butyl]aluminum diethyl etherate ($[\alpha]^{25}_D$ +22.28° (c 6.17, pentane)),[13] was prepared as previously described.[14] All the organoaluminum compounds were stored in sealed capillary glass vials in weighed amounts. The organoaluminum dichlorides were prepared from the trialkylalane by the redistribution with crushed anhydrous $AlCl_3$ in diethyl ether at 0 °C.[3] The solvents were commercial reagent-grade materials, purified by standard methods and redistilled under nitrogen from $LiAlH_4$ before use. GLC analyses were performed on a Perkin-Elmer 3920 B instrument with flame-ionization detectors and using 200 × 0.29 cm columns packed with 8% Carbowax 20M plus 2% KOH on 80–100-mesh Chromosorb W, while preparative GLC was carried out in a Perkin-Elmer F-21 chromatography (300 × 0.80 cm columns, 8% Carbowax 20M plus 2% KOH on 80–100-mesh Chromosorb W). ^1H NMR spectra were obtained by using a Varian A-60 spectrometer. Optical rotations were measured at the 589.6-nm sodium line with a Perkin-Elmer 142 automatic polarimeter.

General Procedure. All reactions were carried out at least in duplicate under a dry nitrogen atmosphere. In a typical small-scale reaction, a three-necked, 25-mL, round-bottomed flask was fitted with a stirring bar, a glass stopcock, a Versilic silicone cap, and a sealed angular piece of glass tubing containing 10.21 mmol of $AlCl_3$. The vessel was charged with 10 mL of ether and cooled at 0 °C, and *i*-Bu_3Al (5.11 mmol) was added from the sealed capillary glass vials. The reaction flask was then turned so that the solid $AlCl_3$ dropped into the trialkylalane solution. After a 5-min agitation, the ether was removed at reduced pressure (0.1 torr), and benzene (72.82 mmol, 6.47 mL) was injected by hypodermic syringe through the cap at the same temperature, followed by the ketone (14.56 mmol). The resulting mixture was stirred at room temperature (ca. 25 °C) for the desired time of aging. At intervals, samples of the mixture (0.4 mL) were withdrawn by a 500-μL hypodermic syringe and quenched in 10% H_2SO_4 solution (1 mL); quantitative and qualitative analyses of the reaction products were performed by GLC on the crude mixture. All products were isolated by preparative GLC, and when necessary their structures were deduced from ^1H NMR and mass spectra.

Asymmetric Reduction of Isopropyl Methyl Ketone. The following procedure is representative of all the experiments. Isopropyl methyl ketone (24.05 mmol, 2.12 g) was added rapidly at 0 °C to a benzene solution (10.7 mL) of (*S*)-(2-methylbutyl)-aluminum dichloride (25.32 mmol) in a flame-dried, two-necked 100-mL flask. A light yellow coloration developed immediately and faded slowly. After 3 h, the benzene was accurately removed at 0.1 torr, 25 mL of pentane was added, and the resulting mixture was cautiously hydrolyzed with dilute sulfuric acid, extracted with pentane, washed with a dilute $NaHCO_3$ solution, and dried (Na_2SO_4). Removal of the solvent and distillation afforded (+)-(*S*)-3-methyl-2-butanol: 2.07 g (93% yield); bp 113 °C; $[\alpha]^{25}_D$ +0.52° (neat).[4]

In an another experiment, isopropyl methyl ketone (26.08 mmol) was reacted in benzene (11.6 mL) with (*S*)-(2-methylbutyl)aluminum dichloride (27.45 mmol). After 3 h, the volatile products[15] were removed at reduced pressure (300 torr), and the reaction mixture was stirred at room temperature for additional 21 h. Hydrolysis was accomplished as above, and the organic products were extracted with pentane. Preparative GLC purification afforded 2-methyl-2-phenylbutane [NMR ($CDCl_3$,Me_4Si) δ 0.67 (3 H, t, CH_3CH_2), 1.27 (6 H, s, $(CH_3)_2C$), 1.67 (2 H, q, CH_2C), 7.30 (5 H, m, C_6H_5)] and (−)-(*R*)-3-methyl-2-phenylbutane: bp 86 °C (21 torr); $[\alpha]^{25}_D$ −2.05° (neat).[9]

