Intramolecular Photocycloadditions of 6,6'-Dimethyl-4,4'-polymethylenedioxy-di-2-pyrones

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Photosensitized reactions of 4,4'-polymethylene-di-2-pyrones **2b-e** afforded [2+2]-cycloadducts **3-5**, site-selectively. The selectivity depended upon the methylene chain length. Namely, the three carbon chain gave a syn head-to-head adduct **3b** at the 3,4-position of the 2-pyrone ring, the four to six carbon chains gave syn head-to-head adducts **4c-e** at the 5,6-position and/or anti head-to-head adducts **5d,e** at the 5,6-position, respectively. The intramolecular cycloaddition mechanism was also explained from results calculated by means of PM3-CI method.

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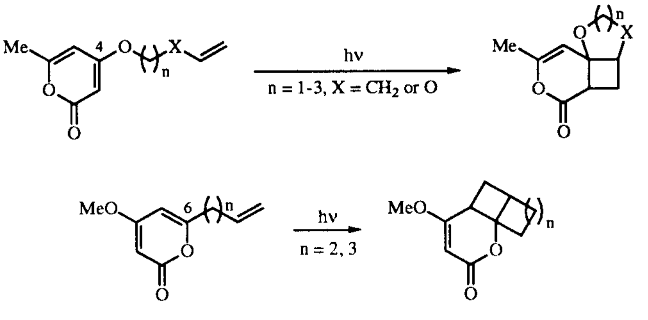
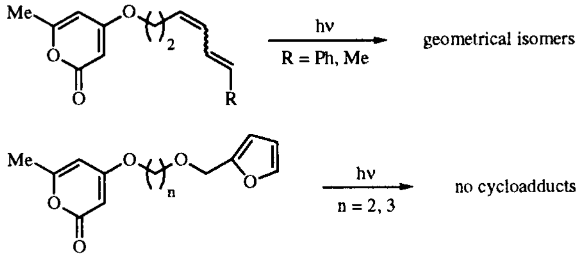
We have previously reported the intramolecular photochemical reactions of 2-pyrones, which are simple heterocyclic dienone system, in order to investigate the intramolecular cycloaddition reactivity. For instance, photoreactions of 4- and 6-ω-enyl-2-pyrones gave two types of oxatricyclic lactones, respectively, depending upon the number of the methylene chain between 2-pyrone and olefinic moiety (Scheme 1) [1]. On the other hand, 4-ω-dienyl-2-pyrones underwent geometrical isomerization and 2-pyrones bearing pendant furans afforded no cycloadducts (Scheme 2) [2]. Since 2-pyrones having dienyl moieties showed different reactivities [3] compared to 2-pyrones having enyl moieties, we have planned to extend this reaction to 4,4'-polymethylene-di-2-pyrones **2** in order to clarify the reactivity of 4π-4π system concerning peri-, site- and stereo-selectivities.

Scheme 1



Scheme 2



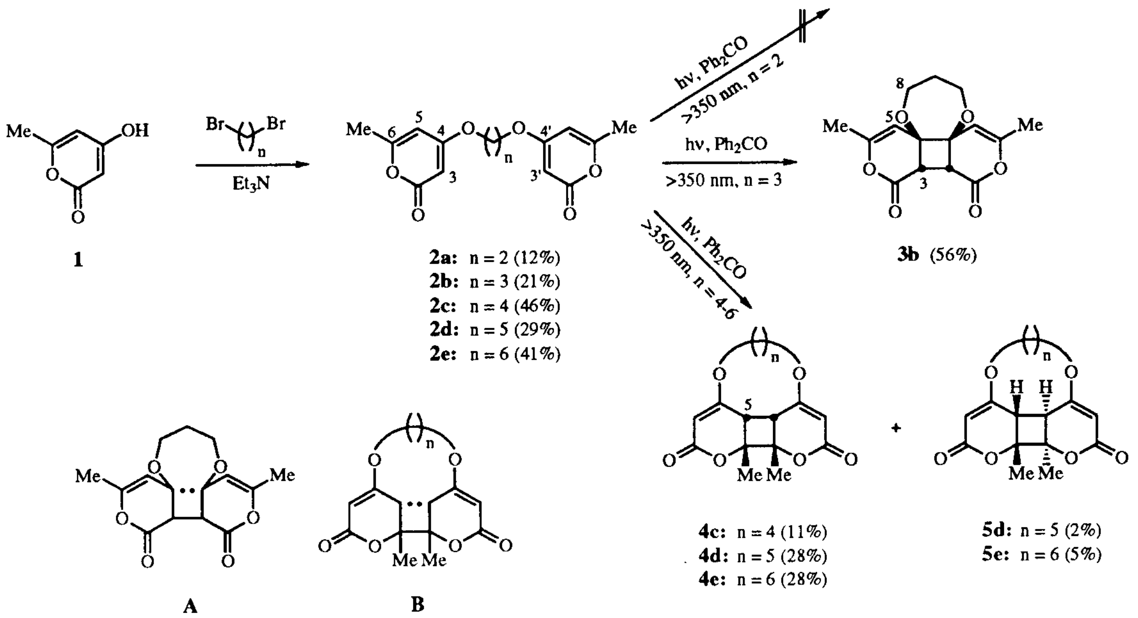
Di-2-pyrones **2a-e** were prepared from dehydrobromination of 4-hydroxy-6-methyl-2-pyrone (**1**) with dibromoalkanes using triethylamine.

