October 1989 Chem. Pharm. Bull. **37**(10) 2803—2806 (1989)

Synthesis of 10-Aryl-3a,9-dihydro-1*H*,3*H*-furo[4,3-*b*][1,5]benzothiazepin-1-ones

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A practical synthetic route for 2-aroyl-4,4-dimethyl-2-buten-4-olides was developed. 10-Aryl-3a,9-dihydro-1*H*,3*H*-furo[4,3-*b*][1,5]benzothiazepin-1-ones were synthesized from 2-aroyl-4,4-dimethyl-2-buten-4-olides and 2-aminothiophenol in good yields.

Keywords benzothiazepinone; 2-aroyl-2-buten-4-olide; *N*-bromosuccinimide; allylic rearrangement; Michael reaction

In the course of our synthetic studies on biologically active heterocyclic compounds using tetronic acids or tetramic acids,[1] we reported the synthesis and biological activity, namely antimicrobial and analgetic activities, of 10-aryl-3,3-dimethyl-2,3,4,10-tetrahydro-1*H*-pyrrolo[3,4-*c*][1,5]benzothiazepin-1-ones (**1**).[2]

As a continuation of our work on the structure–activity relationship of furo- or pyrrolobenzothiazepinones, we planned to synthesize 10-aryl-3,3-dimethyl-3a,9-dihydro-1*H*,3*H*-furo[4,3-*b*][1,5]benzothiazepin-1-ones (**3**), which are isomers of oxaanalogs of **1**.

Schmidt and Zimmer reported that the synthesis of 10-aryl-4,10-dihydro-1*H*,3*H*-furo[3,4-*c*][1,5]benzothiazepin-1-ones (**2**) from 3-(arylmethylene)-2,4(3*H*,5*H*)-furandiones and 2-aminothiophenol in a single operation.[3]

We thought that the title compound **3** might be obtained from 2-aroyl-4,4-dimethyl-2-buten-4-olide (**4**) and 2-aminothiophenol by using a method analogous to that employed previously.[2] Therefore, first of all, we examined the preparation of **4** by a practical method.

Takeda *et al.*[4] reported that 2-benzoyl-4,4-dimethyl-2-buten-4-olide (**4a**) was obtained by reaction of 2-chloro-2-methyl-propanal and ethyl benzoylacetate in aqueous K_2CO_3 solution and subsequent thermal elimination of ethyl benzoylacetate from an intermediary 2-benzoyl-3-(benzoylethoxycarbonylmethyl)-4,4-dimethyl-4-butanolide in excellent yield. We tried to apply this method to the synthesis of **4** having a 4-chloro, 4-methyl or 4-nitro group on the benzene ring, but the desired products were not obtained, probably because of instability of the ethyl aroylacetates employed. Therefore another route was examined.

For the synthesis of **4**, a method using 2-buten-4-olides and aroyl halide in the presence of a base and thermal elimination of α-phenylsulfenyl or α-phenylseleno-2-aroyl-4-butanolides[5] was thought to be possible. Indeed, Hoye *et al.*[6] synthesized 2-benzoyl-2-buten-4-olide by peracid oxidation and then thermolysis of 2-benzoyl-2-phenylsulfenyl-4-butanolide. But they did the reaction in a nuclear magnetic resonance (NMR) tube and the product was not isolated, because of its instability.

