in 60% yield. In ^{1}H NMR spectra of the crude products, no signal was observed assignable to 3-phenyl-5-methyl-5-(chloromethyl)-1,2,4-trioxolane (**16e**).

Ozonolyis of 1b in the Presence of Benzaldehyde (6b) and 2-(Trifluoromethyl)benzaldehyde (6c). To a methylene chloride solution (20 mL) of **1b** (1 mmol), **6b** (4 mmol), and **6c** (1 mmol), was passed 1 mmol of ozone at 0 °C. Column chromatography on silica gel (elution with benzene–hexane, 1:1) afforded 3,5-diphenyl-1,2,4-trioxolane (**13b**) and 3-phenyl-5-(2-(trifluoromethyl)phenyl)-1,2,4-trioxolane (**16a**) in yields of 13% and 25%, respectively.

Ozonolysis of *cis*- and *trans*-1-Phenyl-2-methoxyethene (1b) in the Presence of Trimethylacetaldehyde (6g). When a mixture of *cis*-**1b** (1 mmol) and **6g** (5 mmol) was treated with 1 mmol of ozone in ether at −70 °C, 3-phenyl-5-*tert*-butyl-1,2,4-trioxolane (**16b**) was isolated in 60% yield as a cis–trans mixture, the ratio being 29:71. When *trans*-**1b** was used instead of the cis isomer, a cis–trans mixture of **16b** was obtained in 55% yield, the cis:trans ratio being 30:70.

A similar independence of the ozonide composition on the configuration of the vinyl ether **1b** was found in the reaction in pentane or methylene chloride.

Acknowledgment. Support of part of the work by the Deutsche Forschungsgemeinschaft is greatly acknowledged. M.N. thanks the Deutsche Akademischer Austauschdienst for a travel grant which provided a chance to study the method of ozonolysis on polyethylene at the University of Karlsruhe.

Registry No. *cis*-**1a**, 64304-84-3; *trans*-**1a**, 64304-83-2; *cis*-**1b**, 14371-19-8; *trans*-**1b**, 4110-75-2; *cis*-**1c**, 130011-62-0; *trans*-**1c**, 130011-64-2; *cis*-**1d**, 130011-63-1; *trans*-**1d**, 130011-65-3; **1e**, 40237-72-7; **1f**, 19096-89-0; **3**, 107-31-3; **4a**, 90535-16-3; **4b**, 10027-71-1; **4c**, 130011-66-4; **4d**, 130011-67-5; **4e**, 63704-22-3; **4f**, 16580-35-1; **5a**, 130011-68-6; **5b**, 16204-37-8; **5e**, 16204-36-7; **5f**, 183-84-6; **6a**, 123-11-5; **6b**, 100-52-7; **6c**, 447-61-0; **6d**, 124-13-0; **6e**, 119-61-9; **6f**, 108-94-1; **6g**, 630-19-3; **6h**, 66-25-1; **6i**, 67-64-1; **6j**, 78-95-5; **6k**, 534-07-6; **7a**, 100-09-4; **7b**, 65-85-0; **7d**, 124-07-2; **8**, 79698-42-3; **9**, 4746-86-5; **10**, 35967-47-6; **11**, 101-41-7; *cis*-**13a**, 110003-04-8; *trans*-**13a**, 89902-49-8; *cis*-**13b**, 21072-45-7; *trans*-**13b**, 21072-46-8; *cis*-**13c**, 130011-79-9; *trans*-**13c**, 130011-80-2; **13f**, 129731-36-8; *cis*-**14a**, 130011-69-7; *trans*-**14a**, 130011-75-5; *cis*-**14b**, 130011-70-0; *trans*-**14b**, 130011-76-6; *cis*-**14c**, 130011-71-1; *trans*-**14c**, 130011-77-7; *cis*-**14d**, 130011-72-2; *trans*-**14d**, 130011-78-8; **14e**, 130011-73-3; **14f**, 130011-74-4; *cis*-**15a**, 130011-81-3; *trans*-**15a**, 130011-82-4; **15b**, 130011-83-5; *cis*-**15c**, 130011-84-6; *trans*-**15c**, 130011-85-7; **15d**, 130011-86-8; *cis*-**16a**, 130011-87-9; *trans*-**16a**, 130011-88-0; *cis*-**16b**, 130011-89-1; *trans*-**16b**, 130011-90-4; *cis*-**16c**, 130011-91-5; *trans*-**16c**, 130011-92-6; **16d**, 38481-59-3; *cis*-**16e**, 130011-93-7; *trans*-**16e**, 130011-94-8; **16f**, 130011-95-9; **17a**, 130011-96-0; *cis*-**17b**, 130011-97-1; *trans*-**17b**, 130011-98-2; **17c**, 130011-99-3; *cis*-**18a**, 130012-00-9; *trans*-**18a**, 130012-01-0; *cis*-**18b**, 130012-02-1; *trans*-**18b**, 130012-03-2; **18c**, 130012-04-3; **19a**, 23246-12-0; **19b**, 130012-05-4; **19c**, 130012-06-5; **19d**, 73258-07-8; **19e**, 130012-07-6; **20a**, 130012-08-7; **20b**, 130012-09-8.

Supplementary Material Available: ^{1}H NMR spectra of a mixture of *trans*- and *cis*-**14a**, *trans*-**14a**, *cis*-**14b**, *trans*-**14b**, a mixture of *trans*- and *cis*-**14c**, a mixture of *trans*- and *cis*-**14d**, *cis*-**14d**, and **14e** (8 pages). Ordering information is given on any current masthead page.

A New Chromone and Flavone Synthesis and Its Utilization for the Synthesis of Potentially Antitumorigenic Polycyclic Chromones and Flavones

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A new synthesis of chromones and flavones based on the ortho-directed metalation of methoxymethyl aryl ethers with alkyllithium reagents is described. It entails reaction of the ortho-lithiated intermediates with a conjugated unsaturated aldehyde followed by oxidation of the allylic alcohol product with "periodinane" to yield an ortho-allylic ketone. The latter on heating in acetic acid undergoes loss of the methoxymethyl protecting group and cyclization to a chromanone (or flavanone, if a β-phenyl substitutent is present). Dehydrogenation by treatment with pyrrolidone hydrotribromide (PHT) in dimethyl sulfoxide yields the corresponding chromones (or flavones). This synthetic approach appears general in its applicability. It has been applied to the synthesis of a series of polycyclic chromone and flavone compounds containing the naphthalene and pyrene ring systems that hold promise as agents for the chemoprevention of cancer.

