Intramolecular Photochemical Reactions of 4-(ω-Alkenyloxy)-6-methyl-2-pyrones Having an Alkoxycarbonyl Group at the Olefinic Carbon Chain

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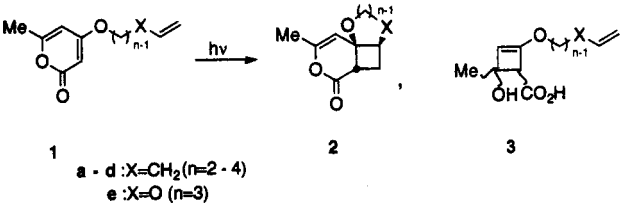
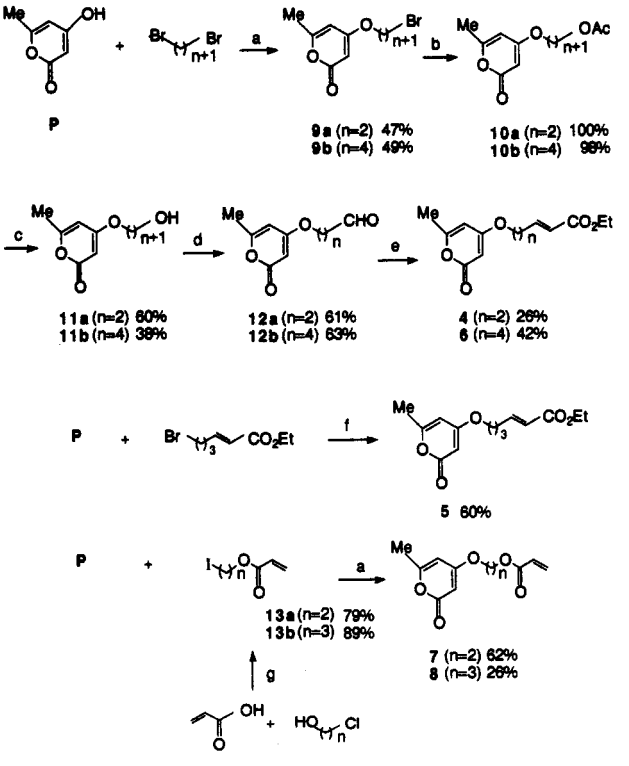
Photochemical reactions of 4-(ω-alkenyloxy)-6-methyl-2-pyrones 4–8 were investigated. Photosensitized reactions of 2-pyrones 4–6 gave intramolecular [2 + 2] cycloadducts 14–16 as oxatricyclic lactones, site-, regio- and stereospecifically, but 7 and 8 gave no products. On the other hand, direct irradiations of 4 and 5 afforded cyclobutenecarboxylic acids 19 and 20, respectively. The intramolecular cycloaddition mechanism was also explained from the excited state of 2-pyrone calculated by means of the MNDO-CI method.

In recent years, intramolecular [2 + 2] photocycloadditions of cyclic α,β-unsaturated enones with remote double bonds have been extensively used to synthesize a variety of interesting compounds including natural products,[1] along with analyzing the mechanisms.[2] Previously, we demonstrated that photochemical reactions of 4-(ω-alkenyloxy)-6-methyl-2-pyrones 1 provided a simple route to synthesize oxatricyclic lactones 2, depending upon the number of the methylene chains between the 2-pyrone ring and olefinic moiety,[3] in addition to the formation of 3 (Scheme I). We have now planned to extend this reaction to 4-(ω-alkenyloxy)-6-methyl-2-pyrones having an alkoxycarbonyl group at the olefinic moiety. In this paper, the photochemical reactions of (ω-alkenyloxy)-2-pyrones 4–8 and the analysis of their regioselectivity about the intramolecular cycloaddition by using MNDO-CI method are described.

Scheme I



Scheme II[a]



[a] Conditions: (a) Et_3N, CH_3CN; (b) NaOAc, EtOH; (c) H_2SO_4, EtOH; (d) PCC, CH_2Cl_2; (e) NaH, $(EtO)_2POCH_2CO_2Et$, THF; (f) DBU, CH_3CN; (g) PTSA, C_6H_6, NaI, acetone.

Results and Discussion

Preparation of Substrates. All of the substrates required for this study were obtained as shown in Scheme II. 2-Pyrones 5, 7, and 8 were prepared from 4-hydroxy-6-methyl-2-pyrone (P) by way of a dehydrohalogenation reaction with proper halogenated substrates. In the case of 4 and 6, additional oxidation and Wittig reaction were carried out.

Photochemical Results. A solution of 4 (7.6 mM) in acetonitrile in the presence of benzophenone as a sensitizer was irradiated with a 400-W high-pressure mercury lamp through a Pyrex filter. The reaction was followed by TLC. After removal of solvent, the residue was chromatographed on silica gel to afford a single photoadduct 14 in 70% yield. Photosensitized irradiations of 5 and 6 in acetonitrile gave also 15 and 16 in 48% and 32% yields, respectively (Scheme III). Similar photoirradiations of 7 and 8 resulted in complex mixtures, respectively. On the other hand, photoirradiations of 4 and 5 without benzophenone gave cyclobutenecarboxylic acids 19 and 20, which were labile, in 15% and 12% yields, respectively.