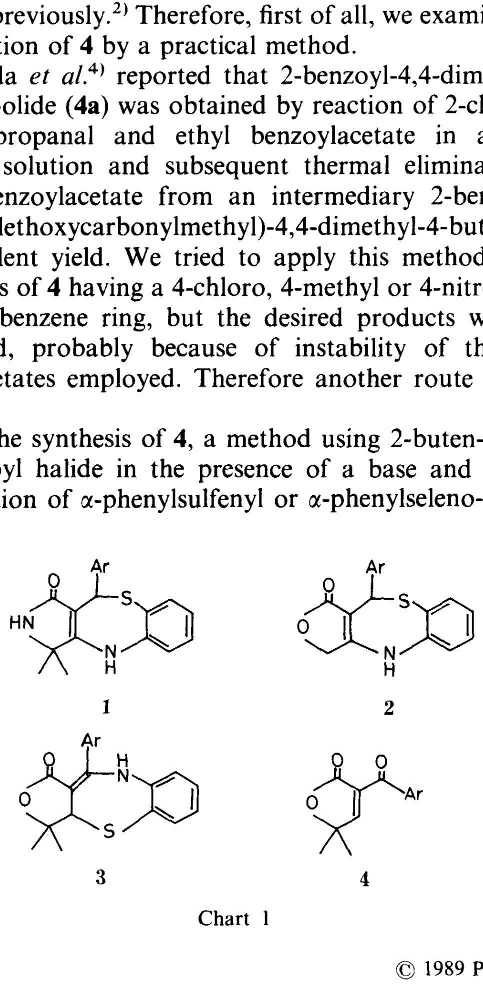


Chart 1

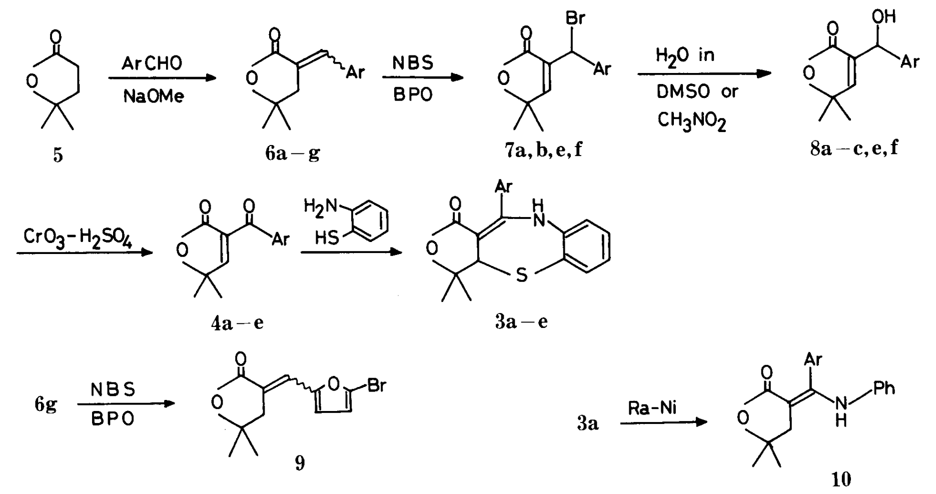
Zimmer *et al.*[7] prepared 2-(α-bromophenylmethyl)-4,4-dimethyl-2-buten-4-olide by bromination of 2-phenylmethylene-4,4-dimethyl-4-butanolide with *N*-bromosuccinimide (NBS).

Therefore we tried to apply this reaction to 2-arylmethylene-4,4-dimethyl-4-butanolide (**6**), in which the aromatic ring was substituted with a chloro, methoxy or nitro group, or replaced by a heterocyclic ring. Thus, 2-(2-chlorophenyl)-methylene-4,4-dimethyl-4-butanolide (**6b**) was synthesized from 4,4-dimethyl-4-butanolide (**5**)[8] and 2-chlorobenzaldehyde in 44.0% yield as a mixture of *E* and *Z*-isomers (1 : 6).[9] Other butanolides **6** were prepared similarly.

When **6b** was treated with NBS in the presence of benzoyl peroxide (BPO), the desired bromide **7b** was isolated in 77.3% yield. In the ^{1}H-NMR spectrum of **7b**, the methine proton signal appears at δ 6.23 as a doublet ($J = 1.5$ Hz). This indicated that the allylic rearrangement had occurred during the reaction as expected.[7] Compounds **6a**, **e**, and **f** were brominated by the same procedure as above to give **7a**,**e**, and **f**. In the case of the 4-methoxy derivative **6c**, the NBS treatment was performed similarly and 2-[α-hydroxy-(4-methoxyphenyl)-methyl]-2-buten-4-olide **8c** was obtained in 66.3% yield. In the case of the 3-nitrophenyl derivative **6d**, isolation of **7d** was not carried out, and the crude bromide was used directly for further chemical transformations. In the case of the 2-furylmethylene derivative **6g**, the desired compound **7g** was not isolated at all, but 2-[(5-bromo-2-furyl)methylene]-4,4-dimethyl-4-butanolide (**9**) was obtained in 37.0% yield.

Next, transformation of the bromides **7** into the alcohols **8** was smoothly performed by the action of water in dimethyl sulfoxide (DMSO) or in nitromethane (in the case of **7a**), except in the case of the pyridyl derivative **7f**, where the yield was low (13.5%). In the case of the 3-nitrophenyl derivative **7d**, as mentioned above, the crude **6d** was used in this transformation reaction, and **8d** was isolated in 49.7% yield based on **6d**, accompanied with **4d** (11.5%) and recovered **6d** (38.6%).