Photoirradiation of a solution of **2b** (n = 3) in acetonitrile in the presence of benzophenone as a sensitizer under nitrogen afforded [2+2]-cycloadduct **3b** in 56% yield as a sole product. Similar photoirradiation of **2c** (n = 4) gave another type of [2+2]-cycloadduct **4c** in 11% yield. Similarly, **2d** (n = 5) and **2e** (n = 6) gave **4d** (28%) and **5d** (2%), and **4e** (28%) and **5e** (5%), respectively, as shown in Scheme 3, but **2a** (n = 2) gave no product.

The structures of **3b**, **4c-e** and **5d,e** were assigned as site-selective intramolecular [2+2]-cycloadducts from the spectral data. For instance, **3b** was assigned as a [2+2]-cycloadduct across the C_3-C_4 and $C_{3'}$-$C_{4'}$ double bonds in **2b** because of showing a strong carbonyl absorption at 1760 cm^{-1} in ir spectrum (potassium bromide) for a γ,δ-unsaturated lactone. The syn head-to-head structure of **3b** was indicated by noting the magnitude of the nOe for two methyne protons (3-H, 5-H) with unequivalent methylene protons (8-CH_2). On the other hand, since products **4e** and **5e** showed strong carbonyl absorptions at 1715 and 1703 cm^{-1}, respectively, for α,β-unsaturated lactone, **4e** and **5e** were assigned as another type of [2+2]-cycloadducts across the C_5-C_6 and $C_{5'}$-$C_{6'}$ double bonds in **2e**. The syn and anti head-to-head structures of **4e** and **5e** were deduced by noting the chemical shift deviation of 5-H (**4e**: δ = 3.19, **5e**: δ = 2.98), which was reasonably explained by the magnetic anisotropy for the C_3-C_4 double bond.

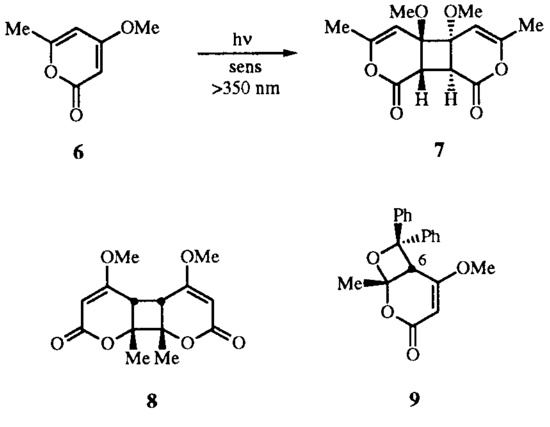
Intermolecular photosensitized dimerization of 4-methoxy-6-methyl-2-pyrone (**6**) gave two types of [2+2]-cycloadducts **7** and **8** along with an oxetane **9**. The structures of **7** and **8** were assigned as [2+2]-cycloadducts across each C_3-C_4, and each C_5-C_6 double bonds, respectively, from the spectral data. The anti head-to-head structure of **7** was mainly deduced from the ^{1}H nmr spectral data of 3-H (δ = 2.90) compared to that of **3b** (syn head-

Scheme 3



to-head, δ = 3.71) and coumarin dimers [4-7], considering the magnetic anisotropy for the carbonyl group of the lactone moiety. The structure of **8** was deduced to be syn head-to-head because of showing similar chemical shift of the bridge head protons with **4e**.