The structures of 14–16 were deduced as intramolecular [2 + 2] cycloadducts from the spectroscopy evidence. For instance, 14, ethyl 10-methyl-8-oxo-2,9-dioxatricyclo-[5.4.0.0^{1,5}]undec-10-ene-*endo*-6-carboxylate showed a strong carbonyl absorption at 1760 cm^{-1} in the IR spectrum (KBr) for a γ,δ-unsaturated lactone. The remarkable feature of the ^{1}H NMR spectrum of 14 was the coupling pattern of 6-H, which occurred at δ 3.13 as a doublet doublet (J = 11.0, 4.4 Hz). The ring junction across the C_1–C_7 double bond in 14 could be deduced as cis-fused, since 14 did not change on treatment with basic alumina, which was used to infer the stereochemistry of ring junctions in [2 + 2] cycloadducts.[4] The stereochemistry of 14 was confirmed

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Scheme III

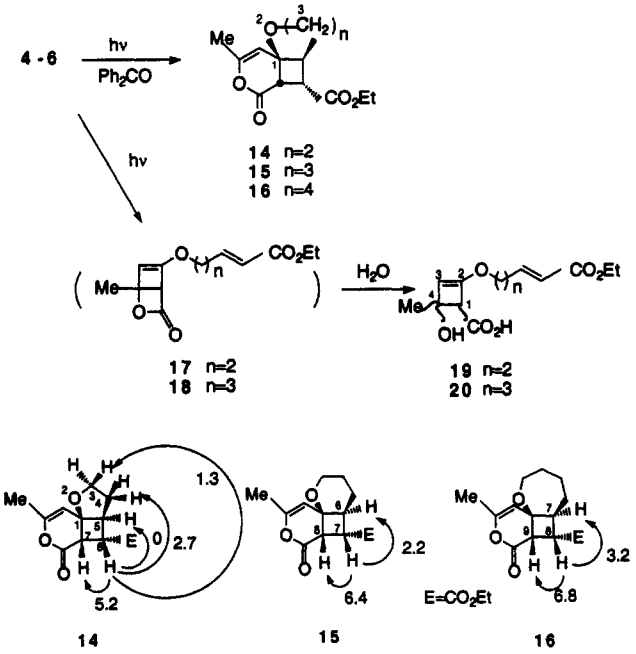


Figure 1. Selected NOE measurements of photocycloadducts 14–16.

by noting the magnitude of the NOE for 5-H/7-H caused by irradiation of 6-H (Figure 1). The stereochemistry of **15** and **16** was also confirmed by NOE measurements. Compounds **19** and **20**, which have been formed through the hydrolyses of bicyclolactones **17** and **18**, were confirmed to be 2-[[4-(ethoxycarbonyl)-*trans*-3-butenyl]oxy- and -[5-(ethoxycarbonyl)-*trans*-4-pentenyl]oxy]-4-hydroxy-4-methylcyclobut-2-ene-1-carboxylic acids, respectively, from the ^{1}H NMR spectra compared with the similar compound.[3]

On the basis of these results as shown in Scheme III, the intramolecular [2 + 2] cycloadditions of **4–6** were found to be site-, regio-, and stereospecific, independent of the alkenyl chain length, and proceed by way of triplet excited states of 2-pyrones. On the other hand, the valence isomerization reactions of **4** and **5** were found to proceed via singlet excited states of 2-pyrones, which had been known as affording cyclobutenecarboxylic acids via bicyclic lactones.[5]

In the direct photoreactions of 4-(ω-alkenyloxy)-2-pyrones which had no chromophores at the olefinic moieties,[3] the intramolecular cycloadditions and valence isomerizations were competitive. In the photosensitized reactions reported here and in a previous report, however, 2-pyrones **1e**[3] and **4–6**, which have electronically different olefinic moieties in the side chains, gave just intramolecular [2 + 2] cycloadducts site-, regio-, and stereospecifically.

We now describe a MNDO-CI treatment of the photoreactions which leads to an understanding of these specificities. The MNDO-CI method has become an increasingly powerful tool for the understanding of cycloaddition reactions.[6] It is reasonable to assume that these intramolecular cycloadditions proceed by way of biradical intermediates of 2-pyrones. The orbital energies and coefficients of triplet excited states (HSOMO and LSOMO) for 2-pyrone were obtained as follows: the optimized

