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6-(ω-Alkenyl)-2-pyrones **3a-c** and **8a,b** were prepared and the photochemical reactions were investigated. Photosensitized reactions of **3b,c** gave intramolecular [2+2]-cycloadducts **11b,c** as tricyclic lactones, site- and regio-specifically. They are not frontier-orbital-controlled adducts. On the other hand, **3a**, **8a,b** afforded cyclobutenecarboxylic acids, **10a**, **14a,b**, respectively. The end-ester group at the side-chain is thought not to be effective for the intramolecular photoaddition.

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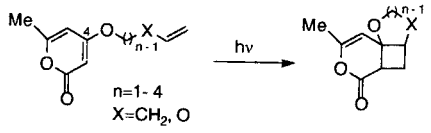
2-Pyrone has a simple heterocyclic skeleton containing an oxygen atom and is a conjugated dienone system in the form of a heterocyclic compound. We previously reported that intramolecular photochemical reactions of 4-(ω-alkenyloxy)-2-pyrones provided a simple route to synthesize oxatricyclic lactones, depending upon the number of the methylene chains between the 2-pyrone ring and olefinic moiety (Scheme 1) [1], in addition to explain the cycloaddition mechanism [2]. We have planned to extended this reaction to 6-(ω-alkenyl)-2-pyrones in order to clarify the reactivity of ω-alkenyl-2-pyrones more in detail, and to synthesize another type of tricyclic lactones.

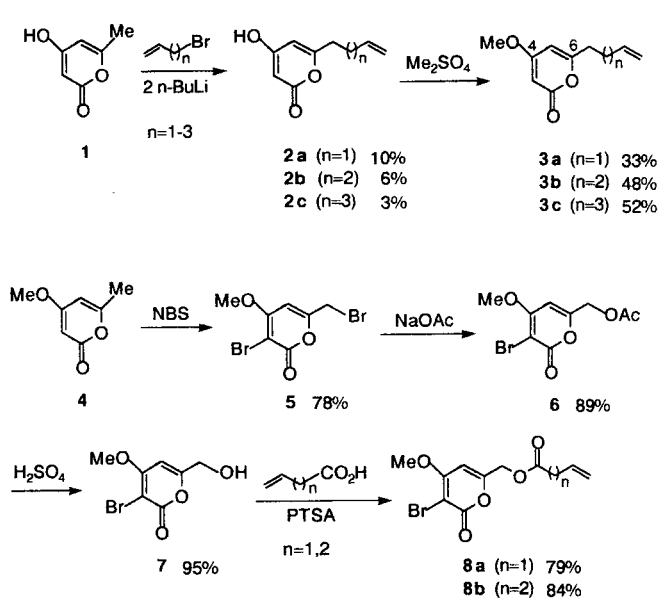
Scheme 1



At first all of the substrates required for this study were prepared as shown in Scheme 2. 2-Pyrones **3a-c** were obtained from dehydrobromination of 4-hydroxy-6-methyl-2-pyrone (**1**) with the proper alkenyl bromides by using butyllithium. In the case of **8a,b**, dehydration of 6-hydroxylmethyl-2-pyrone **7**, which was prepared from 4-methoxy-6-methyl-2-pyrone (**4**) *via* bromination and acetoxylation, with the proper alkenylcarboxylic acids was carried out.

