

Paul Francis Schuda* and Jennifer L. Phillips

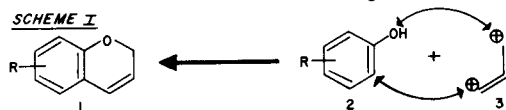
Department of Chemistry, University of Maryland,
College Park, Maryland 20742

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A two-step process for synthesizing 2*H*-1-benzopyrans from phenols and β -halopropionaldehyde acetals is detailed.

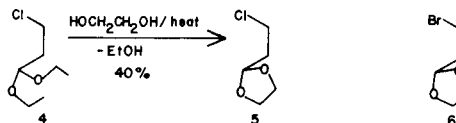
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The 2*H*-1-benzopyran system **1** is being used in our laboratories for a number of synthetic endeavors. Although a considerable amount of work has been reported on the



synthesis of 2,2-dialkyl-2*H*-1-benzopyrans, fewer methods for the preparation of the parent system (**1**) have been developed [1]. These known methods often require multistep transformations or high temperatures, and sometimes suffer from low overall yields and low regioselectivity in the case of unsymmetrically substituted compounds.

Herein, we report the methodology that we have developed for the short (two-step) synthesis of 2*H*-1-benzopyrans (**1**). The construction of the pyran portion was to occur by the reaction of a suitably substituted, electron-rich phenol **2** with the three carbon unit **3** (Scheme I). Three potential equivalents of **3** that are commercially available and/or easily prepared in large quantity [2,3] are the β -halopropionaldehyde alkyl acetals **4-6**. We chose to use **5** because,



(a) it was easy to prepare in large quantities from **4** [2], and (b) its use precluded the formation of by-products in the cyclization reaction that made subsequent purification difficult or impossible.

The first step involves a Williamson ether synthesis between the potassium salt of the phenols **7a-f** with chloroacetal **5** using a catalytic amount of tetra-*n*-butylammonium iodide (TBAI) to give the ether-acetals **8a-f** in the indicated yields (see Table 1). The use of either the sodium phenolate with or without TBAI, or the use of the potassium phenolate led only to a slow and incomplete reaction. These results are reasonable when one considers both the relative shielding abilities of the cations and the rate of cation exchange of Na⁺ and K⁺ for *n*Bu₄N⁺ [4]. Also, the addition of excess iodide (either as *n*Bu₄N⁺I⁻ or KI) does

not appreciably accelerate the reaction, thus indicating that a Finkelstein process of halide exchange is at best a minor process in controlling the reaction speed.

The cyclization of aldehydes and aldehyde acetals onto electron-rich aromatic systems has been used to synthesize benzazepines [5] and 2,2-dialkyl-2*H*-1-benzopyrans [6]. Treatment of the acetals **8a-f** with a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene gave the 2*H*-1-benzopyrans **9a-f** in the indicated yields after chromatography. A variety of Lewis and protic acids were studied in this cyclization. In general, we have found the most effective and reliable one to be *p*-toluenesulfonic acid.

The cyclization is also highly regioselective. In one case studied (**8c**), cyclization gave *ca.* 8:1 mixture of *para:ortho* cyclization products. In the other two possibilities for regioisomer formation (**8e** and **8f** → **9e** and **9f** respectively), we could find no evidence of regioisomer formation using standard spectroscopic and chromatographic analytical techniques. The yield of the cyclization also is best when an electron donating substituent is present at the position *para* to the cyclization site (Table 1).

This methodology provides a short and highly regioselective method of preparing 2*H*-1-benzopyrans from a variety of electron-rich phenols. Although the overall yield in some of the examples is not high [7], the brevity of the overall process and the easy availability of the starting materials may make this alternative the method of choice in some cases.

TABLE I

Entry	R	R'	R''	%Yield of 8	%Yield of 9	ref.
a	H	H	H	78	20	8
b	OMe	H	H	50	14	9,10
c	H	OMe	H	91	44 ^a	10
d	H	H	OMe	88	26	10
e	H	OCH ₂ O	H	100	50	11
f	H	O-CH ₂ -O	H	81	60	—

a. +

EXPERIMENTAL

Proton nmr spectra were recorded on either a Varian EM-360A or Varian XL-100 spectrometer using tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer 281 spectrometer. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Elemental analyses for C and H were performed by Dr. Franz Kasler of the University of Maryland.