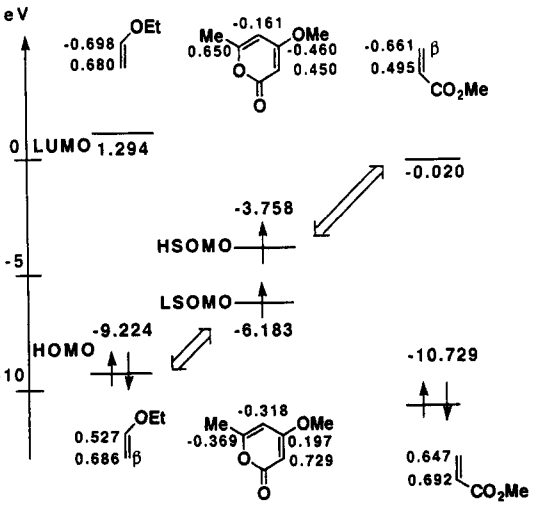
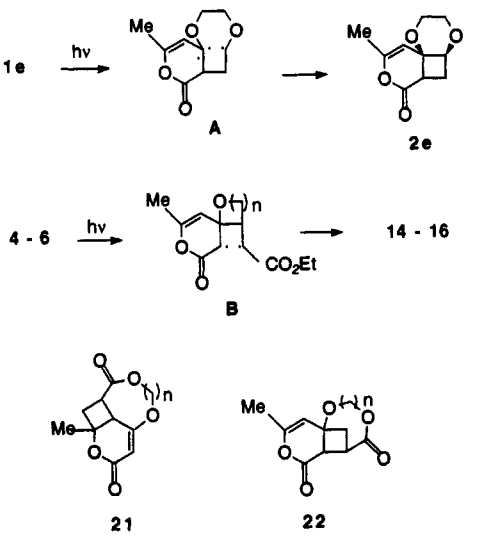


Figure 2. Estimated energies and coefficients of 4-methoxy-6-methyl-2-pyrone and olefins.

Scheme IV



structure of the triplet excited state of 2-pyrone was calculated by using unrestricted Hartree–Fock wavefunction (UHF), and the energies and coefficients were estimated by CI calculation which was carried out by considering 36 configurations of 2-pyrone. In the case of olefins, the optimized structures of the ground states were calculated by restricted Hartree–Fock wavefunction (RHF), and the energies and coefficients were estimated by CI calculations which were performed by taking account of 36 configurations of olefins. It is reasonable to consider that the mechanism of the intramolecular cycloaddition of **1e** is similar to that of reactions between 4-methoxy-6-methyl-2-pyrone and ethyl vinyl ether. Figure 2 shows the estimated orbital energies and coefficients for 4-methoxy-6-methyl-2-pyrone and olefins by using MNDO-CI method.[7]

The energy gap (ΔE) between LSOMO(2-pyrone)-HOMO(ethyl vinyl ether) is smaller than HSOMO(2-pyrone)–LUMO(ethyl vinyl ether), and this frontier orbital interaction is much more important in the photocycloaddition of **1e**. As the coefficient at C-3 in the LSOMO orbital of 2-pyrone and that at C-β in the HOMO orbital of ethyl vinyl ether are larger than any other positions, the initial bond formation is inferred to occur at C(3)–C(β) to

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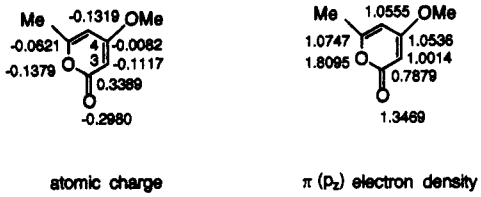

Figure 3. Calculated atomic charge and $\pi(p_z)$ electron density of excited triplet 4-methoxy-6-methyl-2-pyrone.

give a biradical intermediate A which may lead to the adduct **2e** (Scheme IV). The intermediate stabilization can be explained by the so-called "capto-dative substituent effect".[8]

2-Pyrones **4–6** gave the adducts **14–16** by their irradiations. This observation seems to point to a preference for formation of stable biradical B by the initial bonding between C(4) (HSOMO of 2-pyrone) and C(β) (LUMO of methyl acrylate) from the consideration of the energy gap and coeffients in their frontier orbitals (Figure 2). It is reasonable to consider that the endo stereospecificity of the cycloadducts **14–16** is caused from the favorable π orbital interaction between two carbonyl groups of the biradical B in Scheme IV. The lack of intramolecular photocycloadducts **21** and **22** from irradiations of **7** and **8** probably reflects that the approach between two olefinic moieties was disturbed owing to the conjugated carbonyl systems in the side chains.

It is well-recognized that excited triplet enones are polarized as

$$O=\overset{\delta+}{C}-\overset{\delta-}{C}=C$$

in contrast to the ground state. The regioselectivity of the photocycloaddition is explained by means of the polarization interaction of the two substrates. Then we calculated the atomic charge and the electron density of excited triplet 2-pyrone as a dienone by using MNDO-CI method (Figure 3). Both C(3) and C(4) positions of the excited triplet 2-pyrone, however, showed an electron-negative feature. From the results of Figure 3 and properties of ethyl vinyl ether and methyl acrylate, it seems to be difficult to explain the regiospecificity of the photocycloadducts **2e** and **14–16** by means of the polarizations. So it was inferred to be preferable to explain the photocycloaddition mechanism by frontier orbital consideration.

Experimental Section

All melting points are uncorrected. ^{1}H NMR spectra were determined with a JNM-GSX400 (400-MHz) spectrometer (tetramethylsilane as an internal standard), and ^{13}C NMR spectra were mreasured at 100.5 MHz on the JNM-GSX400 instrument using $CDCl_3$ as internal reference. IR spectra were recorded with a JASCO A-3 spectrometer. Low-resolution mass spectral data were obtained with a JMS-OISG instrument at 70 eV. Gas chromatography was performed on a Shimazu GC-12A (nitrogen as carrier gas; 1.7 m × 3 mm column packed with 10% Silicone SE-30 at 170 °C). Photoirradiation was carried out in a Pyrex tube by using a Riko 400W high-pressure mercury lamp equipped with a merry-go-round apparatus. In the case of a photosensitized reaction, a UV 35 filter (Toshiba) which cuts off under 350 nm was used.