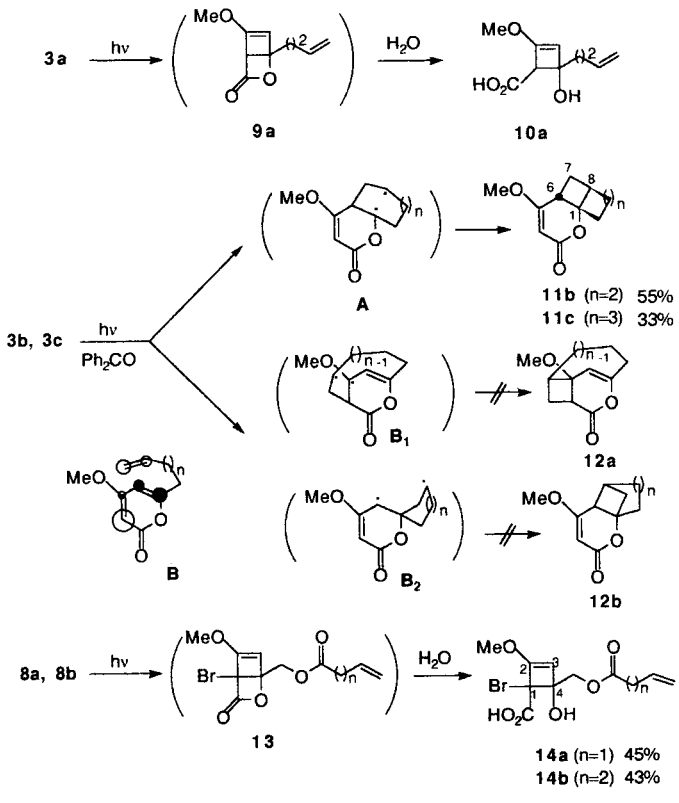
Photoirradiation of a solution of **3b** (n = 2) in acetonitrile in the presence of benzophenone as a sensitizer under nitrogen gave an expected [2+2]-cycloadduct **11b** in 55% yield as a sole product. Similar photoirradiation of **3c** (n = 3) afforded also a sole [2+2]-cycloadduct **11c** in 33% yield as shown in Scheme 3. These results show that the intramolecular photochemical [2+2]-cycloadditions of **3** are site- and regio-specific, and proceed *via* triplet excited states of **3** similar to the case of 4-(ω-alkenyloxy)-2-pyrones [1]. On the other hand, photosensitized irradiation of **3a** did not give the intramolecular [2+2]-cycloadduct but gave cyclobutenecarboxylic acid **10a**, which was difficult to isolate but it was detected by nmr spectroscopy. Similar photoirradiations of **8a** and **8b** afforded cyclobutenecarboxylic acids **13a** and **13b** whose crude yields were 45% and 43%, respectively. These products were difficult to purify by repeated column chromatography. Compounds **10a**, **14a** and **14b** were also obtained in the photoirradiation without benzophenone.

Scheme 2



The structures of **11b** and **11c** were assigned as intramolecular [2+2]-cycloadducts from the spectroscopic data. For instance, **11b**, 5-methoxy-2-oxatricyclo[6.3.0.0^{1,6}]-undec-4-en-3-one, showed a strong carbonyl absorption at 1707 cm^{-1} in the ir spectrum (potassium bromide) for a α,β-unsaturated lactone. The remarkable feature of the ^{1}H nmr spectrum of **11b** was the coupling pattern of 6-H, which appeared at δ 2.89 as a doublet-doublet (J = 9.2, 4.4 Hz). The ring junction across the C_5-C_6 double bond in **3b** could be deduced as *cis*-fused, and the configuration between hydrogens at 6- and 8-positions in **11b** could be assumed as trans by using the same manner cited in the previous report [1]. Compound **14a**, which has been formed through the hydrolysis of bicyclolactone **12a**, was

Scheme 3



assigned as 1-bromo-4-hydroxy-2-methyl-4-(2-oxa-3-oxo-5-hexenyl)-2-cyclobutene-1-carboxylic acid from the ^1H and ^{13}C nmr spectra.

The intramolecular photo[2+2]-cycloadditions of **3b** and **3c**, which had no ester moiety in the side-chain, occurred to afford tricyclic lactones, but in the case of **8a** and **8b**, which had ester group, the valence-isomerization of 2-pyrone ring happened to give cyclobutenecarboxylic acids. There are some reports that ester group is not a favorable one as connecting group between enone and olefin parts [3,4]. But recently, [2+2]-cycloadducts have been obtained in the intramolecular photocycloaddition of oxoesters [5]. These results show that some ester group causes the intramolecular cycloaddition to become delicate. The end-ester group at the side-chain in this system is thought not to be effective for the intramolecular addition. And also the fact that **3a**, which had two methylene units in the side-chain, did not give the intramolecular [2+2]-cycloadduct was thought to be caused by the rigid ring of 2-pyrone.