Scheme 4



On the basis of these results as shown in Scheme 3, the intramolecular [2+2]-cycloadditions of di-2-pyrones **2** proceeded *via* triplet exited states of 2-pyrones and were found to require the presence of at least more than three methylene units. The site-selectivity also depended upon the number of methylene units (n). That is, n = 3 gave syn adduct at the 3,4-position of the 2-pyrone ring, n = 4-6 afforded syn adducts (major products) at the 5,6-positions of 2-pyrones along with anti adducts at the same positions.

Table 1

Estimated Frontier Orbital Interactions Between 4-Methoxy-6-methyl-2-pyrones by PM3-Cl Calculation (γ^2/ev)

	6-6' (HSOMO-LUMO)	3-3' (LSOMO-HOMO)
$(C_iC_r)^2/\Delta\varepsilon$	0.0483	0.0656

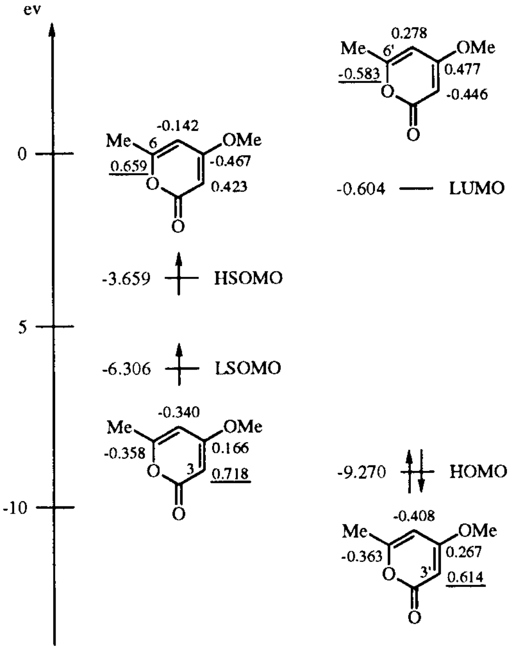


Figure 1. Estimated energies and coefficients of 4-methoxy-6-methyl-2-pyrone.

These site-selectivity were explained reasonably from the frontier-orbital consideration. Figure 1 shows the estimated energies and coefficients of higher singly occupied molecular orbital (HSOMO) and lower one (LSOMO) of the triplet excited state, and the ground state, LUMO and HOMO, for 2-pyrone **6** by using PM3-CI method [8]. Table 1 shows the frontier-orbital interactions (γ^2/ev) between the triplet state and ground state of **6**. Since the interactions, $(CiCr)^2/\Delta\varepsilon$ (in γ^2/ev) have a tendency to be larger between C_3 (LSOMO)- $C_{3'}$ (HOMO), intermediate biradical **A** is prior to occur by way of LSOMO (2-pyrone)-HOMO (2-pyrone) interaction when the number of methylene chain is three which is considered to be suitable to give a cycloadduct **3b**. On the other hand, as the methylene chain becomes more than four, the biradical **A** is assumed to be crowded and labile because of becoming nonplannor structure of the conjugated part in **A**, and then the less-crowded biradical **B** occurs by way of HSOMO (2-pyrone)-LUMO (2-pyrone) interaction to give **4** and **5**.

EXPERIMENTAL

All of the melting points were measured on a Yanagimoto Meltemp apparatus and are uncorrected. The ir, ^{1}H and ^{13}C nmr, and mass spectra were recorded on JASCO A-3, JEOL JNM GSX400, and JEOL JMSOISG spectrometers, respectively. All the photoreactions were monitored by tlc on silica-gel plates.

4,4'-(Ethylenedioxy)-6,6'-dimethyl-**2a**, 6,6'-Dimethyl-4,4'-(trimethylenedioxy)-**2b**, 6,6'-Dimethyl-4,4'-(tetramethylenedioxy)-**2c**, 6,6'-Dimethyl-4,4'-(pentamethylenedioxy)-**2d** and 6,6'-Dimethyl-4,4'-(hexamethylenedioxy)-di-2-pyrone (**2e**).

To a refluxing acetonitrile (45 ml) solution of 4-hydroxy-6-methyl-2-pyrone (**1**) (9.0 g, 71 mmoles) and triethylamine (8.0 g, 79 mmoles) was slowly added 1,2-dibromoethane (5.6 g, 30 mmoles) and the refluxing was continued for 24 hours. After cooling, the reaction mixture was evaporated *in vacuo* and the resulting solid was recrystallized from methanol to give **2a** (1.0 g, 12%). Similar reactions of **1** with 1,3-dibromopropane, 1,4-dibromobutane, 1,5-dibromopentane, and 1,6-dibromohexane gave **2b** (21%), **2c** (46%), **2d** (29%), and **2e** (41%), respectively.