4-[[4-(Ethoxycarbonyl)-*trans*-3-butenyl]oxy]-6-methyl-2-pyrone (4). (1) To a solution of 4-hydroxy-6-methyl-2-pyrone[9] (10.0 g, 79.3 mmol) containing triethylamine (9.6 g, 95.2 mmol) in acetonitrile (50 mL) under reflux was slowly added 1,3-dibromopropane (19.2 g, 95.2 mmol). After addition of 1,3-dibromopropane, the solution was refluxed for 12 h. The reaction mixture was filtered, and the residue was submitted to column chromatography (silica gel, ethyl acetate) to give **9a** (9.2 g, 47%): mp 59–60 °C; IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.21 (3 H, s), 2.31 (2 H, m), 3.53 (2 H, t, J = 6.6 Hz), 4.10 (2 H, t, J = 5.9 Hz), 5.42 (1 H, s), 5.77 (1 H, s); mass spectrum m/z 247 (M^+). Anal. Calcd for $C_9H_{11}BrO_3$: C, 43.74; H, 4.74. Found: C, 44.00; H, 4.54.

(2) A solution of **9a** (9.15 g, 37.0 mmol) and sodium acetate (3.1 g, 37.8 mmol) in ethanol (200 mL) was refluxed for 70 h. After concentration of the reaction mixture, chloroform (50 mL) was added and the filtrate was concentrated to give **10a** (8.4 g, 100%) as a pale yellow oil, which was essentially pure and used for the next step without further purification: IR (neat) 1750, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.07 (3 H, s), 2.11 (2 H, quint, J = 6.2 Hz), 2.21 (3 H, s), 4.02 (2 H, t, J = 6.2 Hz), 4.21 (2 H, t, J = 6.2 Hz), 5.39 (1 H, s), 5.77 (1 H, s); mass spectrum m/z 226 (M^+).

(3) A solution of **10a** (4.4 g, 19.4 mmol) in ethanol (50 mL) containing concentrated sulfuric acid (0.2 mL) was refluxed for 14 h. The reaction mixture was washed with 10% Na_2CO_3 solution and extracted with diethyl ether (4 × 60 mL). After concentration, the extract was chromatographed (silica gel, ethyl acetate) to give **11a** (1.2 g, 34%): mp 70–72 °C; IR (KBr) 3400, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.78 (1 H, br s), 2.03 (3 H, quint, J = 6.2 Hz), 2.21 (3 H, s), 3.81 (2 H, t, J = 6.2 Hz), 4.10 (2 H, t, J = 6.2 Hz), 5.42 (1 H, s), 5.78 (1 H, s); mass spectrum m/z 127 (M^+). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.72; H, 6.50.

(4) To a suspension of pyridinium chlorochromate (8.2 g, 38.0 mmol) in dichloromethane (100 mL) under nitrogen atmosphere was added dichloromethane solution (25 mL) containing **11a** (1.2 g, 7.6 mmol). The reaction mixture was stirred for 3 h at room temperature, washed with water, and extracted with diethyl ether (5 × 100 mL). The combined organic layer was dried ($MgSO_4$) and concentrated to give crude **12a** (1.5 g, 61%), which was used for the next step because it was decomposed by the column chromatography. IR (neat) 1730, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.20 (3 H, s), 2.94 (2 H, m), 4.28 (2 H, m), 5.44 (1 H, s), 5.78 (1 H, s), 9.80 (1 H, s).

(5) To a dry THF (25 mL) suspension of sodium hydride (0.34 g, 8.3 mmol, 60% dispersion in mineral oil) at room temperature under nitrogen atmosphere was added ethyl diethylphosphonoacetate (1.88 g, 8.3 mmol) followed by a THF (5 mL) solution of **12a** (1.52 g, 3.8 mmol). The solution was stirred for 1.5 h. After being quenched into water (30 mL), the aqueous layer was extracted with diethyl ether (5 × 75 mL). The combined organic layer was concentrated and column chromatographed (silica gel, ethyl acetate–benzene (1:2)) to afford **4** (0.3 g, 26%): mp 74–75 °C; IR (KBr) 1725, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (3 H, t, J = 7.0 Hz), 2.21 (3 H, s), 2.68 (2 H, ddt, J = 7.0, 6.2, 1.5 Hz), 4.05 (2 H, t, J = 6.2 Hz), 4.21 (2 H, q, J = 7.0 Hz), 5.38 (1 H, s), 5.78 (1 H, s), 5.94 (1 H, dd, J = 15.8, 1.5 Hz), 6.94 (1 H, dt, J = 15.8, 7.0 Hz); ^{13}C NMR ($CDCl_3$) 14.2, 19.8, 31.1, 60.5, 66.6, 87.9, 100.4, 124.2, 143.0, 162.3, 164.7, 166.0, 170.2; mass spectrum m/z (relative intensity) 252 (M^+, 6) 86 (100). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 62.03; H, 6.39.