Flash chromatography was performed using E. Merck Silica Gel 60 (230-400 mesh). Medium pressure liquid chromatography (mpc) was performed using Whatman LPS-1 silica gel. Thin layer chromatography was performed on E. Merck glass supported Silica Gel 60 (0.25 mm, F-254). Analytical gas chromatography was carried out on a Hewlett-Packard Model 5750 Research Chromatograph (columns, 6 ft, 10% UC-W98, 80-100m).

Ethyl acetate, Skellysolve F, and pentanes were distilled prior to use. Benzene was distilled from calcium hydride and THF was distilled from sodium/benzophenone.

Resorcinol Monobenzyl Ether (7e).

This compound was prepared by the method described by Fitton and Ramage [12] in 27% yield. The yellow waxy crystals had a melting point of 42-45° (lit mp 50-51°); ¹H nmr (deuteriochloroform, 60 MHz): δ 4.85 (s, 1H), 5.71 (s, 1H), 6.19-6.46 (m, 3H), 6.80-7.21 (m, 6H).

2-(2-Chloroethyl)-1,3-dioxolane (5).

β-Chloropropionaldehyde diethyl acetal (4) (50 g, 0.30 mole) and ethylene glycol (20.50 g, 0.33 mole) were placed in a round-bottom flask equipped with a short path condenser apparatus. The reaction mixture was heated and ethanol was distilled over until starting material disappeared as evidenced by nmr analysis of an aliquot. The product was purified by fractional distillation with a 5' Vigreux column to give a colorless liquid (18.26 g, 45%) bp 74-78° (26 mm); ¹H nmr (deuteriochloroform, 100 MHz): δ 2.12 (d of t, 2H, J = 4.6, 7.0 Hz), 3.64 (t, 2H, J = 7.0 Hz), 3.83-3.99 (m, 4H), 5.01 (t, 1H, J = 4.6 Hz); ir (neat): 2975, 2890, 1415, 1130 cm⁻¹.

Anal. Calcd. for C₅H₈ClO₂: C, 43.97; H, 6.64. Found: C, 44.27; H, 6.94.

β-(Phenoxy)propionaldehyde Ethylene Acetal (8a).

Potassium hydride (24.6% mmole) (0.51 g, 12.70 mmoles) was placed in a round-bottomed flask and the oil was washed off with 4 × 1 ml aliquots of petroleum ether. Tetrahydrofuran (10 ml) was added and the suspension cooled to 0° in an ice bath. A solution of phenol (1.00 g, 10.6 mmoles) in 10 ml of THF was added dropwise via an addition funnel over a period of 15 minutes. The mixture was stirred at room temperature for 15 minutes. Tetra-*n*-butylammonium iodide (0.39 g, 1.06 mmoles) was added, immediately followed by a solution of 2-(2-chloroethyl)-1,3-dioxolane (5) (1.59 g, 11.7 mmoles) in 15 ml of THF. The reaction was heated at reflux with stirring for 3 days. The reaction was cooled and filtered through a Celite pad and the salts were washed with THF. The THF was evaporated *in vacuo* and the remaining oil was dissolved in 30 ml ether. The ether was washed with 2 × 30 ml of 10% sodium hydroxide and 30 ml of water, dried over magnesium sulfate and concentrated to yield 1.60 g (78%), of ether 8a. Spectroscopic analysis showed the product was pure enough to be used directly in the next step. An analytical sample was purified by flash chromatography (eluant: 10% ethyl acetate in Skelly F) to give a clear oil; ¹H nmr (deuteriochloroform, 60 MHz): δ 2.13 (d of t, 2H, J = 4.5, 6.0 Hz), 3.8-4.2 (m, 6H), 5.09 (t, 1H, J = 4.5 Hz), 6.85-7.45 (m, 5H); ir (neat): 2980, 2890, 1610, 1505, 1245 cm⁻¹.