On the basis of these results as shown in Scheme 3, the intramolecular cycloaddition of **3** was found to require the presence of more than three methylene units in the side-chain as similar to the case of 4-(ω-alkenyloxy)-2-pyrone [1]. The formation of intramolecular [2+2]-cycloadducts **12a** or **12b** from irradiation of **3b,c** was estimated from the consideration of the frontier-orbital control (LSOMO (2-pyrone) - HOMO (olefin)) such as **B** similar to the case of 4-ω-alkenyloxy-2-pyrone [2]. But the formation of **11** instead of **12a** and **12b** probably reflects that the intermediate $\mathbf{B}_1$ and $\mathbf{B}_2$ were disturbed owing to the enone system having rigid skeleton. Consequently, the addition mechanism of this system is inferred not to be controlled by MO overlapping effect but to be controlled by new insights [6] affected the 2-pyrone triplet lifetime or the stability of the intermediate **A**.

EXPERIMENTAL

All the melting points were measured on a Yanagimoto Meltemp apparatus and are uncorrected. The ir, ^1H 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 using gc, which was performed on a Shimazu GC-12A instrument using a column of Silicon SE-30 (10%) or by tlc on silica-gel plates.

3-Bromo-6-bromomethyl-4-methoxy-2-pyrone (**5**) was prepared according to the method previously described in the literature [7].

6-(3-Butenyl)-4-methoxy- **3a**, 6-(4-Pentenyl)-4-methoxy- **3b**, and 6-(5-Hexenyl)-4-methoxy-2-pyrone (**3c**).

1) To 4-hydroxy-6-methyl-2-pyrone (**1**) (6.0 g, 48 mmoles) dissolved in dry THF (100 ml) at −78° under a nitrogen atmosphere was added *n*-butyllithium (66 ml of 1.6 *M* solution in hexane, 105 mmoles). The mixture was allowed to warm to 0°, stirred to 2 hours, and then allyl bromide (6.1 g, 50 mmoles) was added. The solution was stirred for 12 hours at room temperature, then treated with ice-water (100 ml) and the hexane layer was separated. The aqueous layer was extracted with hexane (3 x 50 ml), then acidified with dilute hydrochloric acid (5%) to *p*H 6. The resulting solution was extracted with diethyl ether (3 x 100 ml), the ether extracts was washed with water followed by brine, and then dried (magnesium sulfate). Chromatography of the crude material obtained from these extracts on silica gel using ethyl acetate-hexane 1:5 v/v mixture gave 6-(3-butenyl)-4-hydroxy-2-pyrone (**2a**) (0.78 g, 10%), which was used for the next step because it was difficult to purify by repeated chromatography. To **2a** (0.78 g, 4.7 mmoles) and anhydrous potassium carbonate (1.36 g, 9.8 mmoles) in 2-butanone (20 ml) was added dimethyl sulfate (0.59 g, 4.7 mmoles). The mixture was heated to reflux under a nitrogen atmosphere for 6 hours. After cooling, the reaction mixture was filtered and evaporated *in vacuo*. Chromatography on silica gel with ethyl acetate-hexane 1:1 v/v mixture yielded **3a** (0.28 g, 33%).

Compound **2a** was obtained as an oil; ^1H nmr (deuteriochloroform): δ 2.42 (m, 2H), 2.58 (m, 2H), 5.05 (m, 2H), 5.58 (s, 1H), 5.78 (m, 1H), 5.98 (s, 1H), 10.95 (bs, 1H).

Compound **3a** was obtained as an oil; ir (neat): 1720, 1650 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.42 (m, 2H), 2.55 (t, 2H), 3.80 (s, 3H), 5.03, 5.08, 5.41, 5.78 (each d, 1H), 5.79 (m, 1H); ms: m/z (relative intensity) 180 (M^+, 100). High-resolution ms Calcd. for $C_{10}H_{12}O_3$: 180.0788. Found: 180.0786.

2) To compound **1** (6.0 g, 48 mmoles) dissolved in dry THF (100 ml) at −78° under a nitrogen atmosphere was added *n*-butyllithium (66 ml, 105 mmoles). The mixture was allowed to warm

to 0°, stirred for 2 hours, and then 4-bromo-1-butene (6.8 g, 50 mmoles) was added. The solution was stirred for 18 hours at room temperature. The same workup mentioned above gave 6-(4-pentenyl)-4-hydroxy-2-pyrone (**2b**) (0.55 g, 6%), which was used for the next step without further purification. To **2b** (0.54 g, 3.0 mmoles) and anhydrous potassium carbonate (0.93 g, 6.7 mmoles) in 2-butanone (20 ml) was added dimethyl sulfate (0.27 g, 2.1 mmoles). The mixture was refluxed for 6 hours, and the same workup using chromatography afforded **3b** (0.28 g, 48%).