Coumarins, chromones, and flavones are pharmacologically important classes of plant products. Some compounds of these classes, notably 5,6- and 7,8-benzoflavone and ellagic acid, have been shown to exhibit significant activity as inhibitors of tumor induction by carcinogenic polycyclic aromatic hydrocarbons (PAHs).[1] In contrast to most other types of tumor-inhibitory compounds, many of which exhibit toxicity, mutagenicity, and other undesirable properties, the coumarin and chromone compounds tend to show minimal side effects. Surprisingly, systematic investigations of their structure–activity relationships have not been conducted. With this objective in mind, we recently devised an efficient novel synthesis of coumarins based on the ortho-directed metalation of methoxymethyl phenolic ethers.[2,3] This method was utilized to prepare a series of substituted coumarins and polycyclic coumarin analogues of PAHs. Preliminary assays of biological activity indicate that several of these compounds exhibit significant antitumor activity. In particular, the polycyclic coumarin analogues of benzo[*a*]pyrenes **1a–c** are strong

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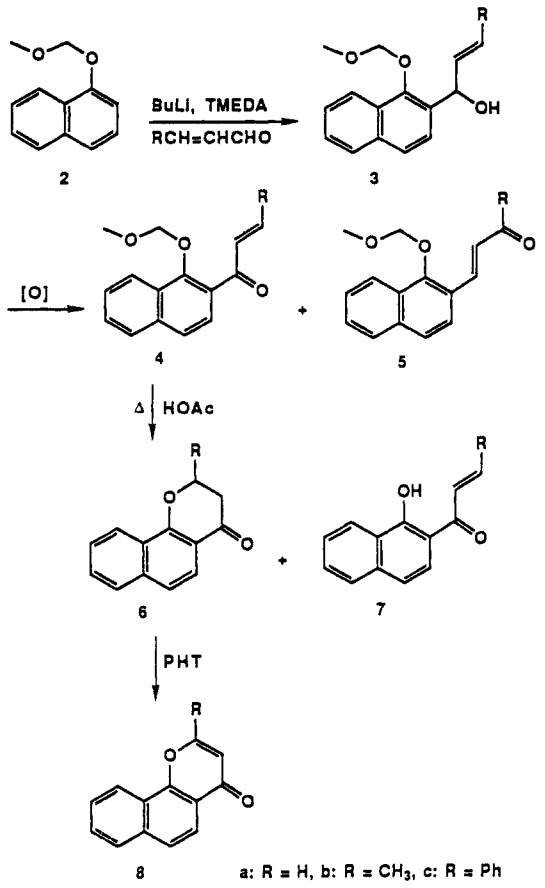
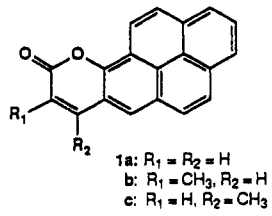
Scheme I



inhibitors of tumor induction when administered prior to the potent carcinogen 7,12-dimethylbenz[*a*]anthracene and are themselves devoid of tumorigenic activity.



We now report extension of this synthetic approach to the preparation of chromones and flavones and utilization of the method to prepare a series of potentially antitumorigenic polycyclic chromones and flavones. The synthetic route employed is based upon the ready availability of polycyclic phenols and the facility of their functionalization via ortho-directed metalation of their methoxymethyl ethers. The general synthetic approach (Scheme I) entails initial reaction of an ortho-lithiated derivative of a methoxymethyl phenolic ether (e.g. **2**) with an allylic aldehyde to yield the corresponding allylic alcohol derivative **3**, followed by oxidation of the latter to a ketone (**4**), deprotection of the phenolic ether, acid-catalyzed cyclization, and dehydrogenation to yield the corresponding chromone or flavone.

In preliminary experiments it was found that direct reaction of the ortho-lithiated derivative of 1-(methoxymethyl)naphthalene (**2**) with acid chlorides afforded only low yields of the desired ketonic intermediates. An indirect route involving reaction of the metalated intermediate with an allylic aldehyde followed by oxidation gave more satisfactory results. Thus, reaction of crotonaldehyde with the 2-lithio salt of **2** furnished smoothly the allylic alcohol **3b**. The attempted oxidative conversion of **3b** to the ketone **4b** with common oxidants such as MnO_2, chromium trioxide–pyridine, and DDQ gave complex mixtures of products. However, reaction of **3b** with the Dess–Martin reagent "periodinane"[4] took place smoothly to furnish **4b** as the predominant product accompanied by a small amount of a second ketone (**5b**) arising from allylic oxidation. With pyridinium dichromate as the oxidant, the rearranged ketone **5b** was the principal product. The isomeric ketones were readily distinguished by NMR analysis. Thus, the NMR spectrum of **5b** showed a characteristic methyl singlet at δ 2.43 and a pair of vinylic doublets at δ 6.75 and 8.16 coupled with each other (J = 17.0 Hz) consistent with its assignment. The spectrum of **4b** showed a more complex splitting pattern, revealing a methyl doublet at δ 1.97 and a pair of vinylic multiplets at δ 6.73–6.77 and 6.87–6.94. The complexity of the splitting pattern of the vinylic protons of **4b** suggests the presence of both *E* and *Z* isomers.

Transformation of the ketone **4b** to the chromanone **6b** was accomplished in a single step by heating in refluxing acetic acid. Removal of the methoxymethyl group and cyclodehydration take place concurrently under these conditions. The uncyclized phenol **7b** was obtained as a minor product of this reaction.

Attempted dehydrogenation of **6b** with various reagents commonly employed for this purpose such as DDQ, SeO_2, and trityl trifluoroacetate[5] gave the chromone **8b** in only low yield. Dehydrogenation was more efficiently accomplished by treatment of **6b** with pyrrolidone hydrotribromide (PHT) in dimethyl sulfoxide.[6] This method is believed to involve initial α-bromination of the carbonyl function followed by dehydrobromination. PHT has been demonstrated to be a selective brominating agent for ketones,[7] and DMSO is known to be an effective solvent–reagent for dehydrobromination.[8]

Similar reaction sequences were employed to synthesize the unsubstituted benzochromone (**8a**) and 7,8-benzoflavone (**8c**) in good overall yield. This synthetic approach was also extended to the preparation of the analogous chromone and flavone derivatives of pyrene (**16a–d**) structurally related to the carcinogenic polycyclic hydrocarbon benzo[*a*]pyrene (Scheme II). Synthesis of the methyl-substituted polycyclic chromone derivative **16b** and the polycyclic flavone **16c** via this route proceeded smoothly to furnish the desired compounds.