Additional Experiments. 2-Methyl-1-butene (0.87 g, 12.39 mmol) was added to [(2-butyl)oxy]aluminum dichloride (12.39 mmol), prepared from 2-butanol and isobutylaluminum dichloride, and the mixture was stirred at room temperature. After 3 h, the olefin, recovered at reduced pressure, was shown to contain 23% of 2-methyl-2-butene. Another run was carried out in benzene (5.5 mL) for 24 h. After hydrolysis with dilute sulfuric acid, GLC analysis of the pentane extracts showed the presence of 2-phenylbutane (53%), 3-methyl-2-phenylbutane (15%), and 2-methyl-2-phenylbutane. (+)-(*S*)-3,3-Dimethyl-2-phenylbutane [1.95 g, 12.00 mmol; $[\alpha]^{25}_D$ + 5.30° (c 6.2, heptane)][11] was added to a benzene (1.0 mL) solution of ethoxyaluminum dichloride (12.00 mmol), prepared from anhydrous ethanol and isobutylaluminum dichloride. The mixture was stirred for 24 h at room temperature, hydrolyzed, and extracted with pentane. GLC purification yielded 1.72 g of (+)-(*S*)-3,3-dimethyl-2-phenylbutane, $[\alpha]^{25}_D$ +5.32° (c 4.81, heptane).[11]

Registry No. 2-Butanone, 78-93-3; 3-methyl-2-butanone, 563-80-4; 3,3-dimethyl-2-butanone, 75-97-8; isobutylaluminum dichloride, 1888-87-5; (*S*)-(2-methylbutyl)aluminum dichloride, 82732-01-2; benzene, 71-43-2.

(13) Giacomelli, G.; Menicagli, R.; Lardicci, L. *J. Org. Chem.* **1973**, *38*, 2370–2376.

(14) Pino, P.; Lardicci L.; Lorenzi, G. P. *Ann. Chim. (Rome)* **1958**, *48*, 1426–1437.

(15) A mixture of 2-methyl-1-butene (81%) and 2-methyl-2-butene (19%) was recovered together with traces of benzene.

Synthesis of a Modified Anthracycline: 4,6,9,11-Tetradeoxydaunomycinone

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Received December 8, 1981

The preparation of a tetradeoxy anthracyclinone is described. The key reaction is the cyclization of the acetylenic coumarin **10** to anthraquinone **11**. Interestingly, the related model system **12** failed to cyclize. The transformation of **11** into the desired compound **13** was effected by straightforward reactions. The key intramolecular cyclization reaction is also useful for the preparation of phthalide quinone **7**.

As a consequence of the potent biological activity exhibited by the anthracyclines, several synthetic approaches to this class of molecules have been reported.[2] While many reports describe research directed toward the synthesis of the parent compounds, an increasing number of publications has focused on the preparation of synthetic analogues. Several deoxy analogues have been synthesized.[3] Among these, the 4-deoxyanthracyclines constitute the largest class. These modified anthracyclines possess

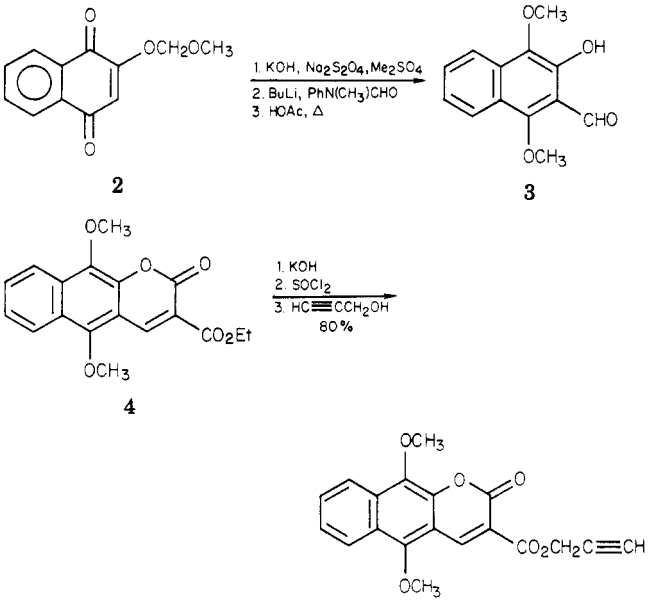
(1) A portion of this paper has been taken from the unfinished Ph.D. thesis of John O. Pezzanite.