Anal. Calcd. for C₁₁H₁₄O₃: C, 68.02; H, 7.27. Found: C, 68.06; H, 7.56.

β-(2-Methoxyphenoxy)propionaldehyde Ethylene Acetal (8b).

Potassium hydride (24.6% in oil) (0.77 g, 19.0 mmoles) was placed in a round-bottomed flask (nitrogen). The oil was washed off with 3 × 4 ml aliquots of petroleum ether. Tetrahydrofuran (20 ml) was added and the

suspension was cooled to 0° in an ice bath. Guaiacol (2.00 g, 16.0 mmoles) in 20 ml of THF was added dropwise over a 15 minute period and the mixture was then stirred at room temperature for 15 minutes. Tetra-*n*-butylammonium iodide (0.59 g, 1.60 mmoles) was added followed by a solution of 2-(2-chloroethyl)-1,3-dioxolane (2.45 g, 18.0 mmoles) in 30 ml of THF. The reaction was heated at reflux with stirring for 4 days, and then cooled and filtered through a Celite pad. The salts were washed with THF. The combined THF was evaporated *in vacuo* and the remaining oil was dissolved in 75 ml of ether, washed with 2 × 50 ml of 10% sodium hydroxide and 50 ml of water. The organic layer was dried over magnesium sulfate and concentrated to yield 1.80 g (50%) of crystalline ether (8b). This was sufficiently pure by spectroscopic analysis to be used directly in the next step. An analytical sample was purified by trituration with petroleum ether to give light pink crystals mp 45°; ¹H nmr (deuteriochloroform, 100 MHz): δ 2.21 (d of t, 2H, J = 4.8, 6.8 Hz), 3.85 (s, 3H), 3.88-4.01 (m, 4H), 4.18 (t, 2H, J = 6.8 Hz), 5.11 (t, 1H, J = 4.8 Hz), 6.90 (s, 4H); ir (chloroform): 3020, 2890, 1505, 1255, 1130 cm⁻¹.

Anal. Calcd. for C₁₂H₁₆O₄: C, 64.27; H, 7.19. Found: C, 64.03; H, 7.34.

β-(3-Methoxyphenoxy)propionaldehyde Ethylene Acetal (8c).

Potassium hydride (24.6% in oil) (0.39 g, 9.70 mmoles) was added to a round-bottomed flask (nitrogen), and washed with 4 × 1 ml aliquots of petroleum ether. Tetrahydrofuran (15 ml) was added and the suspension cooled to 0° in an ice bath. Resorcinol monomethyl ether (1.00 g, 8.10 mmoles) in 15 ml of THF was added dropwise over a 15 minute period. The reaction was then stirred for 15 minutes at room temperature. Tetra-*n*-butylammonium iodide (0.30 g, 0.81 mmole) was added followed immediately by a solution of 2-(2-chloroethyl)-1,3-dioxolane (1.21 g, 8.90 mmoles) in 15 ml of THF. The reaction was heated at reflux for 4 days. The reaction was cooled and filtered through a Celite pad and the salts were washed with THF. The THF was evaporated *in vacuo* and the residue was dissolved in 30 ml of ether. The ether layer was washed with 2 × 25 ml of 10% sodium hydroxide and 25 ml of water, dried over magnesium sulfate and concentrated to give 1.65 g, (91% of ether 8c). This was sufficiently pure by spectroscopic analysis to be used directly in the next step. An analytical sample was purified by flash chromatography (eluant: 10% ethyl acetate in Skelly F) to give a clear oil; ¹H nmr (deuteriochloroform, 100 MHz): δ 2.11 (d of t, 2H, J = 4.8, 6.6 Hz), 3.72 (s, 3H), 3.76-3.95 (m, 4H), 4.07 (t, 2H, J = 6.6 Hz), 5.04 (t, 1H, J = 4.8 Hz), 6.44-6.53 (m, 3H), 7.04-7.28 (m, 1H); ir (neat): 2960, 2885, 1590, 1490, 1155 cm⁻¹.