In the attempted preparation of the unsubstituted chromone **16a** by a similar route, reaction of the intermediate **11a** in refluxing acetic acid gave the desired chromanone **13a** in only low yield (11%); the principal product (38%) was the uncyclized phenol **14a**. When **11a** was treated with hydrochloric acid in ethanol for 10 min, **14a** (80%) was the sole product. And when **11a** was heated at reflux with a slightly higher concentration of HCl in ethanol for 24 h, there was obtained a new product (66%) identified as **15**, arising from addition of ethanol to **14a**. Conversion of **11a** to the corresponding chromanone **13a** was more efficiently accomplished by heating it with HCl in DMSO for 30 min at reflux. This method furnished pure **13a** in 64% yield. Similar reaction of **11a** in refluxing DMF gave **13a** in 24% yield. The cyclized chromanone could also be obtained by treatment of **14a** with KOH in

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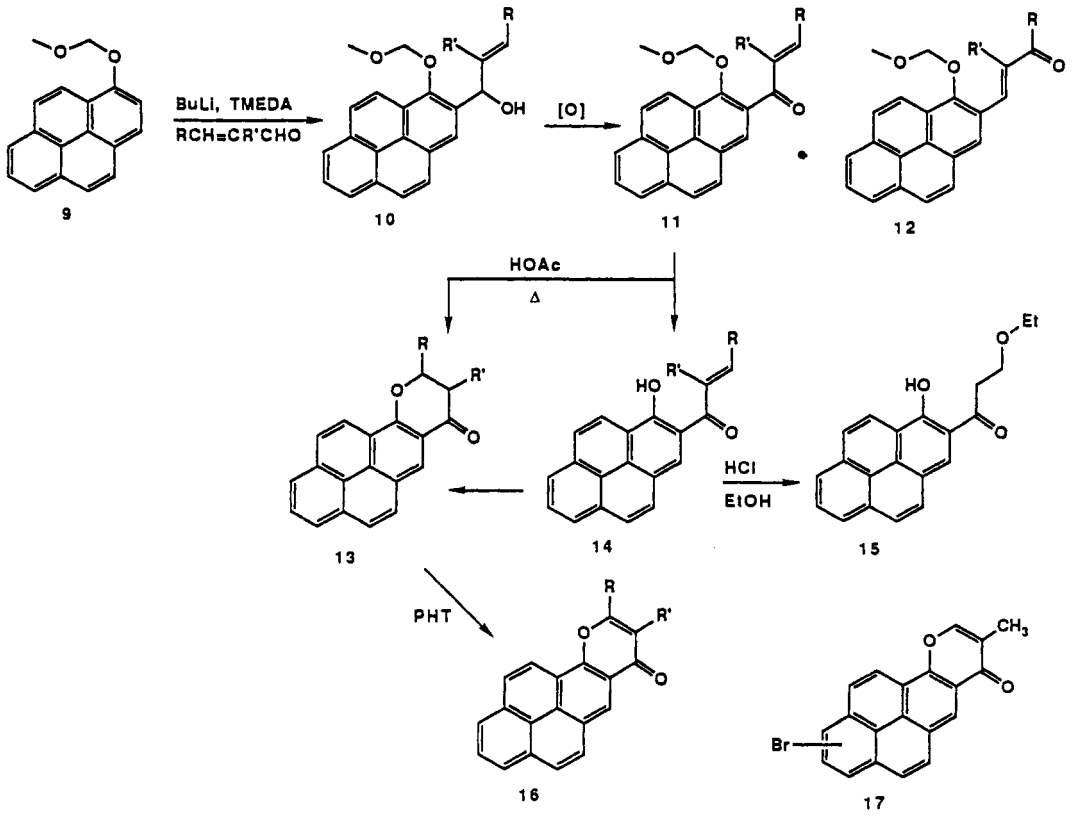
Scheme II



a: R = R' = H; b: R = CH_3, R' = H;
c: R = Ph, R' = H; d: R = H, R' = CH_3.

ethanol, which furnished **13a** in 28% yield. Similarly, reaction of the intermediate **11d** bearing a methyl group adjacent to the carbonyl group took place in refluxing acetic acid to afford a mixture of the corresponding phenol **14d** (36%) and the cyclized chromanone derivative **13d** (27%). When **11d** was heated in ethanolic HCl for 20 min, there was obtained principally the phenol **14d** (89%). However, analogous reaction of **11d** with HCl in DMSO at 165 °C for 15 min converted it smoothly to **13d** (86%). Treatment of **14d** with KOH in ethanol also furnished **13d** (70%).

Dehydrogenation of the chromanones **13a–d** to the corresponding chromones and flavones **16a–d** was readily accomplished by reaction with PHT in DMSO. However, the reaction of **13d** with this reagent afforded in addition to **16d** a second product shown by mass spectral analysis to be a bromo-substituted chromone. Although the site of bromine substitution has not been established, this product is likely to be the 8- or 10-bromo derivative **17**, since pyrene is known to undergo substitution predominantly in these sites.

The methods outlined in Schemes I and II provides convenient synthetic access to chromone and flavone derivatives from readily available methoxymethyl aryl ethers under mild conditions. This ortho-metalation approach complements older established methods[9] and offers significant advantage for the synthesis of polycyclic chromones and flavones.

Studies of the anticarcinogenic properties of these compounds will be undertaken following completion of studies of the analogous polycyclic coumarins that are currently in progress.

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Experimental Section

Methods and Materials. The NMR spectra were obtained on a Varian EM 360 and/or the University of Chicago 500-MHz spectrometer in $CDCl_3$ with Me_4Si as internal standard unless stated otherwise. Integration was consistent with all the molecular structural assignments. Infrared spectra were recorded on a Perkin-Elmer 297 spectrometer. A Waters Prep LC 3000 system was used for HPLC purification. Melting points are uncorrected. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Ga, and all new compounds gave satisfactory microanalyses for C and H within ±0.3% and/or mass spectra consistent with the assigned structures. TLC was carried out on Eastman Kodak silica gel sheets with fluorescent indicator. Florisil (100/200 Å) from U.S. Silica Co. was used for column chromatographic separations unless otherwise noted.

1-Bromopyrene was prepared by the method reported.[10] 1-Acetylpyrene was synthesized from pyrene by Friedel–Crafts acetylation.[11] The Dess–Martin reagent "periodinane" was purchased from the Aldrich Chemical Co. or synthesized by the procedure reported.[4] *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was dried over $LiAlH_4$ and redistilled. Tetrahydrofuran (THF) was freshly distilled from benzophenone ketyl. Ether was dried over sodium. Dimethyformamide was distilled and stored over BaO.

1-Hydroxypyrene. This phenol was initially prepared from 1-bromopyrene by reaction with magnesium followed by treatment with borane and alkaline peroxide by the procedure previously employed for the preparation of 2-hydroxypyrene.[12] Since purification of 1-bromopyrene prepared from pyrene by direct bromination is complicated by the difficulty of removal of secondary brominated products, an alternative synthetic route involving oxidation of 1-acetylpyrene with sodium perborate[13] was

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investigated and found to be superior. To a solution of sodium perborate tetrahydrate (29.88 g, 0.19 mol) in glacial acetic acid (360 mL) was added 1-acetylpyrene (14.64 g, 0.06 mol). The reaction mixture was stirred at room temperature for 27 h under nitrogen, and the reaction was monitored by TLC. It was then poured into ice–water to give a brown oil, which solidified after 3 h. The product was filtered, washed with water, and dried. The crude product (14.3 g) was then dissolved in benzene and passed through a short column of Florisil. Evaporation of the solvent gave 1-acetoxypyrene (12.0 g, 77%): mp 103–104 °C (ethanol) (lit.[11] mp 102 °C).