Next, the desired conjugate dicarbonyl compound **4** was obtained from the alcohol (**8**) by Jones oxidation in good yield, except in the case of the 3-nitrophenyl derivative (**8d**), where many products were formed as judged from thin layer chromatography (TLC). One of them was 3-nitroben-



a: Ar = C_6H_5
b: Ar = 2-ClC_6H_4
c: Ar = 4-$OMeC_6H_4$
d: Ar = 3-$NO_2C_6H_4$
e: Ar = 2-thienyl
f: Ar = 2-pyridyl
g: Ar = 2-furyl

Chart 2

TABLE I. Yields, Physical Constants, and Analytical Data of 3

3	Yields	mp (°C) (Recryst. solv.)	IR ν_{max}^{Nujol} cm^{-1}	^{1}H-NMR $\delta^{a,b)}$	Analysis (%) Calcd (Found)		
					C	H	N
a	83.7	194—195 (EtOH)	3270, 1705, 1620, 1580, 1275, 1050, 760	1.51, 1.57 (each 3H, s, 2 × CH_3), 4.09 (1H, s, SCH), 6.52 (1H, br s, NH), 6.88—7.55 (9H, m, ArH)	69.34	5.82	4.04
					(69.30	5.71	3.93)
					($C_{19}H_{17}NO_2S \cdot 1/2\,C_2H_5OH$)$^{c)}$		
b	91.7	211—215 (C_6H_6–hexane)	3250, 1720, 1630, 1580, 1275, 1045, 750	1.38, 1.40 (each 3H, s, 2 × CH_3), 4.18 (1H, s, SCH), 7.02—7.54 (8H, m, ArH), 9.39 (1H, br s, NH)	63.77	4.51	3.91
					(63.79	4.60	3.89)
					($C_{19}H_{16}ClNO_2S$)		
c	86.0	187—188 (C_6H_6)	3250, 1700, 1610, 1575, 1270, 1040, 750	1.44, 1.51 (each 3H, s, 2 × CH_3), 3.84 (3H, s, OCH_3), 4.10 (1H, s, SCH), 6.99—7.43 (8H, m, ArH), 9.35 (1H, br s, NH)	67.97	5.42	3.96
					(68.07	5.43	3.95)
					($C_{20}H_{19}NO_3S$)		
d	54.0	167—169 (EtOH)	3275, 1710, 1630, 1585, 1530, 1350, 1280, 1060, 760	1.43, 1.51 (each 3H, s, 2 × CH_3), 4.15 (1H, s, SCH), 7.07—8.32 (8H, m, ArH), 9.45 (1H, br s, NH)	59.06	4.69	7.25
					(58.99	4.70	6.95)
					($C_{19}H_{16}N_2O_4S \cdot H_2O$)$^{d)}$		
e	80.5	170—173 ($CHCl_3$–hexane)	3250, 1710, 1625, 1580, 1270, 1050, 775	1.41, 1.48 (each 3H, s, 2 × CH_3), 4.10 (1H, s, SCH), 6.88—7.69 (7H, m, ArH), 9.30 (1H, br s, NH)	61.98	4.59	4.25
					(62.12	4.64	4.38)
					($C_{17}H_{15}NO_2S_2$)		

a) Measured in DMSO-d_6 (**b**—**e**) or $CDCl_3$ (**a**). *b*) br s, broad singlet; m, multiplet; s, singlet. *c*) Exact Mass Calcd for $C_{19}H_{17}NO_2S$: 323.0980. Found: 323.0994. *d*) Exact Mass Calcd for $C_{19}H_{16}N_2O_4S$: 368.0830. Found: 368.0838.

zoic acid. When oxidation of **8d** was performed with pyridinium chlorochromate (PCC) in CH_2Cl_2 in the presence of anhydrous sodium acetate, the desired **4d** was obtained in 85.9% yield. Furthermore, 2-(4-methoxybenzoyl)-4,4-dimethyl-2-buten-4-olide (**4c**) was prepared from 2-(4-methoxyphenyl)methylene-4,4-dimethyl-4-butenolide (**6c**) in 65.0% overall yield without isolation of the intermediates, **7c** and **8c**.

These results indicate that the present synthetic route to 2-aroyl-4,4-dimethyl-2-buten-4-olides (**4**) is practical and economical.