(2) Arcamone, F. "Topics in Antibiotic Chemistry"; Sammes, P. G., Ed.; Halsted Press: New York, 1978; Vol. 2, Chapter 3. Brown, J. R. *Prog. Med. Chem.* **1978**, *15*, 165. Remers, W. A. "The Chemistry of Antitumor Antibiotics"; Wiley Interscience: Somerset, NJ, 1979; Vol. 1, Chapter 2. "Anthracyclines: Current Status and New Developments"; Crooke, S. T.; Reich, S. D., Eds.; Academic Press: New York, 1980. Kelly, T. R., Vaya, J.; Ananthasubramanian, L. *J. Am. Chem. Soc.* **1980**, *102*, 5983 and references therein.

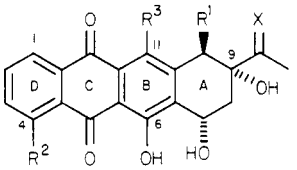
(3) Kim, K. S.; Vanotti, E.; Suarato, A.; Johnson, F. *J. Am. Chem. Soc.* **1979**, *101*, 2483. Parker, K. A.; Kallmerten, J. *Ibid.* **1980**, *102*, 5881. Wong, C. M.; Papien, D.; Schwenk, R.; TeRaa, *J. Can. J. Chem.*, **1971**, *49*, 2712. Kende, A. S.; Belletire, J.; Bently, T. J.; Hume, E.; Airey, J. *J. Am. Chem. Soc.* **1975**, *97*, 4425. Gleim, R. D.; Trenbeath, S.; Mittal, R. S. D.; Sih, C. J. *Tetrahedron Lett.* **1976**, 3385.

0022-3263/82/1947-4337$01.25/0

Scheme I

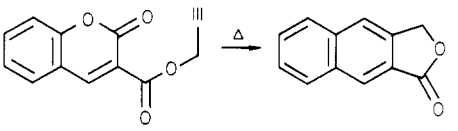


slightly diminished biological activity compared to the parent compounds. However, regiochemical control of the A ring relative to the D ring is not necessary. This represents a considerable synthetic simplification. Recently, 11-deoxyanthracyclines have been isolated and shown to display similar biological activity to known anthracyclines. Importantly, they had fewer dose-limiting side effects.[4] At the onset of our work, no analogue had been prepared that lacked hydroxyl groups at C-4, C-6, C-9, and C-11. The synthesis of this analogue is the subject of this paper.



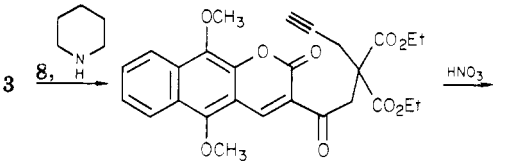
1a (daunomycinone), R^1 = H; R^2 = OCH_3; R^3 = OH; X = O
b (aklavinone), R^1 = CO_2CH_3; R^2 = OH; R^3 = H; X = H_2

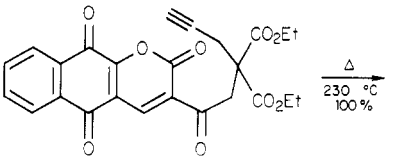
Earlier work in our laboratories had shown that intramolecular Diels–Alder reactions were effective in the construction of substituted benzophthalides.[5] Our plan