To a solution of NaOMe (0.32 g, 6.0 mmol) in methanol (55 mL) was added a solution of 1-acetoxypyrene (0.52 g, 2.0 mmol) in THF (20 mL). The mixture was refluxed for 10 min under nitrogen, then poured over ice, and neutralized with concentrated hydrochloric acid (0.7 mL). The product was filtered, washed, dried, and recrystallized from CCl_4 to furnish 1-hydroxypyrene (0.33 g, 76%): mp 178–180 °C (lit.[11] mp 179 °C).

Synthesis of Methoxymethyl Aryl Ethers. The general procedure based on the method of Yardley and Fletcher[14] is illustrated by the preparation of 1-(methoxymethoxy)naphthalene (**2**). A solution of 1-naphthol (14.4 g, 0.1 mol), dimethoxymethane (44 mL, 0.5 mol), and *p*-toluenesulfonic acid (0.2 g) in CH_2Cl_2 (200 mL) was heated at reflux for 48 h under argon using a Soxhlet apparatus containing type 4-Å molecular sieves (35 g). The molecular sieves were changed three times at 8–12-h intervals. The reaction mixture was allowed to cool, treated with triethylamine to neutralize the acid catalyst, washed with 1 N NaOH and water, and dried over $MgSO_4$. Evaporation of the solvent gave crude **2**. Chromatography on Florisil gave on elution with 4:1 hexanes/THF **2** as a yellow oil (8.16 g, 43%): NMR δ 8.30 (m, 1), 7.73 (m, 1), 7.28–7.57 (m, 4), 7.07 (m, 1), 5.22 (s, 2), 3.40 (s, 3). This product was employed directly in the next step.

1-(Methoxymethoxy)pyrene (9). Similar reaction of 1-pyrenol furnished **9** (74%), mp 68–70 °C (95% ethanol) (lit.[15] mp 64–66 °C): NMR δ 8.41 (d, 1, J = 9.2 Hz), 7.98–8.07 (m, 4), 7.84–7.92 (m, 3), 7.72 (d, 1, J = 8.7 Hz), 5.49 (s, 2), 3.58 (s, 3). This compound was also obtained by an alternative method. A mixture of 1-acetoxypyrene (1.3 g, 5.0 mmol), *p*-toluenesulfonic acid (0.125 g), and methanol (200 mL) was refluxed for 6 h under nitrogen. The solvent was evaporated to dryness and CH_2Cl_2 (100 mL) and dimethoxymethane (30 mL, 34 mmol) were added. Then the procedure described for the preparation of **2** was followed to give **9** (1.18 g, 90%) whose NMR spectrum matched that of an authentic sample.

Synthesis of *o*-Allyl Alcohol Derivatives of Methoxymethyl Aryl Ethers. The general procedure is illustrated by the preparation of **3b**. In a 100-mL round-bottom flask equipped with a pressure-equalizing addition funnel containing *n*-butyllithium (10.4 mL of 2.0 M solution in cyclohexane, 20.7 mmol) were placed **2** (2.6 g, 13.8 mmol), TMEDA (4.2 mL, 27.6 mmol), and 30 mL of dry ether. The round-bottom flask was cooled in an ice bath under argon for 5 min and *n*-butyllithium was added dropwise over 20 min. The solution became black with formation of a brown precipitate. The ice bath was removed and stirring was continued for 1 h at room temperature. Then the funnel was replaced with a funnel containing crotonaldehyde (1.71 mL, 20.7 mmol), and the set-up was cooled in an ice bath under argon for 10 min. Crotonaldehyde was then added dropwise over 5 min, then the ice bath was removed, and stirring was continued for 1 h. On addition of water (30 mL), the yellow precipitate dissolved. The aqueous layer was extracted with ether (2 × 20 mL), combined with the organic layer, and dried over $MgSO_4$. Evaporation of the solvent gave crude **3b**. Chromatography on Florisil and elution with 4:1 hexanes/THF provided **3b** as light yellow oil (3.42 g, 96%): NMR δ 7.94 (d, 1, J = 7.8 Hz), 7.72 (d, 1, J = 7.8 Hz), 7.56 (d, 1, J = 8.7 Hz), 7.36–7.45 (m, 3), 5.75–5.82 (m, 2), 5.65–5.68 (m, 1), 5.14 (d, 1, J = 6.0 Hz), 5.01 (d, 1, J = 6.0 Hz), 3.60 (s, 3), 2.83 (s, 1, exchangeable with D_2O), 1.69 (d, 3, J = 4.9 Hz). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.44; H, 7.05.

Similar reactions of other allylic aldehydes furnished the analogous *o*-allyl alcohol derivatives of methoxymethyl aryl ethers: **3a** (91%), oil decomposed on distillation; NMR δ 7.98 (d, 1, J = 8.2 Hz), 7.78 (d, 1, J = 8.2 Hz), 7.60 (d, 1, J = 8.9 Hz), 7.42–7.49 (m, 3), 6.08–6.16 (m, 1), 5.76–5.80 (m, 1), 5.46 (d, 1, J = 17.0 Hz), 5.26 (d, 1, J = 12.0 Hz), 5.20 (d, 1, J = 6.6 Hz), 5.06 (d, 1, J = 6.6 Hz), 3.65 (s, 3), 3.09 (s, 1, exchangeable with D_2O). Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.58; H, 6.74. **3c** (94%): oil decomposed on distillation; NMR δ 7.99 (d, 1, J = 8.2 Hz), 7.78 (d, 1, J = 8.2 Hz), 7.60 (d, 1, J = 8.9 Hz), 7.51 (d, 1, J = 8.9 Hz), 7.43–7.50 (m, 2), 7.16–7.38 (m, 5), 6.80 (dd, 1, J = 1.5 and 16.3 Hz), 6.50 and 6.46 (pair of d, 1, J = 5.2 Hz), 5.94–5.98 (m, 1), 5.23 (d, 1, J = 6.0 Hz), 5.08 (d, 1, J = 6.0 Hz), 3.67 (s, 3), 3.26 (s, 1, exchangeable with D_2O). Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.72; H, 6.29. Found: C, 78.94; H, 6.40. **10a** (82%): mp 59–61 °C (petroleum ether); NMR δ 8.05–8.21 (m, 5), 7.94–7.98 (m, 3), 6.28–6.35 (m, 1), 6.00–6.03 (m, 1), 5.58 (d, 1, J = 17.2 Hz), 5.37 (d, 1, J = 11.2 Hz), 5.39 (d, 1, J = 6.0 Hz), 5.25 (d, 1, J = 6.0 Hz), 3.71 (s, 3), 3.32 (d, 1, J = 4.4 Hz, exchangeable with D_2O). Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.01; H, 5.61. **10b** (98%): oil decomposed on distillation; NMR δ 8.14–8.17 (m, 2), 8.06–8.08 (m, 2), 8.00 (d, 1, J = 9.3 Hz), 7.88–7.94 (m, 3), 5.88–6.00 (m, 3), 5.32 (d, 1, J = 6.2 Hz), 5.19 (d, 1, J = 6.2 Hz), 3.68 (s, 3), 3.26 (d, 1, J = 3.7 Hz, exchangeable with D_2O), 1.78 (d, 3, J = 6.2 Hz). Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.49; H, 6.07. Found: C, 79.71; H, 6.19. **10c** (83%): mp 111–112 °C (ethanol); NMR δ 7.95–8.24 (m, 8), 7.30–7.47 (m, 3), 6.93 (dd, 1, J = 1.0 and 16.2 Hz), 6.68 (dd, 1, J = 5.9 and 16.2 Hz), 6.20 (m, 1), 5.43 (d, 1, J = 7.5 Hz), 5.29 (d, 1, J = 7.5 Hz), 3.75 (s, 3), 3.44 (d, 1, J = 5.8 Hz, exchangeable with D_2O). Anal. Calcd for $C_{27}H_{22}O_3$: C, 82.21; H, 5.62. Found: C, 82.09; H, 5.67. **10d** (65%): mp 79 °C dec (hexanes); NMR δ 8.23 (d, 1, J = 8.3 Hz), 8.08 (d, 1, J = 8.3 Hz), 8.14 (s, 1), 8.10–8.13 (m, 2), 7.93–7.99 (m, 3), 5.89 (d, 1, J = 7.1 Hz), 5.48 (s, 1), 5.41 (d, 1, J = 7.1 Hz), 5.24 (d, 1, J = 7.1 Hz), 5.19 (s, 1), 3.72 (s, 3), 3.26 (d, 1, J = 7.1 Hz, exchangeable with D_2O), 1.68 (s, 3). Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.49; H, 6.06. Found: C, 79.50; H, 6.09.