4-[[5-(Ethoxycarbonyl)-*trans*-4-pentenyl]oxy]-6-methyl-2-pyrone (5). To a solution of 4-hydroxy-6-methyl-2-pyrone (0.95 g, 7.5 mmol) containing 1,8-diazabicyclo[5.4.0]undec-7-ene (1.26 g, 8.3 mmol) in acetonitrile (100 mL) under reflux was slowly added an acetonitrile (50 mL) solution of ethyl 5-bromo-*trans*-1-pentene-1-carboxylate[10] (2.0 g, 9.0 mmol). The resulting solution was refluxed for 4 h and concentrated in vacuo to give a pale yellow oil, which was chromatographed (silica gel, ethyl acetate–benzene (2:1)) to afford **5** (1.21 g, 60%) as colorless oil: IR (neat) 1735, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (3 H, t, J = 7.0 Hz), 1.95 (2 H, quint, J = 6.2 Hz), 2.20 (3 H, s), 2.36 (2 H, ddt, J = 7.0, 6.2, 1.5 Hz), 3.95 (2 H, t, J = 6.2 Hz), 4.20 (2 H, q, J = 7.0 Hz), 5.37 (1 H, s), 5.77 (1 H, s), 5.86 (1 H, dt, J = 15.4, 1.5 Hz), 6.95 (1 H, dt, J = 15.4, 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.8, 26.9, 28.4, 60.5, 67.6, 87.8, 100.4, 122.4, 146.9, 162.1, 164.8, 166.3, 170.4; mass spectrum m/z (relative intensity) 266 (M^+, 8), 87 (100). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.32; H, 6.76.

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4-[[6-(Ethoxycarbonyl)-*trans*-5-hexenyl]oxy]-6-methyl-2-pyrone (6). The procedure described for **4** afforded **9b** (49%), **10b** (98%), **11b** (38%), **12b** (63%), and **6** (42%), respectively.

9b: pale yellow oil; IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80 (2 H, m), 1.88–1.94 (4 H, m), 2.20 (3 H, s), 3.42 (2 H, t, J = 6.2 Hz), 3.95 (2 H, t, J = 6.2 Hz), 5.38 (1 H, s), 5.78 (1 H, s); mass spectrum m/z 274 (M^+). Anal. Calcd for $C_{11}H_{15}BrO_3$: C, 48.02; H, 5.50. Found: C, 47.92; H, 5.44.

10b: mp 59–61 °C (from benzene); IR (KBr) 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40–1.85 (6 H, m), 2.05 (3 H, s), 2.20 (3 H, s), 3.94 (2 H, t, J = 6.2 Hz), 4.09 (2 H, t, J = 6.6 Hz), 5.38 (1 H, s), 5.77 (1 H, s); mass spectrum m/z 254 (M^+). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.16; H, 7.08.

11b: colorless oil; IR (neat) 3400, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.49–1.82 (6 H, m), 1.52 (1 H, s), 2.20 (3 H, s), 3.68 (2 H, t, J = 6.6 Hz), 3.95 (2 H, t, J = 6.6 Hz), 5.38 (1 H, s), 5.77 (1 H, s); mass spectrum m/z 212 (M^+). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.00; H, 7.54.

12b: colorless oil; IR (neat) 1730, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70–1.95 (4 H, m), 2.20 (3 H, s), 2.43 (1 H, m), 2.54 (1 H, m), 3.96 (2 H, m), 5.39 (1 H, s), 5.78 (1 H, s), 9.80 (1 H, br s); mass spectrum m/z 210 (M^+). Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.50; H, 6.50.

6: mp 40–41 °C; IR (KBr) 1740, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3 H, t, J = 7.0 Hz), 1.61 (2 H, m), 1.79 (2 H, m), 2.20 (3 H, s), 2.26 (2 H, ddt, J = 7.0, 6.2, 1.5 Hz), 3.94 (2 H, t, J = 6.2 Hz), 4.19 (2 H, q, J = 7.0 Hz), 5.37 (1 H, s), 5.76 (1 H, s), 5.84 (1 H, dt, J = 15.4, 1.5 Hz), 6.95 (1 H, dt, J = 15.4, 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.8, 24.3, 27.9, 31.6, 60.2, 68.3, 87.7, 100.5, 122.0, 148.0, 162.1, 164.9, 166.5, 170.5; mass spectrum m/z (relative intensity) 281 (M + 1, 56), 81 (100). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.00; H, 7.21.

4-(1,4-Dioxa-5-oxo-6-heptenyl)-6-methyl-2-pyrone (7). (1) A solution of acrylic acid (45.9 g, 0.637 mol) and 2-chloro-1-ethanol (51.3 g, 0.637 mol) in benzene (50 mL) containing *p*-toluenesulfonic acid (1.5 g) was refluxed for 9 h with a Dean-Stark water separator. The reaction mixture was washed with saturated Na_2CO_3 solution and brine, dried ($MgSO_4$), and concentrated to give brown oil, which was distilled to afford 2-chloroethyl acrylate (31.2 g, 36%): bp 43–45 °C (6 mmHg); ^1H NMR ($CDCl_3$) δ 3.67 (2 H, t, J = 6.2 Hz), 4.42 (2 H, t, J = 6.2 Hz), 5.84 (1 H, dd, J = 10.3, 1.5 Hz), 6.13 (1 H, dd, J = 17.4, 10.3 Hz), 6.42 (1 H, dd, J = 17.4, 1.5 Hz), mass spectrum m/z 134 (M^+). Anal. Calcd for $C_5H_7ClO_2$: C, 44.63; H, 5.24. Found: C, 44.42; H, 5.10.