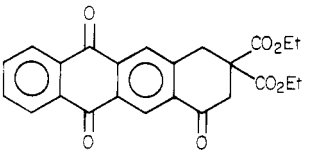


was to extend the reaction to the synthesis of naphthophthalides and then elaborate the lactone subunit to the A ring. The synthetic plan (outlined in Scheme I) began with the methoxymethyl ether **2** of commercially available lawsone.[6] This compound was reductively methylated, metalated with *n*-butyllithium in ether, and transformed into aldehyde **3** by the addition of *N*-methylformanilide.[7] We had previously synthesized[6] **4**, which was transformed into the desired propargyl ester **5**. Attempted cyclization

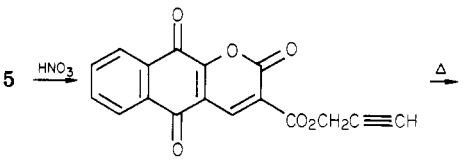
Scheme II

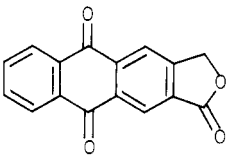






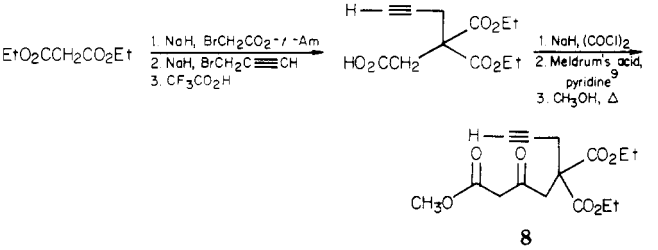
under several conditions afforded either recovered starting material or decomposition products. However, oxidation of the protected hydroquinone with nitric acid[8] furnished quinone **6**, which cyclized in quantitative yield at 230 °C!





The comparative facility with which **6** cyclized is probably attributable to the prior breakup of the aromatic character of the central ring by oxidation. Quinone **7** was characterized by UV, IR, elemental analysis, and mass spectroscopy. Unfortunately, **7** was insoluble in all common NMR solvents, including Me_2SO. The insolubility and inertness of **7** prompted us to modify the overall plan.

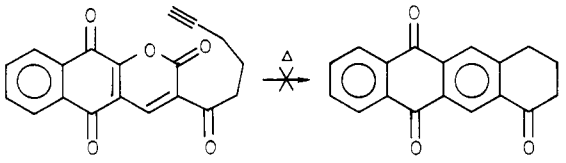
The new plan centered around the creation of the entire A ring by intramolecular cycloaddition. The reaction of aldehyde **3** with keto triester **8** produced **9** in 80% yield. Keto triester **8** is prepared in six steps from diethyl malonate. The cyclization of **9** could not be achieved.



Therefore, nitric acid oxidation was again employed to generate quinone **10** (Scheme II). This compound cyclized

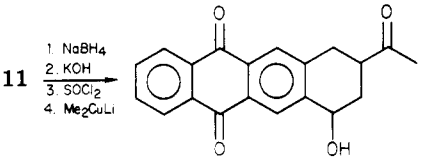
(4) Hori, S.; Shirai, M.; Shinchi, H.; Oki, T.; Inui, T.; Tsukagoshi, S.; Ishizuka, M.; Takeuchi, T.; Umezawa, H. *Gann* **1977**, *68*, 685.
(5) Kraus, G. A.; Pezzanite, J. O.; Sugimoto, H. *Tetrahedron Lett.* **1979**, 853.
(6) Kraus, G. A.; Pezzanite, J. O. *J. Org. Chem.* **1979**, *44*, 2480.
(7) Adams, R.; Lipscomb, R. D. *J. Am. Chem. Soc.* **1949**, *71*, 519.
(8) Schili, G. *Justus Liebigs. Ann. Chem.* **1966**, *691*, 79.

upon heating at 230 °C for 2 h. Interestingly, **12**, an analogue of **10**, was also prepared and subjected to various thermolysis conditions. The cyclization does not occur.