Anal. Calcd. for C₁₂H₁₆O₄: C, 64.27; H, 7.19. Found: C, 64.45; H, 7.19.

β-(4-Methoxyphenoxy)propionaldehyde Ethylene Acetal (8d).

Potassium hydride (24.6% in oil) (0.77 g, 19.2 mmoles) was placed in a round-bottomed flask (nitrogen) and the oil was washed off with 4 × 3 ml aliquots of petroleum ether. Tetrahydrofuran (30 ml) was added and the solution was cooled to 0° in an ice bath. *p*-Methoxyphenol (2 g, 16.1 mmoles) in 30 ml of THF was added dropwise via an addition funnel over a 15 minute period. The reaction was stirred at room temperature for 15 minutes. Tetra-*n*-butylammonium iodide (0.59 g, 1.61 mmoles) was added, followed by a solution of 2-(2-chloroethyl)-1,3-dioxolane (2.45 g, 18.0 mmoles) in 30 ml of THF. The reaction was heated at reflux for 4 days, then cooled and filtered through a pad of Celite. The salts were rinsed with THF and the combined THF was concentrated *in vacuo*. The residue was dissolved in 75 ml of ether and washed with 2 × 75 ml of 10% sodium hydroxide and 75 ml of water. The organic layer was dried (magnesium sulfate) and concentrated *in vacuo* to give 3.15 g (88%) of ether 8d. An analytical sample was purified by flash chromatography (eluant: 10% ethyl acetate in Skelly F) to give a clear oil; ¹H nmr (deuteriochloroform, 100 MHz): δ 2.10 (d of t, 2H, J = 4.8, 6.6 Hz), 3.70 (s, 3H), 3.77-3.94 (m, 4H), 4.03 (t, 2H, J = 6.6 Hz), 5.04 (t, 1H, J = 4.8 Hz), 6.80 (s, 4H); ir (neat): 2980, 1890, 1515, 1230 cm⁻¹.

Anal. Calcd. for C₁₂H₁₆O₄: C, 64.27; H, 7.19. Found: C, 64.12; H, 7.40.

β-(3-Benzyloxyphenoxy)propionaldehyde Ethylene Acetal (8e).

Potassium hydride (24.6% in oil) (0.96 g, 24.0 mmoles) was added to a

round-bottomed flask (nitrogen). The oil was washed off with 4×3 ml aliquots of petroleum ether. Tetrahydrofuran (35 ml) was added and the solution was cooled to 0° in an ice bath. A solution of resorcinol mono-benzyl ether (4.0 g, 20.0 mmoles) in 35 ml of THF was added dropwise over a 15 minute period. The reaction was then stirred at room temperature for 15 minutes. Tetra-*n*-butylammonium iodide (0.74 g, 2.00 mmole) was added followed by 2-(2-chloroethyl)-1,3-dioxolane (2.86 g, 21.0 mmoles) in 35 ml of THF. The reaction was heated at reflux for 3 days. The reaction was cooled and filtered through celite, and the salts washed with THF. The THF was removed *in vacuo* and the remaining oil dissolved in 100 ml of ether. The ether was washed with 2×75 ml of 10% sodium hydroxide and 75 ml of water, dried (magnesium sulfate) and concentrated to give 6.28 g (100%) of ether **8e**. An analytical sample was purified by mpc (eluant: 8% ethyl acetate in Skelly F); ^1H nmr (deuteriochloroform, 100 MHz): δ 2.11 (d of t, 2H, $J = 4.8, 6.5$ Hz), 3.74-3.92 (m, 4H), 4.05 (t, 2H, $J = 6.5$ Hz), 5.03 (t, 1H (containing 2Hs at δ 4.96), $J = 4.8$ Hz), 6.44-6.56 (m, 3H), 7.04-7.40 (m, 6H); ir (chloroform): 2960, 2880, 1590, 1495, 1180, 1145 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{20}\text{O}_4$: C, 71.98; H, 6.71. Found: C, 72.07; H, 6.76.

β -(3,4-Methylenedioxyphenoxy)propionaldehyde Ethylene Acetal (**8f**).