(2) A solution of 2-chloroethyl acrylate (31.2 g, 0.232 mol) and sodium iodide (173.7 g, 1.16 mol) in acetone (150 mL) was refluxed for 22 h. The reaction mixture was diluted with water and extracted with diethyl ether (5 × 100 mL). The combined organic layer was washed with 5% $NaHSO_3$ solution and brine, dried ($MgSO_4$), and concentrated to give **13a** (41.2 g, 79%) as a colorless oil, which was essentially pure and used for the next step without further purification: IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.32 (2 H, t, J = 6.2 Hz), 4.41 (2 H, t, J = 6.2 Hz), 5.89 (1 H, dd, J = 10.3, 1.5 Hz), 6.13 (1 H, dd, J = 17.4, 10.3 Hz), 6.48 (1 H, dd, J = 17.4, 1.5 Hz); mass spectrum m/z 226 (M^+). Anal. Calcd for $C_5H_7IO_2$: C, 26.57: H, 3.12. Found: C, 26.20; H, 2.96.

(3) The similar procedure described for **5** afforded 62% of **7** as a colorless oil: IR (neat) 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21 (3 H, s), 4.19 (2 H, m), 4.50 (1 H, m), 5.41 (1 H, s), 5.82 (1 H, s), 5.90 (1 H, dd, J = 10.4, 1.1 Hz), 6.15 (1 H, dd, J = 17.4, 10.4 Hz), 6.46 (1 H, dd, J = 17.4, 1.1 Hz); mass spectrum m/z 224 (M^+). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 58.70; H, 5.12.

4-(1,5-Dioxa-6-oxo-7-octenyl)-6-methyl-2-pyrone (8). (1) By use of a procedure similar to that described for 2-chloroethyl acetate, 3-chloropropyl acrylate was prepared in 23% yield as a colorless oil: IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15 (2 H, quint, J = 6.2 Hz), 3.64 (2 H, t, J = 6.2 Hz), 4.32 (2 H, t, J = 6.2 Hz), 5.85 (1 H, dd, J = 10.3, 1.5 Hz), 6.13 (1 H, dd, J = 17.4, 10.3 Hz), 6.42 (1 H, dd, J = 17.4, 1.5 Hz); mass spectrum m/z 148 (M^+). Anal. Calcd for $C_6H_9ClO_2$: C, 48.50; H, 6.11. Found: C, 48.21; H, 6.00.

(2) The procedure described for **13a** afforded 89% of **13b** as a pale yellow oil: IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (2 H, quint, J = 6.2 Hz), 3.22 (2 H, t, J = 6.2 Hz), 4.22 (2 H, t, J = 6.2 Hz), 5.85 (1 H, dd, J = 10.3, 1.5 Hz), 6.11 (1 H, dd, J = 17.4, 10.3 Hz), 6.41 (1 H, dd, J = 17.4, 1.5 Hz); mass spectrum m/z 240 (M^+). Anal. Calcd for $C_6H_9IO_2$: C, 30.02; H, 3.78. Found: C, 29.81; H, 3.60.

(3) The procedure described for **7** afforded 26% of **8** as a pale yellow oil: IR (neat) 1740, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.17 (2 H, quint, J = 6.2 Hz), 2.21 (3 H, s), 4.06 (2 H, t, J = 6.2 Hz), 4.32 (2 H, t, J = 6.2 Hz), 5.41 (1 H, s), 5.79 (1 H, s), 5.87 (1 H, dd, J = 10.3, 1.5 Hz), 6.13 (1 H, dd, J = 17.4, 10.3 Hz), 6.42 (1 H, dd, J = 17.4, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 19.8, 27.9, 60.6, 65.2, 87.9, 100.4, 128.1, 131.2, 162.2, 164.8, 166.0, 170.4; mass spectrum m/z 238 (M^+). Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.24; H, 5.63.

Ethyl 10-Methyl-8-oxo-2,9-dioxatricyclo[5.4.0.0^{1,5}]undec-10-ene-*endo*-6-carboxylate (14). A solution of **4** (192 mg, 0.76 mmol) and benzophenone (14 mg, 0.076 mmol) as a sensitizer in acetonitrile (100 mL) under nitrogen atmosphere was irradiated for 2.5 h. The solvent was removed, and the residual liquid was submitted to column chromatography (silica gel, benzene–ethyl acetate (5:2)) to give **14** (134 mg, 70%) as colorless needles: mp 90–92 °C; IR (KBr) 1760, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 7.0 Hz, Me), 1.88 2.06 (each 1 H, m, 4-CH_2), 1.96 (3 H, s, Me), 2.94 (1 H, m, 5-H), 3.13 (1 H, dd, J = 11.0, 4.4 Hz, 6-H), 3.46 (1 H, d, J = 11.0 Hz, 7-H), 3.96, 4.21 (each 1 H, m, 3-CH_2), 4.15 (2 H, q, J = 7.0 Hz, CO_2CH_2), 4.93 (1 H, s, 11-H); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.5, 31.5, 41.5, 42.7, 47.5, 61.5, 67.4, 99.9, 128.3, 151.5, 166.9, 172.1; mass spectrum m/z (relative intensity) 252 (M^+, 8.8), 178 (100). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.92; H, 6.32.