12

There is some analogy in other systems.[10] The rates of ring-forming reactions do increase when quaternary centers are present in the molecule undergoing cyclization. This increase in rate apparently stems from a decrease in the number of conformations unfavorable to cyclization. Quinone **11** was somewhat soluble in polar solvents. Its structure is supported by infrared absorptions at 1733, 1708, and 1682 cm^{-1}, NMR signals at δ 8.8 (d, J = 2 Hz, 1 H), 3.7 (s, 2 H), and 3.2 (s, 2 H) and a high-resolution mass spectrum and elemental analysis consistent with structure **11**. Reduction with sodium borohydride followed by decarboethoxylation afforded an acid that could be converted to methyl ketone **13** by a two-step reaction sequence developed by Johnson and co-workers.[9]



13

This novel synthetic approach to the anthracycline skeleton shows promise for the construction of a variety of A-ring analogues. The plan is a convergent one that could also be useful for development as a regiospecific sequence, provided that suitable CD subunits can be constructed.

Experimental Section

General Procedures. Melting points were taken on a Fisher-Johns melting-point apparatus and are uncorrected.

NMR spectra were determined in the indicated solvent on a Varian A60 or Hitachi Perkin-Elmer R-20B spectrometer; tetramethylsilane was used as an internal standard. Infrared spectra were determined as a neat film or Nujol mull on a Beckman IR4250 or Beckman Acculab 2 spectrophotometer; only significant bands are reported. Exact mass determinations were obtained on a AE1 MS-902 high-resolution mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

1,4-Dimethoxy-2-hydroxy-3-naphthaldehyde (3). To a solution of 4.6 g (21 mmol) of **2** in 80 mL of acetone is added a solution of 15 g of sodium dithionite in 80 mL of water. The mixture is stirred at room temperature for 13 h. It eventually becomes a solution. Most of the acetone is removed under reduced pressure. A solution of 15 g of KOH in 35 mL of water is added in one portion. A light-green solution is obtained. After the reaction mixture is cooled, 30 mL of dimethyl sulfate is added. The green coloration disappears within a few minutes. After a few minutes the ice bath is removed and stirring is continued at room temperature for an additional 7 h. The reaction mixture is extracted twice with ether, and the combined extracts are washed with brine, dried, and concentrated in vacuo. The crude product is chromatographed on silica gel (100 g) with hexane–ether (3/1). The pure product is obtained as a colorless oil, which crystallizes to a waxy solid (mp 33–34 °C) on storage in the refrigerator. The yield is 4.3 g (82%). IR (film) 1680, 1600, 1465, 1375, 1100, 770 cm^{-1}; NMR ($CDCl_3$) δ 3.55 (s, 3 H), 3.9 (s, 6 H), 5.28 (s, 2 H), 6.75 (s, 1 H), 7.45 (m, 2 H), 8.2 (m, 2 H); MS, $C_{14}H_{16}O_4$ requires 248.1049, measured 248.1042. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.71; H, 6.73.

To a solution of 4.0 g (16.1 mmol) of the above compound in 20 mL of dry ether (cooled in an ice slush bath) is added 20 mmol of *n*-butyllithium (as a hexane solution). Stirring is continued at 0 °C for 4 h. A solution of 3.4 g (25 mmol) of *N*-methylformanilide in 5 mL of ether is added by syringe. The precipitated aryllithium immediately dissolves. After a few minutes the solution is diluted with ether, washed with 1 N hydrochloric acid and brine, dried, and then concentrated in vacuo. The residue is dissolved in 30 mL of acetic acid and 1 mL of water. The solution is refluxed gently for 4.5 h, cooled, and concentrated in vacuo. The residue is taken up in ether, washed twice with water and brine, dried, and concentrated in vacuo. The crude product is chromatographed on 100 g of silica gel with hexane ether (3/1). The aldehyde **3** is obtained as a bright-orange solid in 53% yield: mp 105–106 °C (aqueous ethanol); IR (mull) 3100, 1660, 1570, 1510, 775, 720 cm^{-1}; NMR ($CDCl_3$) δ 10.95 (s, 1 H), 10.55 (s, 1 H), 8.2 (m, 2 H), 7.6 (m, 2 H), 4.15 (s, 3 H), 4.05 (s, 3 H); MS, $C_{13}H_{12}O_4$ requires 232.0725, measured 232.0736. Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.11; H, 5.27.