Compound **2a** had mp 240-241° (colorless plates); ir (potassium bromide): 1710, 1660, 1560 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.22 (s, 6H), 4.27 (s, 4H), 5.43 (s, 2H), 5.81 (s, 2H); ms: m/z (relative intensity) 278 (M^+, 100).

Anal. Calcd. for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.23; H, 5.07.

Compound **2b** had mp 162-163°(colorless needles); ir (potassium bromide): 1745, 1655, 1570 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.21 (s, 6H), 2.24 (quint, 2H, J = 5.8 Hz), 4.09 (t, 4H, J = 5.8 Hz), 5.40 (s, 2H), 5.77 (s, 2H); ms: m/z (relative intensity) 292 (M^+, 100).

Anal. Calcd. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.64, H, 5.51.

Compound **2c** had mp 231-232° (colorless plates); ir (potassium bromide): 1713, 1651, 1570 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.93 (m, 4H), 2.21 (s, 6H), 4.00 (m, 4H), 5.38 (s, 2H), 5.76 (s, 2H); ms: m/z (relative intensity) 306 (M^+, 100).

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.68; H, 5.91.

Compound **2d** had mp 144.5-145.0° (colorless needles); ir (potassium bromide): 1721, 1655, 1570 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.57 (m, 2H), 1.83 (m, 4H), 2.21 (s, 6H), 3.96 (t, 4H, J = 6.4 Hz), 5.38 (s, 2H), 5.77 (s, 2H); ms: m/z (relative intensity) 320 (M^+, 100).

Anal. Calcd. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.62, H, 6.37.

Compound **2e** had mp 176-177° (colorless crystals); ir (potassium bromide): 1715, 1650, 1560 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.47 (m, 4H), 1.79 (m, 4H), 2.20 (s, 6H), 3.94 (t, 4H, J = 6.4 Hz), 5.37 (s, 2H), 5.76 (s, 2H); ms: m/z (relative intensity) 334 (M^+, 78), 127 (100).

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.42; H, 6.64.

9,16-Dimethyl-2,6,10,15-tetraoxatetracyclo$[11.4.0.0^{1,7}.0^{7,12}]$-heptadecane-8,16-diene-11,14-dione (syn head-to-head adduct) (**3b**).

A solution of **2b** (0.22 g, 0.75 mmole) and benzophenone (0.01 g, 0.06 mmole) in acetonitrile (100 ml) was irradiated for 26 hours under nitrogen with a 400 W high-pressure mercury lamp through a UV 35 filter (Toshiba) which cuts off under 350 nm. The solvent was removed *in vacuo* and the residue was chromatographed using ethyl acetate-hexane 1:1 v/v mixture to give **3b** (0.12 g, 56%).

Compound **3b** had mp 173-174° (colorless plates); ir (potassium bromide): 1760, 1700 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.84 (m, 1H), 1.93 (s, 6H), 2.20 (m, 1H), 3.71 (s, 2H), 3.77 (ddd, 2H, J = 13.2, 10.0, 3.0 Hz), 3.93 (dt, 2H, J = 13.2, 4.6 Hz), 5.20 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 19.4, 33.7, 41.9, 63.9, 81.3, 96.4, 152.1, 164.4; ms: m/z (relative intensity) 292 (M^+, 100).

Anal. Calcd. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.79; H, 5.67.

11,12-Dimethyl-3,8,13,18-tetraoxatetracyclo$[8.3^{2,12}.3^{9,11}.2.0]$-octadecane-2(15),9(16)-diene-14,17-dione (syn head-to-head adduct) (**4c**).

A solution of **2c** (0.46 g, 1.5 mmoles) and benzophenone (0.27 g, 1.5 mmoles) in chloroform (200 ml) was irradiated for 144 hours using the same apparatus. After the solvent was removed, the residue was washed with ethyl acetate and filtered. The resulting solid was recrystallized from ethanol to give **4c** (0.05 g, 11%).