Compound **2b** was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 1.78, 2.05, 2.45, 4.97 (each m, 2H), 5.58 (s, 1H), 5.74 (m, 1H), 5.94 (s, 1H), 10.97 (bs, 1H).

Compound **3b** was obtained as an oil; ir (neat): 1730, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.77 (quint, 2H), 2.11 (m, 2H), 2.45 (t, 2H), 3.79 (s, 3H), 5.01 (m, 2H), 5.41, 5.76 (each s, 1H), 5.77 (m, 1H); ms: m/z (relative intensity) 194 (M$^+$, 100).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.20; H, 7.03.

3) To compound **1** (3.8 g, 30 mmoles) dissolved in dry THF (60 ml) at −78° under a nitrogen atmosphere was added *n*-butyllithium 38 ml, 60 mmoles). The mixture was allowed to 0°, stirred for 2 hours, and then 5-bromo-1-pentene (5.0 g, 34 mmoles) was added. The solution was stirred for 17 hours at room temperature. The same workup gave 6-(5-hexenyl)-4-hydroxy-2-pyrone (**2c**) (0.16 g, 3%), which was used for the next step without further purification. To **2c** (0.15 g, 0.8 mmole) and anhydrous potassium carbonate (0.23 g, 1.7 mmoles) in 2-butanone (20 ml) was added dimethyl sulfate (0.08 g, 0.6 mmole). The mixture was refluxed for 1 hour, and the same workup using chromatography gave **3c** (0.09 g, 52%).

Compound **2c** was obtained as an oil; ^{1}H nmr (deuteriochloroform): δ 1.49, 1.58, 2.00, 2.32, 4.90 (each m, 2H), 5.48 (s, 1H), 5.72 (m, 1H), 5.85 (s, 1H), 9.97 (bs, 1H).

Compound **3c** was obtained as an oil; ir (neat): 1725, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.53, 1.63, 2.03, 2.32 (each m, 2H), 3.80 (m, 3H), 5.00 (m, 2H), 5.40 (s, 1H), 5.74 (m, 1H), 5.75 (s, 1H); ms: m/z (relative intensity) 208 (M$^+$, 8), 125 (100).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.38; H, 7.56.

3-Bromo-4-methoxy-6-(2-oxa-3-oxo-5-hexenyl)-2-pyrone (**8a**) and 3-Bromo-4-methoxy-6-(2-oxa-3-oxo-6-heptenyl)-2-pyrone (**8b**).

1) A solution of 3-bromo-6-bromomethyl-4-methoxy-2-pyrone (**5**) [6] (2.7 g, 9.0 mmoles) and sodium acetate (0.74 g, 9.0 mmoles) in ethanol (100 ml) was refluxed for 22 hours, and then the solvent was evaporated *in vacuo*. After adding chloroform (20 ml) to the resulting mixture, sodium bromide was filtered and the filtrate was concentrated to give 6-acetoxymethyl-3-bromo-4-methoxy-2-pyrone (**6**) (2.2 g, 89%), which was essentially pure and used for the next step without further purification.

Compound **6** had mp 130-133°; ir (potassium bromide): 1740, 1720, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.16, 4.02 (each s, 3H), 4.87 (s, 2H), 6.30 (s, 1H); ms: m/z (relative intensity) 276 (M$^+$, 23), 234 (100).

Anal. Calcd. for $C_9H_9O_5Br$: C, 39.02; H, 3.27. Found: C, 38.76; H, 3.31.

2) A solution of **6** (1.1 g, 4.0 mmoles) containing concentrated sulfuric acid (0.2 ml) in ethanol (20 ml) was refluxed for 11 hours. After concentrated the solvent *in vacuo* and treated with 10% sodium carbonate solution, the resulting solution was extracted with chloroform (20 ml x 5) to give 3-bromo-6-hydroxymethyl-4-methoxy-2-pyrone (**7**) (0.89 g, 95%).

Compound **7** had mp 142-145° (lit [8], mp 134-140°); ir (potassium bromide): 1740, 1720, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.65 (bs, 1H), 4.03 (s, 3H), 4.50 (s, 2H), 6.42 (s, 1H); ms: m/z (relative intensity) 234 (M$^+$, 60), 205 (100).