Potassium hydride (0.35 g, 8.70 mmoles) was placed in a round-bottomed flask (nitrogen). The oil was washed off with 4×1 ml aliquots of petroleum ether. Tetrahydrofuran (10 ml) was added and the suspension cooled to 0° in an ice bath. A solution of sesamol (1 g, 7.25 mmoles) in 10 ml of THF was added dropwise over a 15 minute period. The reaction was then stirred at room temperature for 15 minutes. Tetra-*n*-butylammonium iodide (0.27 g, 0.72 mmole) was added followed by 2-(2-chloroethyl)-1,3-dioxolane (1.03 g, 7.60 mmoles) in 10 ml of THF. The reaction was heated at reflux for 3 days. The reaction was cooled and filtered through a Celite pad and the salts washed with THF. The THF was removed *in vacuo* and the remaining oil was dissolved in 25 ml of ether and washed with 2×25 ml of 10% sodium hydroxide and 25 ml of water. The organic layer was dried (magnesium sulfate) and concentrated to give 1.40 g (81%) of crystalline ether **8f**. The ether was used directly in the next step. An analytical sample was purified by trituration with petroleum ether to give white crystals mp $56\text{--}57^\circ$; ^1H nmr (deuteriochloroform, 100 MHz): δ 2.11 (d of t, 2H, $J = 4.8, 6.6$ Hz), 3.83-3.98 (m, 4H), 4.04 (t, 2H, $J = 6.6$ Hz), 5.07 (t, 1H, $J = 4.8$ Hz), 5.89 (s, 2H), 6.27-6.73 (m, 3H); ir (chloroform): 3020, 2980, 2900, 1510, 1490, 1480, 1190 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_5$: C, 60.50; H, 5.92. Found: C, 60.84; H, 6.00.

2H-1-Benzopyran (**9a**) (lit [8]).

A solution of β -(phenoxy)propionaldehyde ethylene acetal (**8a**) (1.50 g, 7.73 mmoles) in 30 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (459 mg) was added and the solution heated at reflux for 3 days. A solution of 20 ml of 10% sodium hydroxide was added and the solution cooled to room temperature. The layers were separated and the organic layer washed with 20 ml of 10% sodium hydroxide and 20 ml of water. The aqueous layers were extracted with 20 ml of benzene. The organic layers were combined and dried (magnesium sulfate) and concentrated *in vacuo*. The crude oil was purified by flash chromatography (eluant: pentane) to yield 0.21 g (20%) of 2H-1-benzopyran as a clear oil; ^1H nmr (deuteriochloroform, 60 MHz): δ 4.70 (d of d, 2H, $J = 2.0, 3.5$ Hz), 5.59 (d of t, 1H, $J = 3.5, 10$ Hz), 6.20-7.08 (m, 5H); ir (neat): 2840, 1485, 1235, 1200 cm^{-1} .

8-Methoxy-2H-1-benzopyran (**9b**) (lit [9,10]).

A solution of ether (**8b**) (1.00 g, 4.50 mmoles) in 20 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (65 mg) was added and the solution was heated at reflux for 3 days. At this time 10 ml of 10% sodium hydroxide was added and the reaction was cooled to room temperature. The aqueous phase was separated and the organic layer washed with 10 ml of 10% sodium hydroxide and 10 ml of water. The aqueous layers were extracted with 20 ml of benzene and the combined organic layers were dried (magnesium sulfate) and concentrated *in vacuo*. The crude product was purified by mpc (eluant: 3%

ethyl acetate in Skelly F) to yield 100 mg (14%) of a light yellow oil; ^1H nmr (deuteriochloroform, 100 MHz): δ 3.85 (s, 3H), 4.87 (d of d, 2H, $J = 1.8, 3.5$ Hz), 5.72-5.82 (m, 1H), 6.34-6.85 (m, 4H); ir (neat): 2965, 2840, 1485, 1275, 1215 cm^{-1} .

7-Methoxy-2H-1-benzopyran (**9c**) (lit [10]).