With the desired Michael acceptor **4** in our hands, we next examined the synthesis of the title compound **3**. When 2-(2-chlorobenzoyl)-2-buten-4-olide (**4b**) was treated with 2-aminothiophenol in ethanol in the presence of concentrated HCl, Michael type addition reaction and subsequent intramolecular dehydration took place to give 10-(2-chlorophenyl)-3a,9-dihydro-1*H*,3*H*-furo[4,3-*b*][1,5]benzothiazepin-1-one (**3b**) in 91.7% yield.[2)] Other ene-dicarbonyl compounds (**4**) were allowed to react similarly and the desired compounds (**3**) were obtained in good yields. The structures of **3** were assigned on the basis of elemental analysis, infrared (IR), ^{1}H-NMR and mass spectral data, and some chemical reactions. In the ^{1}H-NMR spectraum of **3b**, the methine and NH proton signals appear at δ 4.09 and 6.52, each as a singlet, respectively. In the mass spectra (MS) of **3a** and **3d**, the base peak is at *m*/*z* 246 in both cases, which corresponds to M − Ar. When **3a** was treated with acetic anhydride in pyridine or methyl iodide in acetone in the presence of potassium carbonate, the starting material was recovered in both cases. Finally, when **3a** was treated with Raney-Ni in ethanol, compound **10** was isolated in 31.3% yield. Biological activity testing of the obtained compounds is under way.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus, model MP-S3, and are uncorrected. IR spectra were measured with a Hitachi 260-30 infrared spectrometer, and ^{1}H-NMR spectra were measured with a JEOL JNM-FX200 (200 MHz) spectrometer using tetramethylsilane (TMS) as an internal standard. MS were measured with a JEOL JMS-HX 100 instrument.

2-(2-Chlorophenyl)methylene-4,4-dimethyl-4-butanolide (6b) A solution of 4,4-dimethyl-4-butanolide (**5**)[8] (8.0 g, 70.1 mmol) and 2-chlorobenzaldehyde (10.0 g, 71.7 mmol) in dry benzene (39 ml) was added to a suspension of sodium methoxide (4.0 g, 74.9 mmol) in dry benzene (35 ml) at 10 °C under an N_2 atmosphere. The reaction mixture was stirred at room temperature overnight and then refluxed for 1 h. After cooling, the reaction mixture was acidified with 20% H_2SO_4 until pH 1—2. The separated organic phase was washed with brine and dried over Na_2SO_4. The crude product obtained by removal of the solvent was purified by SiO_2 column chromatography (chloroform) to give 7.30 g (44.0%) of pure **6b** as a colorless oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3060, 1750, 1655, 1600, 960. ^{1}H-NMR ($CDCl_3$) δ: E:Z=1:6 E-isomer: 1.48 (6H, s, 2×CH_3), 2.98 (2H, d, J=1.5 Hz, CH_2), 7.18—7.49 (4H, m, ArH), 7.90 (1H, t, J=1.5 Hz, =CHAr); Z-isomer: 1.42 (6H, s, 2×CH_3), 3.68 (2H, d, J=1.5 Hz, CH_2), 7.18—7.49 (4H, m, ArH), 6.75 (1H, t, J=1.5 Hz, =CHAr). Exact mass Calcd for $C_{13}H_{13}ClO_2$: 236.0604. Found: 236.0620.

The following compounds (**6a**,**c**—**g**) were prepared in the same manner.

2-Phenylmethylene-4,4-dimethyl-4-butanolide (6a)[7] 17.03 g (74.1%). bp 124—125 °C (0.25 Torr). IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3050, 1745, 1660, 1610, 960. ^{1}H-NMR ($CDCl_3$) δ: E:Z=4:5 E-isomer: 1.49 (6H, s, 2×CH_3), 3.04 (2H, d, J=3 Hz, CH_2), 7.20—7.50 (5H, m, ArH), 7.57 (1H, t, J=3 Hz, =CHAr); Z-isomer: 1.42 (6H, s, 2×CH_3), 3.56 (2H, d, J=2 Hz, CH_2), 6.77 (1H, t, J=2 Hz, =CHAr), 7.20—7.50 (5H, m, ArH).

2-(4-Methoxyphenyl)methylene-4,4-dimethyl-4-butanolide (6c) 8.87 g (32.4%). mp 114.5—116 °C (ethanol). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1725, 1640, 1600, 930. ^{1}H-NMR ($CDCl_3$) δ: 1.49 (6H, s, 2×CH_3), 3.00 (2H, d, J=3 Hz, CH_2), 3.85 (3H, s, OCH_3), 6.95 and 7.43 (each 2H, d, J=9 Hz, ArH), 7.52 (1H, t, J=3 Hz, =CHAr). *Anal.* Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.35; H, 6.94.