Anal. Calcd. for $C_7H_7O_4Br$: C, 35.77; H, 3.00. Found: C, 35.68; H, 3.01.

3) A solution of **7** (1.0 g, 4.3 mmoles), 3-butenoic acid (0.48 g, 4.4 mmoles) and *p*-toluenesulfonic acid (0.05 g) in benzene (5 ml) was refluxed for 27 hours by using a Dean-Stark apparatus. The reaction mixture was washed with saturated sodium carbonate solution, dried (magnesium sulfate), and concentrated to give **8a** (1.0 g, 79%), which was recrystallized from benzene-carbontetrachloride = 1:10 v/v mixture.

A solution of **7** (1.2 g, 5.1 mmoles), 4-pentenoic acid (0.61 g, 6.1 mmoles) and *p*-toluenesulfonic acid (0.05 g) was refluxed for 26 hours. The similar workup mentioned above gave **8b** (1.1 g, 84%).

Compound **8a** had mp 106-108°; ir (potassium bromide): 1740, 1720, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.20 (d, 2H, J = 6.8 Hz), 4.01 (s, 3H), 4.90 (s, 2H), 5.22 (d, 1H, J = 10.0 Hz), 5.24 (d, 1H, J = 16.0 Hz), 5.90 (m, 1H), 6.28 (s, 1H); ms: m/z (relative intensity) 304 (M + 2, 26), 302 (M$^+$, 26), 236 (100).

Anal. Calcd. for $C_{11}H_{11}O_5Br$: C, 43.59; H, 3.66. Found: C, 43.72; H, 3.58.

Compound **8b** had mp 125-128°; ir (potassium bromide): 1740, 1720, 1650 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.42 (m, 2H), 2.52 (t, 2H, J = 7.6 Hz), 4.01 (s, 3H), 4.88 (s, 2H), 5.03 (d, 1H, J = 10.4 Hz), 5.08 (d, 1H, J = 17.2 Hz), 5.82 (m, 1H); ms: m/z (relative intensity) 318 (M + 2, 7), 316 (M$^+$, 6), 125 (100).

Anal. Calcd. for $C_{12}H_{13}O_5Br$: C, 45.46; H, 4.13. Found: C, 45.58; H, 4.03.

4-(3-Butenyl)-4-hydroxy-2-methoxy-2-cyclobutenecarboxylic Acid (**10a**).

A solution of **3a** (135 mg, 0.75 mmole) in acetonitrile (100 ml) was irradiated under nitrogen with a 400 W high-pressure mercury lamp through a Pyrex tube for 2.5 hours at room temperature. The solvent was then removed *in vacuo* and the residue was chromatographed using ethyl acetate to give a mixture (oil, 97 mg) containing **10a**, which was difficult to purify but was detected by ^{1}H nmr spectroscopy.

Compound **10a** had ^{1}H nmr (deuteriochloroform): δ 2.25, 2.36 (each m, 2H, CH_2), 3.18 (s, 1H, OH), 3.70 (s, 3H, Me), 3.72 (s, 1H, CH), 5.02 (m, 2H, $=CH_2$), 5.10 (s, 1H, =CH), 5.78 (m, 1H, $CH=CH_2$).

5-Methoxy-2-oxatricyclo[6.3.0.0^{1,6}]undec-4-en-3-one (**11b**).

A solution of **3b** (40 mg, 0.22 mmole) and benzophenone (4 mg, 0.02 mole) in acetonitrile (30 ml) was irradiated for 1 hour. After the solvent was removed, the residue was chromatographed using ethyl acetate-hexane 1:10 v/v mixture to give **11b** (22 mg, 55%).

Compound **11b** had mp 78-80°; ir (potassium bromide): 1707, 1630 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.55-2.10 (m, 8H, CH_2), 2.89 (dd, 1H, J = 9.2, 4.4 Hz, 6-H), 2.97 (m, 1H, 8-H), 3.75 (s, 3H, Me), 5.18 (s, 1H, =CH); ^{13}C nmr (deuteriochloroform): δ 24.1, 26.2, 31.3, 38.3, 39.1, 45.5, 55.9, 87.3, 89.1, 166.5, 174.2; ms: m/z (relative intensity) 194 (M$^+$, 10), 150 (100).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.95; H, 7.10.