Compound **4c** had mp 315-317° (colorless plates); ir (potassium bromide): 1721 (sh), 1717, 1638 (sh), 1634 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.56 (s, 6H), 1.80 (m, 2H), 2.12 (m, 2H), 3.21 (s, 2H), 4.08 (ddd, 2H, J = 11.6, 6.0, 3.2 Hz), 4.14 (ddd, 2H, J = 11.2, 8.4, 2.8 Hz), 5.21 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 22.8, 25.9, 42.3, 69.1, 81.7, 93.1, 164.2, 166.2; ms: m/z (relative intensity) 306 (M^+, 100).

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.76; H, 5.93. Found: C, 62.63; H, 5.86.

12,13-Dimethyl-3,9,14,19-tetraoxatetracyclo$[9.3^{2,13}.3^{10,12}.2.0]$-nonadecane-2(16),10(17)-diene-15,18-dione (syn head-to-head adduct) (**4d**) and (anti head-to-head adduct) (**5d**).

A solution of **2d** (0.48 g, 1.5 mmoles) and benzophenone (0.03 g, 0.15 mmole) in acetonitrile (200 ml) was irradiated for 138 hours. The solvent was removed and the residue was chromatographed using ethyl acetate-hexane 1:1 v/v mixture to give **4d** (0.13 g, 28%) and **5d** (0.01 g, 2%).

Compound **4d** had mp 313-315° (colorless needles); ir (potassium bromide): 1721, 1692 (sh), 1638, 1620 (sh) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.54 (s, 6H), 1.67 (m, 1H), 1.73 (m, 4H), 1.81 (m, 1H), 3.19 (s, 2H), 4.01 (m, 4H), 5.20 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 17.7, 22.1, 22.2, 42.4, 65.9, 82.0, 92.3, 164.3, 165.7; ms: m/z (relative intensity) 320 (M$^+$, 100).

Anal. Calcd. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.51; H, 6.33.

Compound **5d** had mp 197-202°; ir (potassium bromide): 1709 (sh), 1703, 1698 (sh), 1640 (sh), 1632, 1622 (sh); ^{1}H nmr (deuteriochloroform): δ 1.51 (s, 6H), 1.61 (m, 2H), 1.82 (m, 4H), 3.10 (s, 2H), 4.02 (dt, 2H, J = 11.0, 6.4 Hz), 4.08 (dt, 2H, J = 11.0, 6.4 Hz), 5.25 (s, 2H); ms: m/z (relative intensity) 320 (M$^+$, 100).

13,14-Dimethyl-3,10,15,20-tetraoxatetracyclo[10.3^{2,14}.3^{11,13}.2.0]eicosane-2(17),11(18)-diene-16,19-dione (syn head-to-head adduct) (**4e**) and (anti head-to-head adduct) (**5e**).

A solution of **2e** (0.50 g, 1.5 mmoles) and benzophenone (0.03 g, 0.15 mmole) in dichloromethane (200 ml) was irradiated for 141 hours. The solvent was removed and then ethyl acetate (15 ml) was added to the reaction mixture. The resulting solid was filtered and recrystallized from ethyl acetate to give **4e** (0.14 g, 28%) and the filtrate was chromatographed using ethyl acetate to give **5e** (0.03 g, 5%).

Compound **4e** had mp 311-312° (colorless needles); ir (potassium bromide): 1715, 1632 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.34 (m, 2H), 1.54 (s, 6H), 1.66 (m, 2H), 1.75 (m, 4H), 3.19 (s, 2H), 3.95 (m, 4H), 5.20 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 22.1, 24.0, 27.1, 42.6, 68.8, 82.1, 91.5, 164.5, 166.7; ms: m/z (relative intensity) 334 (M$^+$, 100).

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 64.66; H, 6.33. Found: C, 64.64; H, 6.55.

Compound **5e** had mp 211-212° (colorless plates); ir (potassium bromide): 1703, 1642 (sh), 1634 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.33 (m, 2H), 1.51 (s, 6H), 1.71 (m, 4H), 1.84 (m, 2H), 2.98 (s, 2H), 3.80 (ddd, 2H, J = 12.4, 9.6, 2.8 Hz), 4.15 (ddd, 2H, J = 9.6, 5.0, 1.8 Hz), 5.10 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 18.3, 23.3, 26.5, 46.6, 68.6, 84.9, 89.3, 165.0, 170.6; ms: m/z (relative intensity) 334 (M$^+$, 100).

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 64.66; H, 6.33. Found: C, 64.70; H, 6.58.