2-(3-Nitrophenyl)methylene-4,4-dimethyl-4-butanolide (6d) 3.22 g (25.2%). mp 108—115 °C (2-propanol–hexane). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1740, 1650, 920. ^{1}H-NMR ($CDCl_3$) δ: 1.51 (6H, s, 2×CH_3), 3.10 (2H, d, J=3 Hz, CH_2), 7.61 (1H, t, J=3 Hz, =CHAr), 7.65—8.33 (4H, m, ArH). *Anal.* Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 62.99; H, 5.32; N, 5.66.

2-(2-Thienyl)methylene-4,4-dimethyl-4-butanolide (6e) 6.06 g (33.2%). mp 114—116.5 °C (2-propanol). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3100, 1730, 1630, 930. ^{1}H-NMR ($CDCl_3$) δ: 1.52 (6H, s, 2×CH_3), 2.94 (2H, d, J=2.8 Hz, CH_2), 7.16 (1H, dd, J=4, 5 Hz, ArH), 7.33 (1H, d, J=4 Hz, ArH), 7.55 (1H, d, J=5 Hz, ArH), 7.75 (1H, t, J=2.8 Hz, =CHAr). *Anal.* Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81. Found: C, 63.27; H, 5.80.

2-(2-Pyridyl)methylene-4,4-dimethyl-4-butanolide (6f) 2.17 g (53.8%). mp 254—257 °C (ethanol). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3030, 1740, 1660, 1590, 965. ^{1}H-NMR ($CDCl_3$) δ: E:Z=1:4 E-isomer: 1.50 (6H, s, 2×CH_3), 3.35 (2H, d, J=3 Hz, CH_2), 7.16—8.70 (4H, m, ArH), 7.49 (1H, t, J=3 Hz, =CHAr); Z-isomer: 1.42 (6H, s, 2×CH_3), 3.75 (2H, d, J=1 Hz, CH_2), 7.04 (1H, t, J=1 Hz, =CHAr), 7.16—8.70 (4H, m, ArH). *Anal.* Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.93; H, 6.46; N, 7.19.

2-(2-Furyl)methylene-4,4-dimethyl-4-butanolide (6g) 5.34 g (39.6%). Oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3030, 1740, 1725, 1655, 920. ^{1}H-NMR ($CDCl_3$) δ: 1.44 and 1.49 (each 3H, s, 2×CH_3), 3.07 (2H, d, J=3 Hz, CH_2), 6.52—7.56 (3H, m, ArH), 7.31 (1H, t, J=3 Hz, =CHAr). Exact mass Calcd for $C_{11}H_{12}O_3$: 192.0786. Found: 192.0785.

2-[α-Bromo(2-chlorophenyl)methyl]-4,4-dimethyl-2-buten-4-olide (7b) NBS (0.59 g, 3.29 mmol) and BPO (3 mg, 0.01 mmol) were added successively to a solution of **6b** (0.78 g, 3.29 mmol) in dry CCl_4 (18.8 ml) and the whole was refluxed for 2 h. After cooling, the precipitates formed were filtered off. The filtrate was concentrated *in vacuo* to give a residue, which was crystallized from 2-propanol to furnish 3.33 g (63.7%) of **7b** as colorless needles. mp 100.5—102 °C. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3080, 1740, 1645, 965. ^{1}H-NMR ($CDCl_3$) δ: 1.51 and 1.53 (each 3H, s, 2×CH_3), 6.23 (1H, d, J=1.5 Hz, CHBr), 7.24—7.56 (5H, m, ArH and =CH). *Anal.* Calcd for $C_{13}H_{12}BrClO_2$: C, 49.48; H, 3.83. Found: C, 49.73; H, 3.90.

The following compounds (**7a**,**e**,**f**) were prepared in the same manner.

2-(α-Bromophenylmethyl)-4,4-dimethyl-2-buten-4-olide(7a)[7] 3.33 g (63.7%). mp 97.0—98.5 °C (2-propanol). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3075, 1740, 1630, 1600, 960. ^{1}H-NMR ($CDCl_3$) δ: 1.47 and 1.53 (each 3H, s, 2×CH_3), 5.76 (1H, d, J=1 Hz, CHBr), 7.29—7.52 (6H, m, ArH and =CH).

2-[α-Bromo(2-thienyl)methyl]-4,4-dimethyl-2-buten-4-olide (7e) 1.69 g (56.4%). mp 128—135 °C (benzene). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3080, 1735, 1630, 970. ^{1}H-NMR ($CDCl_3$) δ: 1.47 and 1.74 (each 3H, s, 2×CH_3), 5.24 (1H, d, J=1 Hz, CHBr), 7.21 (1H, dd, J=4, 5 Hz, ArH), 7.50 (1H, d, J=4 Hz, ArH), 7,74 (1H, d, J=5 Hz, ArH), 7.76 (1H, s, =CH). This compound was relatively unstable and was used for the next reaction after measurement of its IR and ^{1}H-NMR spectra.

