1' double bond in the excited state. Therefore, (5a) *via* (EX-Ca) is predominantly formed. In addition, this assumption appears to be consonant with the enhanced regioselectivity at a low temperature for better kinetic control.

On the other hand, the photolysis of the 4'-methyl analogue (3b) most interested us. A similar irradiation of (3b) in acetone for 40 h at 5-10 °C furnished exclusively the straight adduct (4b)[11] [colorless prisms, mp 53-54 °C] in 82.5% yield, and the cross adduct (5b) could not be detected (HPLC) out of the given conditions. The exclusive formation of (4b) is also explicable in terms of the preferential formation of exciplex (EX-Sb); it is likely that a non-bonding steric repulsion around C_1 position is more important than that of C_2 position in each of the exciplexes, and a steric hindrance between the methyl group and the cyclopentane ring in (EX-Cb) may result in the exclusive formation of (EX-Sb) to give (4b).

In contrast, a similar irradiation of 5',5'-dimethyl analogue (3c) gave the cross adduct (5c)[11] [colorless prisms, mp 93 °C] together with the major product

(6)[9, 11] [colorless needles, mp 68 °C] arising from the biradical intermediate (BR-Cc) by an intramolecular hydrogen abstraction.[10] The regiochemical course of this reaction can also be controlled by the non-bonding steric repulsion around C_1 position on (EX-Sc). Thus the reaction proceeds exclusively *via* (EX-Cc) to give (5c) and (6). Table 3 shows the product distributions in various conditions, and reveals that the reaction course is apparently influenced by temperature and by solvent in a slight degree, but the photo-ene product (6) was always a major product in the given examples.

Table 3. Effects of Reaction Temperature and Solvents on the Product Ratios of (5c):(6)[a)]

Solvent	Temp.; °C	
	-70±3	5-10
CH_3CN		22:78
EtOH	17:83	23:77
Acetone	17:83 (12.7:71.2)[b)]	28:72
AcOEt	18:82	30:70
Et_2O	21:79	33:67
Benzene		29:71
Hexane	26:74	42:58 (34.6:51.9)[b)]

a,b) See footnote in Table 2.

In short, from a synthetic point of view the high regioselectivity with respect to the photocycloaddition of the 4'-methyl analogue (3b) yielding the straight adduct (4b) will provide us with an efficient synthetic pathway leading to the pseudoguaiane ring. Further studies on this intriguing synthetic transformation are in progress.

REFERENCES AND NOTES

1) For a recent review, see S.W. Baldwin, "Organic Photochemistry," Vol. 5, ed. by A. Padwa, Marcel Dekker, Inc., New York, 1981, pp. 123-225.
2) H. Seto, S. Hirokawa, Y. Fujimoto, and T. Tatsuno, Chem. Lett., 1983, 989.
3) M.J. Begley, M. Mellor, and G. Pattenden, J. Chem. Soc., Perkin Trans. I, 1983, 1905.
4) For a recent review on the intramolecular photocycloaddition and cyclobutane fragmentation sequence, see W. Oppolzer, Acc. Chem. Res., 15, 135 (1982).
5) T.K. Devon and A.I. Scott, "Handbook of Naturally Occurring Compounds," Vol. II, Terpenes, Academic Press, New York, 1972; "Terpenoids and Steroids," ed. by J.R. Hanson (Specialist Periodical Reports), The Royal Society of Chemistry, London, Vol. 1-11.
6) For a similar example, see W. Oppolzer and T. Godel, J. Am. Chem. Soc., 100, 2583 (1978).
7) Pattenden *et al.* reported (see ref. 3) that acetylation of (2a) [Ac_2O, *p*-TsOH] led to a mixture of (3a) and (3Ea) which was separable by GLC. However, our results obviously showed that (3a) reported by them consisted of (3a) and (3Za).
8) E.J. Corey, J.D. Bass, R. LeMahieu, and R.B. Mitra, J. Am. Chem. Soc., 86, 5570 (1964); R.O. Loutfy and P. de Mayo, *ibid.*, 99, 3559 (1977), R.A. Caldwell and D. Creed, Acc. Chem. Res., 13, 45 (1980).
9) The stereochomistry was tentatively assigned on the basis of its formation mechanism.
10) The intramolecularity of this reaction has been well documented; see Y. Tamura, H. Ishibashi, and M. Ikeda, J. Org. Chem., 41, 1277 (1976); A.J. Wexler, J.A. Hyatt, P.W. Raynolds, C. Cottrell, and J.S. Swenton, J. Am. Chem. Soc., 100, 512 (1978).
11) All new compounds gave satisfactory analytical and spectral properties. Selected data for (4b), (5c), and (6) are as follows: IR spectra were recorded in CCl_4. Absorption bands are shown in cm^{-1}. NMR spectra were measured at 400 MHz for ^1H and at 22.5 MHz for ^{13}C in $CDCl_3$, and the chemical shifts are given in ppm (δ) relative to the internal TMS. The multiplicity and *J* values (Hz) are in parentheses. (4b): IR 1736; ^1H-NMR 1.12(3H, s), 1.55-1.88(4H), 1.92-2.14(3H), 1.98(3H, s), 2.33-2.44(4H), 2.68(1H, ddd, 17.6, 12.0, 9.5); ^{13}C-NMR 21.2, 22.5 (q), 25.4, 26.0, 36.3, 38.1, 38.4, 45.1(t), 37.4, 64.2, 85.6, 169.4, 216.0(s). (5c): IR 1735, 1716; ^1H-NMR 0.93(3H, s), 1.25(3H, s), 1.64(1H, ddd, 14, 9.5, 5), 1.77(1H, dddd, 16.5, 8.5, 5, 3.5), 1.86-2.09(3H), 2.00(3H,s), 2.14(1H, ddd, 15.5, 10, 4), 2.24(1H, ddd, 14, 11, 6), 2.35(1H, ddd, 19.5, 8.5, 5.5), 2.41(1H, ddd, 19.5, 9, 4), 2.65(1H, ddd, 15.5, 10.5, 7.5), 2.88(1H, t, 3); ^{13}C-NMR 20.9, 22.6, 24.7(q), 21.0, 22.9, 25.8, 36.0, 38.3(t), 47.5(d), 35.2, 73.5, 88.1, 169.5, 210.0(s). (6): IR 1733(sh), 1725; ^1H-NMR 1.57-1.83(4H), 1.95(3H, br s), 1.96 (3H, s), 1.90-2.13(3H), 2.39(1H, dt, 16.8, 6.5), 2.51(1H, ddd, 16.8, 8.3, 6.6), 2.67(1H, m), 2.83(1H, t, 9.3), 3.42(1H, t, 6.4), 5.04(2H, m); ^{13}C-NMR 21.8, 24.8(q), 20.2, 20.4, 26.3, 32.1, 37.8, 113.0(t), 43.7, 55.1(d), 96.3, 145.9, 169.5, 208.5(s).

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