A solution of ether **8c** (2.0 g, 8.90 mmoles) in 35 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (60 mg) was added and the reaction heated at reflux for 24 hours. At this time, 15 ml of 10% sodium hydroxide was added and the reaction cooled to room temperature. The aqueous layer was separated and the organic layer washed with 20 ml of 10% sodium hydroxide and 20 ml of water. The aqueous phases were extracted with 25 ml of benzene and the combined benzene layers dried (magnesium sulfate) and concentrated to yield crude 7-methoxy-2H-1-benzopyran. The crude oil was purified by mpc (eluant: 2% ethyl acetate in Skelly F) to yield 0.56 g (39%) of a light yellow oil; ^1H nmr (deuteriochloroform, 100 MHz): δ 3.72 (s, 3H), 4.75 (d of d, 2H, $J = 1.8, 3.5$ Hz), 5.49-5.66 (m, 1H), 6.28-6.46 (m, 3H), 6.79-6.88 (m, 1H); ir (neat): 2960, 2850, 1600, 1510, 1280, 1200 cm^{-1} .

6-Methoxy-2H-1-benzopyran (**9d**) (lit [10]).

A solution of ether (**8d**) (0.50 g, 2.23 mmoles) in 10 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (55 mg) was added and the solution was heated at reflux for 3 days. At this time 5 ml of 10% sodium hydroxide was added and the reaction was cooled to room temperature. The aqueous layer was separated and the benzene washed with 5 ml of 10% sodium hydroxide and 10 ml of water. The combined aqueous layers were extracted with 10 ml of benzene. The combined organic layers were dried (magnesium sulfate) and concentrated *in vacuo* to give the crude chromene. This was purified by mpc (eluant: 3% ethyl acetate in Skelly F) to yield 92 mg, 26% of a light yellow oil; ^1H nmr (deuteriochloroform, 100 MHz): δ 3.73 (s, 3H), 4.72 (d of d, 2H, $J = 1.7, 3.5$ Hz), 5.70-5.87 (m, 1H), 6.31-6.83 (m, 4H); ir (neat): 2960, 2840, 1490, 1205 cm^{-1} .

7-Benzyloxy-2H-1-benzopyran (**9e**) (lit [11]).

A solution of ether **8e** (2.00 g, 6.70 mmoles) in 35 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (85 mg) was added and the reaction heated at reflux for 24 hours. A solution of 20 ml of 10% sodium hydroxide was added and the reaction was cooled to room temperature. The layers were separated and the organic layer washed with 20 ml of 10% sodium hydroxide and 20 ml of water. The aqueous layers were extracted with 20 ml of benzene and the combined organic layers were dried (magnesium sulfate) and concentrated to give the crude chromene **9e**. This was purified by mpc (eluant: 2% ethyl acetate in Skelly F) to yield 0.80 g (50%) of white crystals mp $57\text{--}58^\circ$; ^1H nmr (deuteriochloroform, 100 MHz): δ 4.76 (d of d, 2H, $J = 2.0, 4.0$ Hz), 4.98 (s, 2H), 5.57 (d of t, 1H, $J = 4.0$ Hz, 10 Hz), 6.26-6.52 (m, 3H), 6.58-6.68 (m, 1H), 7.35 (s, 5H); ir (chloroform): 3010, 2840, 1640, 1500, 1275, 1170 cm^{-1} .

6,7-Methylenedioxy-2H-1-benzopyran (**9f**).

A solution of ether **8f** (2.00 g, 8.40 mmoles) in 35 ml of benzene was placed in a round-bottomed flask (under nitrogen). *p*-Toluenesulfonic acid (40 mg) was added and the solution heated at reflux for 12 hours. At this time 20 ml of 10% sodium hydroxide was added and the reaction was cooled to room temperature. The aqueous layer was separated and the organic layer washed with 20 ml of 10% sodium hydroxide and 20 ml of water. The combined aqueous layers were extracted with 20 ml of benzene and the combined benzene layers were dried (magnesium sulfate) and concentrated *in vacuo* to yield crude chromene **9f**. The crude chromene was purified by mpc (eluant: 2% ethyl acetate in Skelly F) to yield 0.90 g, 60% of white crystals mp $37\text{--}39^\circ$; ^1H nmr (deuteriochloroform, 100 MHz): δ 4.68 (d of d, 2H, $J = 1.6, 3.7$ Hz), 5.54-5.71 (m, 1H), 5.85 (s, 2H), 6.23-6.45 (m, 3H); ir (chloroform): 3020, 2900, 2870, 1485, 1270, 1125 cm^{-1} .