2-[α-Bromo(2-pyridyl)methyl]-4,4-dimethyl-2-buten-4-olide (7f) 0.48 g (39.1%). Oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3080, 1750, 1590, 965. ^{1}H-NMR ($CDCl_3$) δ: 1.48 and 1.54 (each 3H, s, 2×CH_3), 5.82 (1H, s, CHBr), 7.27—8.64 (5H, m, ArH and =CH). MS m/z: 282.

2-(α-Hydroxyphenyl)methyl-4,4-dimethyl-2-buten-4-olide (8a) Water (4.2 ml) was added to a solution of **7a** (2.809 g, 10 mmol) in nitromethane (20.8 ml), and the resulting solution was refluxed for 2 h, stirred at room temperature overnight, and then concentrated *in vacuo*. The residue was dissolved in chloroform, washed with brine, and dried over Na_2SO_4. Removal of the solvent gave 2.753 g of crude **8a**, which was purified by SiO_2 column chromatography (benzene–ethyl acetate, 10:3) to afford 2.115 g (96.5%) of pure **4a** as a colorless oil. This compound was relatively unstable and used for the next reaction after measurement of its IR and ^{1}H-NMR spectra. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3400, 3070, 1735, 1600, 960. ^{1}H-NMR ($CDCl_3$) δ: 1.45 and 1.47 (each 3H, s, 2×CH_3), 3.21 (1H, br s, OH), 5.55 (1H, br s, C$\underline{H}$OH), 6.98 (1H, d, J=1 Hz, =CH), 7.29—7.44 (5H, m, ArH).

2-[α-Hydroxy(2-chlorophenyl)methyl]-4,4-dimethyl-2-buten-4-olide (8b) Water (1 ml) was added to a solution of **7b** (0.50 g, 1.58 mmol) in DMSO (5 ml), and the resulting solution was stirred at 60—70 °C for 2 h. After dilution with chloroform, the whole was washed successively with H_2O and brine, and dried over Na_2SO_4. Removal of the solvent gave 0.38 g (94.0%) of **8b** as an oil. This compound was relatively unstable and used for the next reaction after measurement of the IR and ^{1}H-NMR spectra. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3425, 3070, 1740, 1629, 1600, 965. ^{1}H-NMR ($CDCl_3$) δ: 1.44 and 1.47 (each 3H, s, 2×CH_3), 3.6 (1H, br s, OH), 5.93 (1H, br s, C$\underline{H}$OH), 6.83 (1H, d, J=1 Hz, =CH), 7.25—7.40 (4H, m, ArH).

The following compounds (**8e**, **f**) were prepared in the same manner.

2-[α-Hydroxy(2-thienyl)methyl]-4,4-dimethyl-2-buten-4-olide (8e) 0.67 g (99.1%). Oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3500, 3070, 1740, 1630, 960. ^{1}H-NMR ($CDCl_3$) δ: 1.49 and 1.51 (each 3H, s, 2×CH_3), 3.32 (1H, br s, OH), 5.82 (1H, br s, C$\underline{H}$OH), 6.92—7.30 (3H, m, ArH), 7.17 (1H, d, J=1 Hz, =CH). This compound was unstable and was used for the next reaction after measurement of its IR and ^{1}H-NMR spectra.

2-[α-Hydroxy(2-pyridyl)methyl]-4,4-dimethyl-2-buten-4-olide (8f) Stirring was continued for 15 h. 0.07 g (13.5%). Oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3350, 3070, 1740, 1590, 960. ^{1}H-NMR ($CDCl_3$) δ: 1.41 and 1.50 (each 3H, s, 2×CH_3), 5.59 (1H, br s, C$\underline{H}$OH), 7.26-8.54 (4H, m, ArH), 7.31 (1H, d, J=2 Hz, =CH). No satisfactory elemental analysis could be obtained.