2-[[4-(Ethoxycarbonyl)-*trans*-3-butenyl]oxy]-4-hydroxy-4-methylcyclobut-2-ene-1-carboxylic Acid (19). A solution of **4** (87 mg, 0.34 mmol) without benzophenone in acetonitrile (45 mL) was irradiated for 3 h and the usual workup yielded **19** (14 mg, 15%) as a pale yellow oil, which was difficult to purify by repeated chromatography: IR (neat) 3000–2500, 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3 H, t, J = 7.0 Hz, Me), 2.00 (3 H, s, Me), 2.55 (2 H, dt, J = 7.0, 6.2 Hz, CH_2CH=CH), 3.66 (1 H, s, OH), 3.72 (1 H, s, 1-H), 4.20 (2 H, q, J = 7.0 Hz, CO_2CH_2), 4.22 (2 H, t, J = 6.2 Hz, OCH_2), 5.89 (1 H, s, 3-H), 5.90 (1 H, d, J = 15.8 Hz, CH=CH), 6.90 (1 H, dt, J = 15.8, 7.0 Hz, CH=CH), 9.10 (1 H, br s, CO_2H); ^{13}C NMR ($CDCl_3$) δ 14.2, 26.1, 31.3, 38.6, 60.4, 62.7, 118.6, 119.0, 123.7, 143.9, 153.2, 166.4, 169.8.

Ethyl 11-Methyl-9-oxo-2,10-dioxatricyclo[6.4.0.0^{1,6}]dodec-11-ene-*endo*-7-carboxylate (15). A solution of **5** (400 mg, 1.5 mmol) and benzophenone (27 mg, 0.15 mmol) in acetonitrile (200 mL) was irradiated for 16 h, and the usual workup yielded **15** (190 mg, 48%) as a pale yellow oil: IR (neat) 1745, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 7.0 Hz, Me), 1.45–1.70 (4 H, m, CH_2CH_2), 1.89 (3 H, s, Me), 2.69 (1 H, m, 6-H), 3.17 (1 H, dd, J = 10.1, 1.4 Hz, 7-H), 3.73 (2 H, m, OCH_2), 3.80 (1 H, d, J = 10.1 Hz, 8-H), 4.15 (2 H, q, J = 7.0 Hz, CO_2CH_2), 5.00 (1 H, s, 12-H); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.2, 21.8, 25.5, 40.6, 41.9, 62.0, 69.9, 103.3, 127.7, 150.8, 166.1, 170.8; mass spectrum m/z (relative intensity) 266 (M^+, 7.2), 83 (100). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 62.98; H, 7.05.

2-[[5-(Ethoxycarbonyl)-*trans*-4-pentenyl]oxy]-4-hydroxy-4-methylcyclobut-2-ene-1-carboxylic Acid (20). A solution of **5** (400 mg, 1.5 mmol) in acetonitrile (200 mL) was irradiated for 6 h, and the usual workup yielded **20** (51 mg, 12%) as a pale yellow oil, which was difficult to purify by repeated chromatography: IR (neat) 3000–2500, 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, J = 7.0 Hz, Me), 1.82 (2 H, quint, J = 6.2 Hz, CH_2), 2.25 (3 H, s, Me), 3.00 (2 H, dt, J = 7.0, 6.2 Hz, CH_2CH=CH), 3.18 (1 H, s, OH), 3.67 (1 H, s, 1-H), 4.13 (2 H, t, J = 6.2 Hz, OCH_2), 4.19 (2 H, q, J = 7.0 Hz, CO_2CH_2), 5.80 (1 H, s, 3-H), 5.83 (1 H, d, J = 15.4 Hz, CH=CH), 6.93 (1 H, dt, J = 15.4, 7.0 Hz, CH=CH), 9.10 (1 H, br s, CO_2H); ^{13}C NMR ($CDCl_3$) δ 14.2, 19.0, 27.1, 28.7, 30.9, 45.3, 60.3, 63.0, 119.8, 122.1, 147.6, 150.6, 165.9, 174.2.

Ethyl 12-Methyl-10-oxo-2,11-dioxatricyclo[7.4.0.0^{1,7}]tridec-12-ene-*endo*-8-carboxylate (16). A solution of **6** (294 mg, 1.05 mmol) and benzophenone (19 mg, 0.11 mmol) in acetonitrile (140 mL) was irradiated for 20 h, and the usual workup yielded **16** (95 mg, 32%) as a pale yellow oil: IR (neat) 1770, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (3 H, t, J = 7.0 Hz, Me), 1.65–2.00 (6 H, m, CH_2), 1.92 (3 H, s, Me), 2.96 (1 H, dd, J = 11.6, 3.3 Hz, 8-H), 3.46, 3.73 (each 1 H, m, OCH_2), 3.54 (1 H, d, J = 11.6 Hz, 9-H),

4.11 (2 H, q, J = 7.0 Hz, CO_2CH_2), 5.25 (1 H, s, 13-H); ^{13}C NMR ($CDCl_3$) δ 13.9, 19.5, 28.4, 31.9, 40.4, 42.2, 49.4, 61.4, 66.0, 73.2, 100.7, 127.7, 150.8, 166.1, 171.3; mass spectrum m/z (relative intensity) 280 (M^+, 89), 206 (100). Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.09; H, 7.09.