Synthesis of *o*-Allyl Ketone Derivatives of Methoxymethyl Aryl Ethers. The general procedure is illustrated by the preparation of **4b**. To a solution of "periodinane" (4.7 g, 11.2 mmol) in CH_2Cl_2 (150 mL) was added a solution of **3b** (2.2 g, 8.6 mmol). The resulting yellow solution was stirred for 3 h at room temperature and the color of the solution changed to green. The reaction mixture was diluted with ether (500 mL), and the resulting suspension was added to 1.3 M NaOH (100 mL). This was stirred until it separated into two clear layers. The ether layer was washed with 1.3 M NaOH (2 × 50 mL) and water (100 mL). The organic layer was dried over $MgSO_4$ and evaporated to give crude **4b**. Chromatography on a column of Florisil gave **4b** on elution with 4:1 hexanes/THF as a yellow oil (1.22 g, 56%, decomposed on distillation): NMR δ 7.50–8.25 (m, 6), 6.87–6.94 (m, 1), 6.73–6.77 (m, 1), 5.09 (s, 2), 3.51 (s, 3), 1.97 (dd, 3, J = 2.0 and 6.9 Hz); IR (neat) 1670, 1620 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.17; H, 6.11. Further elution gave **5b** (0.14 g, 7%), mp 57–59 °C (petroleum ether); NMR δ 8.13 (d, 1, J = 17.0 Hz), 8.08–8.12 (m, 1), 7.78–7.82 (m, 1), 7.58–7.64 (m, 2), 7.50–7.53 (m, 2), 6.76 (d, 1, J = 17.0 Hz), 5.19 (s, 2), 3.69 (s, 3), 2.43 (s, 3); IR (KBr) 1705, 1680, 1630, 1620, 1580 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.77; H, 6.35. Oxidation of **3b** with pyridinium dichromate afforded **4b** and **5b** in the ratio of 1:2.3.

Similar oxidations of the alcohols **3a**, **3c**, and **10a–d** provided the analogous ketones. **4a** (74%), decomposed on distillation: NMR δ 8.26–8.29 (m, 1), 7.84–7.87 (m, 1), 7.67 (d, 1, J = 9.0 Hz), 7.56–7.61 (m, 3), 7.07 (dd, 1, J = 10.5 and 17.5 Hz), 6.36 (dd, 1, J = 1.3 and 17.5 Hz), 5.94 (dd, 1, J = 1.3 and 10.5 Hz), 5.13 (s, 2), 3.53 (s, 3); IR (neat) 1670, 1630, 1605, 1575, 1510 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.11; H, 5.70. **5a** (5%): NMR δ 9.88 (d, 1, J = 8.0 Hz), 7.42–8.31 (m, 6), 6.58–7.07 (m, 2), 5.23 (s, 2), 3.70 (s, 3). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.30; H, 5.87. **4c** (46%), purified by HPLC on a Zorbax Sil column eluted with 9:1 to 7:3 hexane/THF gradient in 20 min: NMR δ 8.26–8.28 (m, 1), 7.84–7.86 (m, 1), 7.62–7.70 (m, 4), 7.55–7.60 (m, 4), 7.44 (d, 1, J = 16.3 Hz), 7.36–7.39 (m, 2), 5.13 (s, 2), 3.48 (s, 3); IR (neat) 1670, 1635, 1610, 1585 cm^{-1}. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.79. Found: C, 79.39; H, 5.81. **5c** (7%): MS 318 (M^+), 257 ($M^+ - CH_3OCH_2O$), 105 (100, C_6H_5CO); NMR δ 7.12–8.51 (m, 13), 5.17 (s, 2), 3.65 (s, 3). **11a**

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(87%), mp 78–80 °C (ethanol): NMR δ 8.38–8.54 (m, 2), 8.25 (s, 1), 7.99–8.17 (m, 5), 7.12 (dd, 1, J = 10.3 and 17.5 Hz), 6.35 (dd, 1, J = 1.6 and 17.1 Hz), 6.01 (dd, 1, J = 1.6 and 17.1 Hz), 5.21 (s, 2), 3.55 (s, 3); IR (KBr) 1665, 1630, 1600, 1550 cm^{-1}. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.58; H, 5.19. **12a** (2%): mp 149–151 °C (ethanol); NMR δ 9.84 (d, 1, J = 8.0 Hz), 8.27–8.34 (m, 3), 8.08–8.16 (m, 3), 7.97–8.02 (m, 3), 7.03 (dd, 1, J = 7.6 and 15.7 Hz), 5.33 (s, 2), 3.67 (s, 3); IR (KBr) 1665, 1620 cm^{-1}. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.47; H, 5.19. **11b** (76%): mp 82–84 °C (ethanol); NMR δ 8.39 (d, 1, J = 9.3 Hz), 8.19 (s, 1), 8.06–8.14 (m, 3), 7.94–7.99 (m, 3), 6.88–6.96 (m, 1), 6.82 (dd, 1, J = 1.2 and 15.5 Hz), 5.20 (s, 2), 3.56 (s, 3), 1.99 (dd, 3, J = 1.2 and 6.8 Hz): IR (KBr) 1655, 1625, 1555 cm^{-1}. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 80.19; H, 5.37. **12b** (6%): mp 121–123 °C (ethanol); NMR δ 8.27–8.32 (m, 3), 8.06–8.13 (m, 3), 7.93–7.98 (m, 3), 6.99 (d, 1, J = 16.7 Hz), 5.29 (s, 2), 3.70 (s, 3), 2.48 (s, 3); IR (KBr) 1650, 1620 cm^{-1}. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.89; H, 5.51. **11c** (70%): mp 98–99.5 °C (ethanol); NMR δ 8.44 (d, 1, J = 9.2 Hz), 8.35 (s, 1), 8.14–8.18 (m, 3), 8.00–8.05 (m, 3), 7.62 (dd, 2, J = 16.6 and 19.6 Hz), 7.60–7.63 (m, 2), 7.38–7.40 (m, 3), 5.26 (s, 2), 3.55 (s, 3); IR (KBr) 1680, 1630, 1600 cm^{-1}. Anal. Calcd for $C_{27}H_{20}O_3$: C, 82.63; H, 5.14. Found: C, 82.57; H, 5.19. **11d** (84%): mp 109–110 °C (ethanol); NMR δ 8.39 (d, 1, J = 8.33 Hz), 7.96–8.17 (m, 7), 6.06 (s, 1), 5.68 (s, 1), 5.22 (s, 2), 3.57 (s, 3), 2.18 (s, 3); IR (KBr) 1660 cm^{-1}. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.86; H, 5.52.