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{O}_3$: C, 68.18; H, 4.50. Found: C, 68.32; H, 4.56.

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REFERENCES AND NOTES

- [1a] S. Wawzonek in "Heterocyclic Compounds", Vol 2, R. C. Elderfield, ed, John Wiley and Sons, New York NY, 1951, p 277; [b] "Chromenes Chromanones, and Chromones", G. P. Ellis, ed, John Wiley and Sons, New York, NY, 1977; [c] W. K. Anderson and E. J. LaVoie, *J. Org. Chem.*, **38**, 3832 (1973); [d] E. E. Schweizer, A. T. Wehman and D. M. Nycz, *ibid.*, **38**, 1583 (1973); [e] G. Cardillo, R. Cricchio and L. Merlino, *Tetrahedron*, **27**, 1875 (1971); [f] K. C. Majumdar and B. S. Thyagarajan, *J. Heterocyclic Chem.*, **9**, 489 (1972); [g] C. E. Cook and C. E. Twine, *J. Chem. Soc., Chem. Commun.*, 791 (1968); [h] J. Hlubcek, E. Ritchie and W. C. Taylor, *Aust. J. Chem.*, **24**, 2347 (1971); [i] J. Hlubcek, E. Ritchie and W. C. Taylor, *ibid.*, **23**, 1881 (1970); [j] I. Iwai and I. Ide, *Chem. Pharm. Bull.*, **11**, 1042 (1963); [k] J. Nickl, *Chem. Ber.*, **91**, 1371 (1958); [l] P. Anastasis and P. E. Brown, *J. Chem. Soc., Perkin Trans. I*, 2013 (1982).
- [2] E. G. Witzemann, W. L. Evans, H. Hass and E. F. Schroeder, "Organic Synthesis", Coll Vol II, p 137.
- [3] G. Buchi and H. Wuest, *J. Org. Chem.*, **34**, 1122 (1969).
- [4a] A. McKillop, J. C. Fiaud and R. P. Hug, *Tetrahedron*, **30**, 1379 (1974); [b] M. Fedorynski, K. Wojeiechoski, A. Matacz and M. Makosza, *J. Org. Chem.*, **43**, 4682 (1978).
- [5a] S. M. Weinreb and J. Auerbach, *J. Am. Chem. Soc.*, **97**, 2503 (1975); [b] R. F. Newton, M. Sainsbury and P. L. R. Stanley, *Heterocycles*, **19**, 2037 (1982).
- [6a] W. M. Bandaranayake, L. Crombie and D. A. Whiting, *J. Chem. Soc. (C)*, 811 (1971); [b] F. Camps, J. Coll, A. Messeguer and M. A. Pericas, *J. Heterocyclic Chem.*, **17**, 207 (1980).
- [7] The resulting 2*H*-1-benzopyrans are in general very sensitive and unless they are stored in the cold (0°C), will decompose over varying periods of time, depending on the structure. These compounds are also very sensitive to acid. This fact may offer a possible explanation for the low material recovery and yield of products in some of the cyclization reactions.
- [8a] W. E. Parham and L. D. Huestis, *J. Am. Chem. Soc.*, **84**, 813 (1962); [b] E. E. Schweizer, *ibid.*, **86**, 2744 (1964).
- [9] E. E. Schweizer, J. Liehr and D. J. Monaco, *J. Org. Chem.*, **33**, 2416 (1968).
- [10] W. K. Anderson and E. J. LaVoie, *ibid.*, **38**, 3832 (1973).
- [11] J. C. Breytenbach and G. J. H. Rall, *J. Chem. Soc., Perkin Trans. I*, 1804 (1980).
- [12] A. O. Fitton and G. R. Ramage, *J. Chem. Soc.*, 4870 (1962).