7,8-Dimethoxy-5,10-dimethyl-4,11-dioxatricyclo[6.4.0.0^{2,7}]dodeca-5,9-diene-3,12-dione (**7**), 6,9-Dimethoxy-1,2-dimethyl-3,12-dioxatricyclo[6.4.0.0^{2,7}]dodeca-5,9-diene-4,11-dione (**8**) and 5-Methoxy-1-methyl-7,7-diphenyl-2,8-dioxabicyclo[4.2.0]oct-4-en-3-one (**9**).

A solution of 4-methoxy-6-methyl-2-pyrone (**6**) (2.1 g, 15 mmoles) and benzophenone (0.6 g, 3 mmoles) in acetonitrile (100 ml) was irradiated for 211 hours using a UV 35 filter. After the solvent was removed, the residue was chromatographed using ethyl acetate-hexane 1:1 v/v mixture to give **7** (0.31 g, 15%) which was recrystallized from ethanol, and **9** (0.65 g, 13%) which was recrystallized from hexane. A solution of **6** (4.2 g, 30 mmoles) and xanthone (2.4 g, 12 mmoles) in acetonitrile (300 ml) was irradiated for 203 hours. The solvent was removed and the same workup mentioned above gave **7** (0.03 g, 2%) and **8** (0.01 g, 0.6%) along with the recovery of **6** (2.7 g, 64%).

Compound **7** had mp 191-192° (colorless plates); ir (potassium bromide): 1775, 1694 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.07 (s, 6H), 2.90 (s, 2H), 3.14 (s, 6H), 5.08 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 19.5, 39.4, 51.5, 80.2, 97.1, 153.1, 163.6; ms: m/z (relative intensity) 280 (M$^+$, 0.1), 112 ($C_6H_8O_2$, 100).

Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 59.72; H, 5.77.

Compound **8** had mp 217-218° (colorless plates); ir (potassium bromide): 1710, 1630 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.54 (s, 6H), 3.16 (s, 2H), 3.69 (s, 6H), 5.21 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 21.9, 42.4, 56.0, 82.4, 91.5, 164.2, 167.4; ms: m/z (relative intensity) 281 (M$^+$+1, 0.2), 112 ($C_6H_8O_2$, 100).

Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 59.84; H, 5.71.

Compound **9** had mp 149-150° (colorless needles); ir (potassium bromide): 1721, 1715 (sh), 1649 (sh), 1632 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.64 (s, 3H), 3.34 (s, 3H), 4.11 (s, 1H), 4.99 (s, 1H), 7.18-7.48 (m, 10H); ^{13}C nmr (deuteriochloroform): δ 27.9, 51.5, 55.8, 87.5, 92.1, 103.2, 125.8, 126.3, 127.8, 127.9, 128.6, 140.1, 144.4, 164.1, 167.6; ms: m/z (relative intensity) 322 (M$^+$, 0.1), 140 ($C_7H_8O_3$, 100). The nOe enhancement between 6-H and the *ortho* phenyl proton was observed to be 25%.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.30; H, 5.69.

REFERENCES AND NOTES

[1a] T. Shimo, M. Yasuda, J. Tajima, and K. Somekawa, *J. Heterocyclic Chem.*, **28**, 745 (1991); [b] T. Shimo, J. Tajima, T. Suishu, and K. Somekawa, *J. Org. Chem.*, **56**, 7150 (1991); [c] T. Shimo, S. Matsuzaki, and K. Somekawa, *J. Heterocyclic Chem.*, **31**, 387 (1994).

[2] T. Shimo, S. Ueda, and K. Somekawa, *J. Heterocyclic Chem.*, **32**, 341 (1995).

[3a] M. Van Meerbeck, S. Toppet, and F. C. De Schryver, *Tetrahedron Letters*, 2247 (1972); [b] F. G. West, C. E. Chase, and A. M. Arif, *J. Org. Chem.*, **58**, 3794 (1993).

[4] K. Muthuramu and V. Ramamurthy, *J. Org. Chem.*, **47**, 3976 (1982).

[5] F. D. Lewis, D. K. Howard, and J. D. Oxman, *J. Am. Chem. Soc.*, **105**, 3344 (1983).

[6] L. H. Leenders, E. Schouteden, and F. C. De Schryver, *J. Org. Chem.*, **38**, 957 (1973).

[7] K. Kuthuramu, N. Rammath, and V. Ramamurthy, *J. Org. Chem.*, **48**, 1872 (1983).

[8] K. Somekawa, T. Shimo, and T. Suishu, *Bull. Chem. Soc. Japan*, **65**, 3541 (1992).