Synthesis of Chromanones and Flavanones. The general procedure may be illustrated by the preparation of **6b**. A solution of **4b** (1.14 g, 4.4 mmol) in glacial acetic acid (50 mL) was heated at reflux for 6 h and poured into ice–water (200 mL). The resulting suspension was extracted with CH_2Cl_2 (3 × 50 mL) and washed with water (3 × 50 mL), 5% $NaHCO_3$ (100 mL), and water (100 mL). The organic layer was dried over $MgSO_4$ and evaporated to give a brown oil. Chromatography on Florisil gave **7b** in 9% yield on elution with 4:1 hexanes/THF. Further elution gave **6b** as yellow oil (0.68 g, 71%), which crystallized on standing. Recrystallization from petroleum ether (35–60 °C) gave 0.55 g (58%) of **6b** as short white needles: mp 57–58 °C (lit.[16] bp 164–168 °C at 0.7 mm); NMR δ 8.28 (d, 1, J = 8.5 Hz), 7.82 (d, 1, J = 8.5 Hz), 7.74 (d, 1, J = 7.9 Hz), 7.55–7.59 (m, 1), 7.46–7.51 (m, 1), 7.35 (d, 1, J = 8.5 Hz), 4.73–4.81 (m, 1), 2.74–2.78 (m, 2), 1.65 (d, 3, J = 7.0 Hz); IR (KBr) 1670, 1620, 1575, 1510 cm^{-1}.

Similar reactions of the ketones **4a**, **4c**, and **11a–d** in acetic acid gave the analogous chromanones and flavanones. **6a** (eluted with 1% acetone in CH_2Cl_2): (57%), mp 102–103 °C (ethanol) (lit.[17] mp 104.5 °C); NMR δ 8.24 (d, 1, J = 8.5 Hz), 7.84 (d, 1, J = 8.5 Hz), 7.74 (d, 1, J = 7.9 Hz), 7.56–7.60 (m, 1), 7.47–7.51 (m, 1), 7.36 (d, 1, J = 8.5 Hz), 4.73 (t, 2, J = 6.8 Hz), 2.88 (t, 2, J = 6.8 Hz); IR (KBr) 1665, 1625, 1600, 1570, 1510 cm^{-1}. **7a** was also obtained as a minor product (8%) of this synthesis. **6c** (eluted with CH_2Cl_2): (54%), mp 126–127 °C (ethanol) (lit.[18] mp 126 °C); NMR δ 8.32 (d, 1, J = 8.5 Hz), 7.89 (d, 1, J = 8.5 Hz), 7.77 (d, 1, J = 7.9 Hz), 7.37–7.61 (m, 8), 5.66 (dd, 1, J = 2.5 and 12.4 Hz), 3.17 (dd, 1, J = 13.9 and 16.4 Hz), 2.98 (dd, 1, J = 2.5 and 16.4 Hz); IR (KBr) 1675, 1620, 1595, 1570, 1500 cm^{-1}. **7c** was obtained as a minor product (8%) of this synthesis. **13a** (eluted with CH_2Cl_2) (11%): mp 139–141 °C (95% ethanol); NMR δ 8.57 (s, 1), 8.37 (d, 1, J = 9.5 Hz), 7.79–8.08 (m, 6), 4.83 (t, 2, J = 6.5 Hz), 3.04 (t, 2, J = 6.5 Hz); IR (KBr) 1650, 1625, 1600, 1590, 1550 cm^{-1}. Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.81; H, 4.44. Found: C, 83.99; H, 4.32. **13a** was more efficiently obtained (64% purified yield) from reaction of **11a** (0.32 g, 1 mmol) with 1 M HCl (1.0 mL) in refluxing DMSO (20 mL) for 30 min. **13a** was also obtained (24%) from analogous reaction of **11a** in refluxing DMF for 24 h. **14a** (38%), mp 144–146 °C (95% ethanol); NMR δ 13.19 (s, 1, exchangeable with D_2O), 8.41–8.52 (m, 2), 7.92–8.07 (m, 4), 7.75–7.83 (m, 2), 7.63 (dd, 1, J = 10.9 and 16.9 Hz), 6.68 (dd, 1, J = 1.6 and 16.9 Hz), 6.07 (dd, 1, J = 1.6 and 10.9 Hz); IR (KBr) 1635, 1590, 1400 cm^{-1}. Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.81; H, 4.44. Found: C, 83.69; H, 4.49. **13b** (refluxed for 24 h) (eluted with CH_2Cl_2) (73%): mp 142–144 °C (95% ethanol); NMR δ 8.57 (s, 1), 8.42 (d, 1, J = 9.5 Hz), 7.80–8.09 (m, 6), 4.84–4.92 (m, 1), 2.87–2.97 (m, 2), 1.73 (d, 3, J = 6.4 Hz); IR (KBr) 1670, 1630, 1600, 1555 cm^{-1}. Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.65; H, 5.11. The free phenol **14b** was not isolated from this reaction. **13c** (41%): mp 185–186 °C (ethanol); NMR δ 8.65 (s, 1), 8.47 (d, 1, J = 8.8 Hz), 7.44–8.14 (m, 11), 5.80 (dd, 1, J = 2.3 and 13.6 Hz), 3.35 (dd, 1, J = 13.6 and 16.6 Hz), 3.16 (dd, 1, J = 2.3 and 16.6 Hz); IR (KBr) 1670, 1625, 1600, 1550 cm^{-1}. Anal. Calcd for $C_{25}H_{16}O_2$: C, 86.18; H, 4.63. Found: C, 86.28; H, 4.65. The phenol **14c** was obtained as a coproduct of this reaction. It was purified by chromatography on a silica gel column eluted with 9:3 hexanes/benzene to give **14c** (32%), mp 206–207 °C (benzene); NMR δ 13.82 (s, 1 H, exchangeable with deuterium oxide), 8.53–8.55 (m, 2), 7.93–8.06 (m, 7), 7.93 (d, 1, J = 8.7 Hz), 7.80 (d, 1, J = 8.7 Hz), 7.75–7.77 (m, 2), 7.48 (s, 2); IR (KBr) 1613, 1595, 1580, 1550, cm^{-1}. Anal. Calcd for $C_{25}H_{16}O_2$: C, 86.18; H, 4.63. Found: C, 86.15; H, 4.67.