2-[α-Hydroxy(4-methoxyphenyl)methyl]-4,4-dimethyl-2-buten-4-olide (8c) NBS (0.3 g, 1.7 mmol) and BPO (2 mg, 0.01 mmol) were added to a solution of **6c** (0.37 g, 1.6 mmol) in dry CCl_4 (10 ml) and the whole was refluxed for 1 h. After cooling, the precipitates formed were filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (benzene–ethyl acetate, 5:1) to give 0.26 g (66.3%) of **8c** as an oil. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3425, 1740, 1600, 955. ^{1}H-NMR ($CDCl_3$) δ: 1.45 and 1.48 (each 3H, s, 2×CH_3), 3.80 (3H, s, OCH_3), 5.50 (1H, s, C$\underline{H}$OH), 6.90 and 7.32 (each 2H, d, J=9 Hz, ArH), 6.99 (1H, s, =CH). Exact mass Calcd for $C_{14}H_{16}O_4$: 248.1049. Found: 248.1077.

2-[α-Hydroxy(3-nitrophenyl)methyl]-4,4-dimethyl-2-buten-4-olide (8d) and 4,4-Dimethyl-2-(3-nitrobenzoyl)-2-buten-4-olide (4d) A solution of **6d** (7.0 g, 28.3 mmol), NBS (5.3 g, 29.7 mmol) and BPO (24 mg, 0.1 mmol) in dry CCl_4 (130 ml) was refluxed for 2.5 h. After concentration *in vacuo*, the residue was dissolved in DMSO (87 ml). H_2O (18 ml) was added to the above solution and the whole was stirred at 60—70 °C for 5 h, then allowed to cool. Chloroform was added to the above solution, and the whole was washed successively with H_2O and brine, and dried over Na_2SO_4. Removal of the solvent gave 8.97 g of crude product, which was purified by SiO_2 column chromatography (chloroform), providing 2.70 g (38.6%) of recovered **6d**, 0.85 g (11.5%) of oxidized **4d**, and 3.71 g (49.7%) of **8d** (eluted in that order). **4d**: mp 92—93 °C (2-propanol). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3050, 1750, 1605, 1525, 1350, 960. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (6H, s, 2×CH_3), 7.72—8.67 (4H, m, ArH), 8.02 (1H, s, =CH). *Anal.* Calcd for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.86; H, 4.30; N, 5.39. **8d**: mp 152—156 °C (benzene). IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3475, 1725, 1530, 1350. ^{1}H-NMR ($CDCl_3$) δ: 1.48 and 1.50 (each 3H, s, 2×CH_3), 3.40 (1H, br s, OH), 5.68 (1H, s, C$\underline{H}$OH), 7.06 (1H, d, J=1 Hz, =CH), 7.57—8.30 (4H, m, ArH). *Anal.* Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.07; H, 5.00; N, 5.34.

2-(5-Bromo-2-furyl)methylene-4,4-dimethyl-4-butanolide (9) A mixture of **6g** (1.0 g, 5.2 mmol), NBS (1.4 g, 5.7 mmol) and BPO (4 mg, 0.02 mmol) in dry CCl_4 (30 ml) was refluxed for 1 h. After cooling, the precipitates formed were filtered off. The filtrate was concentrated *in vacuo* and the residue was purified by SiO_2 column chromatography (benzene–ethyl acetate, 25:1) to give 0.52 g (37.0%) of **9** as colorless needles after recrystallization from 2-propanol. mp 75—77 °C. IR ν_{max}^{Nujol} cm^{-1}: 3100, 1730, 1650, 960. ^1H-NMR ($CDCl_3$) δ: 1.49 (6H, s, $2\times CH_3$), 3.04 (2H, d, $J=3$ Hz, CH_2), 6.45 and 6.59 (each 1H, d, $J=3$ Hz, ArH), 7.20 (1H, t, $J=3$ Hz, =CH). *Anal.* Calcd for $C_{11}H_{11}BrO_3$: C, 48.73; H, 4.09. Found: C, 48.72; H, 4.19.

2-Benzoyl-4,4-dimethyl-2-buten-4-olide (4a)[4] Jones' reagent (0.5 ml) was added dropwise to a stirred solution of **8a** (0.3 g, 1.4 mmol) in acetone under ice-cooling. When **8a** had disappeared on TLC, 2-propanol was added to the above solution. The whole was concentrated *in vacuo*, treated with H_2O, and extracted with ether. The ether layer was washed with brine and dried over Na_2SO_4. Removal of the solvent *in vacuo* gave 0.28 g (95.4%) of **4a** as a colorless oil. bp 151—154 °C (0.45 Torr) (lit.[4] bp 145—150 °C (1 Torr)). mp 60—63 °C (2-propanol) (lit.[4] mp 65—66 °C). IR ν_{max}^{Nujol} cm^{-1}: 3070, 1750, 1655, 1620, 960. ^1H-NMR ($CDCl_3$) δ: 1.62 (6H, s, $2\times CH_3$), 7.46—7.54 (2H, m, ArH), 7.59—7.67 (1H, m, ArH), 7.78 (1H, s, =CH), 7.83—7.89 (2H, m, ArH).