5-Methoxy-2-oxatricyclo[6.4.0.0^{1,6}]dodec-4-en-3-one (**11c**).

A solution of **3c** (80 mg, 0.38 mmole) and benzophene (9 mg, 0.04 mmole) in acetonitrile (30 ml) was irradiated for 7 hours. The same workup mentioned above afforded **11c** (26 mg, 33%).

Compound **11c** was obtained as an oil; ir (neat): 1705, 1633 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.30-2.30 (m, 8H, CH_2), 2.51 (m, 1H, 8-H), 2.85 (t, 1H, J = 7.0 Hz, 6-H), 3.70 (s, 3H, Me), 5.10 (s, 1H, 4-H); ms: m/z (relative intensity) 208 (M^+, 2), 125 (100).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.30; H, 7.60.

1-Bromo-4-hydroxy-2-methoxy-4-(2-oxa-3-oxo-5-hexenyl)-2-cyclobutene-1-carboxylic Acid (**14a**) and 1-Bromo-4-hydroxy-2-methoxy-4-(2-oxa-3-oxo-6-heptenyl)-2-cyclobutene-1-carboxylic Acid (**14b**).

A solution of **8a** (228 mg, 0.75 mmole) in acetonitrile (100 ml) was irradiated for 5 hours. The similar workup and chromatography using ethyl acetate-hexane 1:1 v/v mixture gave crude cyclobutenecarboxylic acid **14a** (110 mg, 45%), which was difficult to purify by repeated chromatography. A solution of **8b** (238 mg, 0.75 mmole) in acetonitrile (100 ml) was irradiated for 4 hours. The same workup gave crude cyclobutenecarboxylic acid **14b** (109 mg, 43%).

Compound **14a** was obtained as an oil; ir (neat): 3000-2500, 1740 (br) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.12 (d, 2H, J = 6.8 Hz, CH_2), 3.15 (s, 1H, OH), 3.68 (s, 3H, Me), 3.75 (s, 2H, CH_2), 5.18 (m, 2H, $=CH_2$), 5.20 (s, 1H, =CH), 5.88 (m, 1H, $CH=CH_2$); ^{13}C nmr (deuteriochloroform): δ 36.7, 52.4, 67.3, 68.8, 72.9, 118.7, 119.3, 120.7, 129.3, 161.1, 169.2; ms: m/z (relative intensity) 322 (M+2, 2), 320 (M^+, 2), 141 (100).

Compound **14b** was obtained as an oil; ir (neat): 3000-2500, 1740 (br) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.38 (m, 2H, CH_2), 2.45 (t, 2H, J = 7.2 Hz, CH_2), 3.60 (s, 1H, OH), 3.72 (s, 3H, Me), 3.76 (s, 2H, CH_2), 5.00 (m, 2H, $=CH_2$), 5.10 (s, 1H, =CH), 5.80 (m, 1H, $CH=CH_2$); ms: m/z (relative intensity) 193 ($M-C_6H_7O_4$+2, 31), 191 ($M-C_6H_7O_4$, 32), 147 (100).

REFERENCES AND NOTES

[1] T. Shimo, M. Yasuda, J. Tajima and K. Somekawa, *J. Heterocyclic Chem.*, **28**, 745 (1991).

[2] T. Shimo, J. Tajima, T. Suishu and K. Somekawa, *J. Org. Chem.*, **56**, 7150 (1991).

[3] M. C. Pirrung and S. A. Thomson, *Tetrahedron Letters*, **27**, 2703 (1986).

[4] N. Katagiri, T. Haneda, H. Watamabe and C. Kaneko, *Chem. Pharm. Bull.*, **34**, 2646 (1986).

[5] S. L. Blanc, J.-P. Pete and O. Piva, *Tetrahedron Letters*, **34**, 635 (1993).

[6] D. I. Schuster, G. Lem and N. A. Kaprinidis, *Chem. Rev.*, **93**, 3 (1993).

[7] R. Bacardit, M. Moreno-Manãs and R. Pleixats, *J. Heterocyclic Chem.*, **19**, 157 (1982).

[8] P. de March, M. Moreno-Manãs, R. Pi, I. Ripoll and F. Sánchez-Ferrando, *J. Heterocyclic Chem.*, **22**, 1537 (1985).