The chromanone **13d** was most efficiently prepared by reaction of **11d** (495 mg, 1.5 mmol) with 1 M HCl (1.5 mL) in DMSO (30 mL) at 165 °C for 15 min. The mixture was allowed to cool, then poured into water, filtered, and worked up conventionally to yield **13d** (370 mg, 86%), mp 135–136 °C (ethanol); NMR δ 8.57 (s, 1), 8.37 (d, 1, J = 9.0 Hz), 8.07 (d, 1, J = 8.3 Hz), 8.03 (d, 2, J = 9.0 Hz), 7.95 (t, 1, J = 8.3 Hz), 7.90 (d, 1, J = 9.0 Hz), 7.81 (d, 1, J = 9.0 Hz), 4.82 (dd, 1, J = 6.8 and 21.2 Hz), 4.44 (apparent t, 1, J = 21.2 Hz), 3.08–3.15 (m, 1), 1.36 (d, 3, J = 7.6 Hz); IR (KBr) 1670, 1635, 1600, 1550 cm^{-1}. Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.95; H, 4.93. Acidic ethanolysis of **11d** followed by base-catalyzed cyclization also afforded **13d**. A solution of **11d** (1.5 g, 4.5 mmol) in ethanol (45 mL) and 1 M HCl (0.6 mL) was heated on a steam bath for 20 min, cooled, filtered, and worked up in the usual way to yield **14d** (1.14 g, 89%): mp 115–116 °C (ethanol); NMR δ 12.83 (s, 1, exchangeable with deuterium oxide), 8.53 (d, 1, J = 8.8 Hz), 8.46 (s, 1), 7.94–8.09 (m, 4), 7.82 (dd, 2, J = 9.2 and 20.4 Hz), 5.88 (s, 1), 5.58 (s, 1), 2.24 (s, 3); IR (KBr) 1635, 1600 cm^{-1}. Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.65; H, 4.97. To a solution of **14d** (1.0 g, 3.5 mmol) in ethanol (45 mL) was added 1% aqueous KOH (1.2 mL). The resulting solution was heated at reflux for 1 h, cooled, and neutralized with 1 M HCl to give **13d** as a yellow powder (0.7 g, 70%): mp 135–136 °C (ethanol); the NMR spectrum agreed closely with that of the chromanone obtained by the direct route.

Acidic ethanolysis of **11a** led to initial rapid formation of **14a** followed by further slow conversion to **15**. A solution of **11a** (0.55 g, 1.74 mmol) and 0.3 mL of 1 M HCl in ethanol (15 mL) was heated at reflux for 10 min and cooled to room temperature to precipitate **14a** (0.38 g, 80%), identical in its properties with **14a** obtained from the reaction of **11a** in acetic acid. A solution of **11a** (0.30 g, 0.95 mmol) and 0.2 mL of 1 M HCl in ethanol (20 mL) was heated at reflux and similar volumes of 1 M HCl were added after 10 min, 20 min, 30 min, 1 h, 2 h, 3 h, and 4 h. After 24 h at reflux, the solution was poured into 50 mL of cold water, extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated to dryness. The residue was purified by chromatography on a silica gel column eluted with CH_2Cl_2 to yield **15** (0.20 g, 66%): mp 119–121 °C (ethanol); NMR δ 13.20 (s, 1, exchangeable with deuterium oxide), 8.50 (d, 1, J = 9.2 Hz), 8.43 (s, 1), 7.92–8.07 (m, 4), 7.76–7.83 (m, 2), 3.98 (t, 2, J = 6.8 Hz), 3.55–3.61 (m, 4), 1.22 (t, 3, J = 6.8 Hz). Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.13; H, 5.71.

Synthesis of Chromones and Flavones. The general procedure is typified by the preparation of **8b**. To a stirred solution of **6b** (0.42 g, 2.0 mmol) in Me_2SO (25 mL) was added PHT (1.2 g, 2.4 mmol) in Me_2SO (25 mL). The reaction mixture was stirred for 6 h at 80–90 °C and then poured into water (500 mL). It was extracted with ether (3 × 50 mL) and the combined organic layer was washed with brine (50 mL), dried over $MgSO_4$, and evaporated to give crude **8b**. Chromatography on Florisil gave on elution with 9:1 CH_2Cl_2/acetone a light yellow powder that was recrystallized from 95% ethanol to afford **8b** as white needles (0.18 g, 42%): mp 177–179 °C (lit.[19,20] mp 174–174.5 °C and 178–179 °C); NMR

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δ 8.45 (d, 1, J = 8.5 Hz), 8.10 (d, 1, J = 8.5 Hz), 7.88 (d, 1, J = 8.5 Hz), 7.71 (d, 1, J = 8.5 Hz), 7.60-7.69 (m, 2), 6.30 (s, 1), 2.50 (s, 3); IR (KBr) 1650, 1635 cm^{-1}.