Registry No. **4**, 136721-16-9; **5**, 136721-17-0; **6**, 136721-18-1; **7**, 136721-19-2; **8**, 136721-20-5; **9a**, 136721-21-6; **9b**, 136721-22-7; **10a**, 136721-23-8; **10b**, 136721-24-9; **11a**, 136721-25-0; **11b**, 136721-26-1; **12a**, 136721-27-2; **12b**, 136721-28-3; **14**, 136721-29-4; **15**, 136721-30-7; **16**, 136721-31-8; **19**, 136721-32-9; **20**, 136721-33-0; P, 675-10-5; $Br(CH_2)_3Br$, 109-64-8; $Br(CH_2)_5Br$, 111-24-0; (*E*)-$Br(CH_2)_3CH{=}CHCO_2Et$, 71032-10-5; $H_2C{=}CHCO_2H$, 79-10-7; $HO(CH_2)_2Cl$, 107-07-3; Ph_2CO, 119-61-9; 2-chloroethyl acrylate, 2206-89-5; 3-chloropropyl acrylate, 5888-79-9; ethyl (diethylphosphono)acetate, 867-13-0.

Anodic Oxidation of α-Substituted *p*-Xylenes. Electronic and Stereoelectronic Effects of α-Substituents in the Deprotonation of Alkylaromatic Radical Cations[1]

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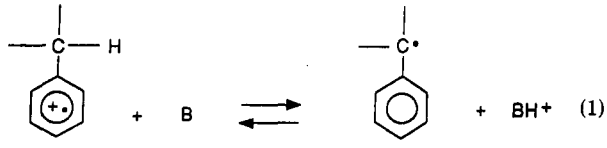
The effect of α-substituents on the deprotonation rate from the benzylic position of alkylaromatic radical cations, $k(CH_2Z)/k(CH_3)$, has been investigated by determining the intramolecular selectivity in the anodic oxidation in acetic acid of α-Z-substituted *p*-xylenes **1** (Z = H, OMe, OH, Me, *tert*-butyl, OAc, COOMe, CN), 5,6-dimethylindan **4** (R = H), and 2,2,5,6-tetramethylindan **4** (R = Me). Some oxidations induced by CAN have also been carried out. It has been found that, with the exception of when Z = *tert*-butyl, the deprotonation rate of $1^{\bullet+}$ is always faster from the CH_2Z group than from the CH_3 group, independently of the electron-donating or electron-withdrawing nature of Z. The electron-donating groups (OH, OMe, Me), however, exert a larger effect than the electron-withdrawing ones (COOMe, CN). The negligible deprotonation rate from CH_2-*t*-Bu has been ascribed to stereoelectronic effects (the bulky *tert*-butyl group does not allow the C–H bonds to be collinear with the π-system), the suggestion being nicely confirmed by the observation that the deprotonation rate from the position 1(3), relative to that from the 5(6)-methyl group, is almost identical in the radical cations of **4** (R = H and Me). The effect of the other α-substituents is mainly of electronic nature and has been rationalized on the basis of a variable transition-state structure for the deprotonation process. It is suggested that with +R groups most of the charge, in the transition state, has been transferred to the C_α–H bond where it can be stabilized by the α-substituent. With electron-withdrawing groups less charge transfer has taken place and the rate-enhancing effects of these groups is ascribed to their capability to significantly decrease the strength of the C_α–H bond.

Alkylaromatic radical cations are among the strongest carbon acids in solution (pK_a as negative as −30 or more in DMSO![3]) undergoing proton loss from an α-carbon, as shown in eq 1.



(1)

This process presents several aspects of theoretical and practical interest, and accordingly, it has been the object of intense investigations in the last decade. In particular, great attention has been given to the knowledge of the structural factors influencing the deprotonation rate and the position of the equilibrium.

By means of thermochemical cycles the pK_a values of a great number of alkylaromatic radical cations have been evaluated,[4] and today we have satisfactory information on the way these values are affected by the substrate structure. The factors which play the major role in this respect are the C_α–H bond energy and the oxidation potential of the parent substrate. In general, the thermodynamic acidity of an alkylaromatic radical cation decreases as the oxidation potential of the neutral substrate is lowered, i.e., by the presence of electron-donating ring substituents.

Information concerning structural effects on the kinetic acidity of alkylaromatic radical cations has come (directly) from laser photolysis[5] or pulse radiolysis[6] experiments as well as (indirectly) from kinetic[7] and intramolecular se-

(1) Part of this research has been presented as a main Section Lecture at the 32nd IUPAC Congress, Stockolm, 1989.[2]

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