The following compounds (**4b,c,e**) were prepared in the same manner.

2-(2-Chlorobenzoyl)-4,4-dimethyl-2-buten-4-olide (4b) 0.23 g (90.2%). mp 74—77 °C (2-propanol–hexane). IR ν_{max}^{Nujol} cm^{-1}: 3075, 1740, 1670, 1620, 1590, 960. ^1H-NMR ($CDCl_3$) δ: 1.57 (6H, s, $2\times CH_3$), 7.35—7.53 (4H, m, ArH), 7.89 (1H, s, =CH). *Anal.* Calcd for $C_{13}H_{11}ClO_3$: C, 62.29; H, 4.42. Found: C, 62.11; H, 4.47.

2-(4-Methoxybenzoyl)-4,4-dimethyl-2-buten-4-olide (4c) 0.15 g (67.6%). mp 94—95 °C (2-propanol). IR ν_{max}^{Nujol} cm^{-1}: 3090, 1755, 1640, 1600, 1570, 965. ^1H-NMR ($CDCl_3$) δ: 1.61 (6H, s, $2\times CH_3$), 3.89 (3H, s, OCH_3), 6.96 and 7.85 (each 2H, d, $J=9$ Hz, ArH), 7.73 (1H, s, =CH). *Anal.* Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.19; H, 5.69.

Compound **4c** was also prepared in 65.0% overall yield from **6c** without isolation of the intermediates, **7c** and **8c**.

4,4-Dimethyl-2-thenoyl-2-buten-4-olide (4e) 0.55 g (71.9%). mp 132—135 °C (2-propanol). IR ν_{max}^{Nujol} cm^{-1}: 3080, 1760, 1640, 1620, 960. ^1H-NMR ($CDCl_3$) δ: 1.61 (6H, s, $2\times CH_3$), 7.18—7.86 (3H, m, ArH), 7.89 (1H, s, =CH). *Anal.* Calcd for $C_{11}H_{10}O_3S$: C, 59.44; H, 4.53. Found: C, 59.29; H, 4.47.

4,4-Dimethyl-2-(3-nitrobenzoyl)-2-buten-4-olide (4d) A solution of **8d** (0.10 g, 0.38 mmol) in dry CH_2Cl_2 (2.5 ml) was added to a suspension of PCC (0.12 g, 0.6 mmol), sodium acetate (9 mg, 0.1 mmol), and Celite (0.11 g) in dry CH_2Cl_2 (0.8 ml) and the resulting mixture was stirred for 1.5 h at room temperature. After further addition of PCC (41 mg), stirring was continued for another 2.5 h. Usual work-up and recrystallization from 2-propanol gave **4d** (85 mg, 85.9%). mp 92—93 °C. IR and ^1H-NMR spectral data and elemental analysis data were presented above.

10-(2-Chlorophenyl)-3,3-dimethyl-3a,9-dihydro-1*H*,3*H*-furo[4,3-*b*][1,5]benzothiazepin-1-one (3b) 2-Aminothiophenol (2.0 g, 16 mmol) and concentrated HCl (1.4 ml, 17.3 mmol) were added to a solution of **4b** (4.0 g, 16 mmol) in ethanol (48 ml) and the whole was refluxed for 1.5 h. After concentration *in vacuo*, the residue was crystallized from benzene to give 5.25 g, of **3b** as colorless plates.

Other compounds (**3a,c—e**) were prepared in the same manner, and yields, melting points, elemental analyses, IR, and ^1H-NMR spectral data are listed in Table I.

2-(α-Anilinophenylmethylene)-4,4-dimethyl-4-butanolide (10) A mixture of **3a** (1.0 g, 3.1 mmol) and Ra-Ni (prepared from 2.0 g of Al-Ni alloy) in ethanol (20 ml) was refluxed overnight. After filtration, the filtrate was concentrated *in vacuo* to leave a black oil (0.96 g), which was purified by SiO_2 column chromatography (hexane–acetone, 4:1) to give 0.28 g (31.3%) of **10** as colorless needles after recrystallization from 2-propanol. mp 140—141.5 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250, 1675, 1620, 1595, 980. ^1H-NMR ($CDCl_3$) δ: 1.41 (6H, s, $2\times CH_3$), 2.62 (2H, s, CH_2), 6.86—7.38 (10H, m, ArH), 10.11 (1H, br s, NH). *Anal.* Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.81; H, 6.58; N, 4.73.

References and Notes

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