Similar dehydrogenation of the other chromanones and flavanones gave the analogous chromones and flavones. **8a** (eluted with 2% acetone in CH_2Cl_2) (51%): mp 123-124 °C (95% ethanol) (lit.[17] mp 125 °C); NMR δ 8.45 (d, 1, J = 8.6 Hz), 8.13 (d, 1, J = 8.9 Hz), 8.02 (d, 1, J = 6.2 Hz), 7.91 (d, 1, J = 8.6 Hz), 7.75 (d, 1, J = 8.9 Hz), 7.63-7.70 (m, 2), 6.49 (d, 1, J = 6.2 Hz); IR (KBr) 1630, 1560 cm^{-1}. **8c** (65%): mp 153-155 °C (MeOH) (lit.[21] mp 154 °C); NMR δ 8.58-8.62 (m, 1), 8.16 (d, 1, J = 8.9 Hz), 7.98-8.03 (m, 2), 7.91-7.93 (m, 1), 7.77 (d, 1, J = 8.9 Hz), 7.67-7.71 (m, 2), 7.53-7.58 (m, 3), 6.85 (s, 1); IR (KBr) 1650, 1640, 1580 cm^{-1}. **16a** (28%): mp 207-209 °C (95% ethanol); NMR δ 8.83 (s, 1), 8.58 (d, 1, J = 10.0 Hz), 8.13-8.22 (m, 4), 7.95-8.07 (m, 3), 6.56 (d, 1, J = 6.8 Hz); IR (KBr) 1640, 1630 cm^{-1}. Anal. Calcd for $C_{19}H_{10}O_2$: C, 84.43; H, 3.73. Found: C, 84.56; H, 3.90. **16b** (40%): mp 212-214 °C (95% ethanol); NMR δ 8.74 (s, 1), 8.49 (d, 1, J = 10.0 Hz), 8.09-8.17 (m, 3), 7.90-8.02 (m, 3), 6.36 (s, 1), 2.59 (s, 3); IR (KBr) 1640 cm^{-1}. Anal. Calcd for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25. Found: C, 84.38; H, 4.38. **16c** (84%): mp 231-232 °C (ethanol); NMR δ 8.86 (s, 1), 8.71 (d, 1, J = 7.5 Hz), 7.95-8.23 (m, 8), 7.57-7.63 (m, 3), 7.03 (s, 1); IR (KBr) 1635, 1600, 1580, 1560 cm^{-1}. Anal. Calcd for $C_{25}H_{14}O_2$: C, 86.69; H, 4.07. Found: C, 86.63; H, 3.99. **16d** (eluted with 15:1 $CH_2Cl_2/CHCl_3$) (44%): mp 188-189 °C (ethanol); NMR δ 8.90 (s, 1), 8.63 (dd, 1, J = 1.5 and 9.7 Hz), 8.22 (d, 2, J = 8.7 Hz), 8.17 (d, 1, J = 7.4 Hz), 8.12 (s, 1), 8.07 (t, 1, J = 8.7 Hz), 8.04 (d, 1, J = 7.4 Hz), 7.98 (dd, 1, J = 1.5 and 9.7 Hz), 2.23 (s, 3); IR (KBr) 1650, 1630, 1610 cm^{-1}. Anal. Calcd for $C_{20}H_{12}O_2$: C, 84.48; H, 4.26. Found: C, 84.19; H, 4.34. The second fraction was collected, evaporated and passed through a column of neutral alumina (activity 1), and eluted with $CHCl_3$ to give **17** (27%); mp 236-237 °C (ethanol); NMR δ 8.81 (s, 1), 8.58 (d, 1, J = 10.9 Hz), 8.48 (d, 1, J = 8.9 Hz), 8.25 (d, 1, J = 8.9 Hz), 8.10 (s, 1), 8.02 (d, 1, J = 10.9 Hz), 7.95 (d, 1, J = 8.9 Hz), 7.88 (d, 1, J = 8.9 Hz), 2.21 (s, CH_3); IR (KBr) 1635, 1595 cm^{-1}; MS 363 (100, M^+). **16d** was also prepared by catalytic dehydrogenation of **13d** (0.11 g, 0.4 mmol) over 10% Pd/C (100 mg) in refluxing triethylene glycol dimethyl ether (8 mL) for 5 h under nitrogen. The solution was cooled and filtered, and the filtrate was poured into ice-water to give **16d** as a yellow powder (65 mg, 58%) whose NMR spectrum matched that of an authentic sample.

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Registry No. **2**, 7382-37-8; **3a**, 129986-82-9; **3b**, 129986-81-8; **3c**, 129986-83-0; **4a**, 129986-90-9; **4b**, 129986-88-5; **4c**, 129986-92-1; **5a**, 129986-91-0; **5b**, 129986-89-6; **5c**, 129987-13-9; **6a**, 16563-51-2; **6b**, 21568-05-8; **6c**, 6051-86-1; **7a**, 129987-00-4; **7b**, 129986-99-8; **7c**, 125574-15-4; **8a**, 3528-23-2; **8b**, 54965-49-0; **9**, 115560-65-1; **10a**, 129986-84-1; **10b**, 129986-85-2; **10c**, 129986-86-3; **10d**, 129986-87-4; **11a**, 129986-93-2; **11b**, 129986-95-4; **11c**, 129986-97-6; **11d**, 129986-98-7; **12a**, 129986-94-3; **12b**, 129986-96-5; **13a**, 129987-01-5; **13b**, 129987-03-7; **13c**, 129987-04-8; **13d**, 129987-06-0; **14a**, 129987-02-6; **14c**, 129987-05-9; **14d**, 129987-07-1; **15**, 129987-08-2; **16a**, 129987-09-3; **16b**, 129987-10-6; **16c**, 129987-11-7; **16d**, 129987-12-8; **17**, 129987-14-0; H_2C=CHCHO, 107-02-8; (*E*)-PhCH=CHCHO, 14371-10-9; H_2C=$C(CH_3)$CHO, 78-85-3; 1-acetylpyrene, 3264-21-9; 1-acetoxypyrene, 78751-40-3; 1-hydroxypyrene, 5315-79-7; 1-naphthol, 90-15-3; (*E*)-crotonaldehyde, 123-73-9.

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Preparation and Reactivity of Methyl 3,3-Bis(4-(dimethylamino)pyridinium-1-yl)propenoate Dichloride

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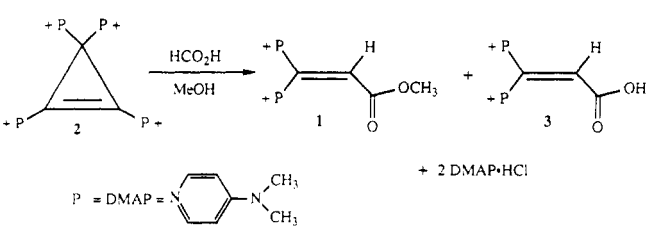
The preparation, structure, and reactivity of methyl 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoate dichloride (**1**) are discussed. 1,2,3,3-Tetrakis(4-(dimethylamino)pyridinium-1-yl)cyclopropene tetrachloride (**2**) was converted to **1** with formic or acetic acid in methanol. A mechanism for the conversion of **2** to **1** is suggested. Hydrolysis of **1** under basic conditions gave 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoic acid (**3**), which has a pK_a of 2. The X-ray structure of **1** shows that the pyridinium rings are both twisted with respect to the double bond; the resulting high steric hindrance prevent Diels-Alder reactions with dienes despite the electrophilic nature of the system.

We have recently reported the preparation and some reactions of 1,2,3,3-tetrakis(4-(dimethylamino)-pyridinium-1-yl)cyclopropene tetrachloride (**2**).[1,2] Compound **2** has been shown to undergo nucleophilic attack at the double bond followed by ring opening to give allyl anions substituted with *N*-pyridinium cations, which in some cases undergo electrocyclic ring closure to give indolizines.[1-4] In this paper we report the conversion of **2** to 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoic acid, **3**, and its esters, along with the properties of this unique acrylic system.

Results and Discussion

Compound **2** was found to react with formic or acetic acids in methanol to give **1** and **3**. The reaction produces 2 equiv of 4-(dimethylamino)pyridine hydrochloride, DMAP·HCl. The reaction of **2** as the chloride salt with



formic acid in ethanol gave ethyl 3,3-bis(4-dimethylamino)pyridinium-1-yl)propenoate, **4**, DMAP·HCl, and **3**. The ratio of acrylic acid to ester is dependent both on the

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