Propargyl Ester 5. To a suspension of 3.28 g (10 mmol) of ethyl ester **4** in 50 mL of 95% ethanol is added a solution of 10 g of KOH in 10 mL of water. The mixture is refluxed for 2 h, cooled to room temperature, and acidified with concentrated hydrochloric acid. The acidified mixture is partitioned between methylene chloride and brine. The organic layer is dried and concentrated in vacuo. The crude carboxylic acid thus obtained is sufficiently pure for the next step or it can be recrystallized from acetone/95% ethanol, mp 250–252 °C (dec). The carboxylic acid is suspended in 50 mL of chloroform and 5 mL of thionyl chloride is added. The solution is refluxed for 2 h and concentrated in vacuo. The last traces of thionyl chloride are removed by adding benzene followed by concentration in vacuo. The crude acid chloride, a crystalline substance, is suspended in 50 mL of methylene chloride and cooled in an ice slush bath. To this is added 5 mL of pyridine followed by 3 mL of propargyl alcohol. The mixture is stirred overnight at room temperature, diluted with ether, and washed with 1 N hydrochloric acid and then brine. After drying and concentration in vacuo, crude crystalline **5** is obtained and is sufficiently pure for the next step. The yield of **5** is 2.7 g (80%): mp 192–194 °C (ethyl acetate); IR (mull) 3265, 2130, 1745, 1715, 1615 cm^{-1}; NMR ($CDCl_3$) δ 9.05 (s, 1 H), 8.3 (m, 2 H), 7.7 (m, 2 H), 5.1 (d, J = 3 Hz, 2 H), 4.25 (s, 3 H), 4.0 (s, 3 H), 2.6 (t, J = 3 Hz, 1 H); MS, $C_{19}H_{14}O_6$ requires 338.0790, measured 338.0805. Anal. Calcd for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17. Found: C, 67.61; H, 4.16.

Quinone 6. To a suspension of 2.7 g of propargyl ester **5** in 40 mL of acetic acid is added 10 mL of concentrated nitric acid. The orange suspension becomes a yellow solution and then a yellow precipitate forms. The mixture is stirred an additional 10 min and poured into 250 mL of water. The precipitate is filtered, washed with water, and allowed to air-dry. The crude product is recrystallized from acetone. Yield of **6** is 2.2 g (90%): mp 206–207 °C (acetone); IR (mull) 3260, 2130, 1745, 1725, 1675 cm^{-1}; NMR (Me_2SO-d_6SO) δ 8.70 (s, 1 H), 8.0 (m, 4 H), 5.05 (d, J = 3 Hz, 2 H), 3.3 (t, J = 3 Hz, 1 H); MS, $C_{17}H_8O_6$ requires 308.0321, measured 308.0321. Anal. Calcd for $C_{17}H_8O_6$: C, 66.24; H, 2.62. Found: C, 66.01; H, 2.55.

Lactone 7. A suspension of 2.0 g of quinone **6** in 15 mL of toluene in a sealed tube is placed in a silicone oil bath heated to 230 °C. The initial reaction mixture becomes a light-brown solution after 10 min. After approximately 1 h the product crystallizes from the *hot* solution. After cooling, the product is filtered and dried on the vacuum pump. The yield is quantitative and the lactone **7** is obtained in analytical purity. No NMR spectrum could be obtained on this substance due to its extreme insolubility. **7**: mp >265 °C dec; IR (mull) 1775, 1675 cm^{-1}; MS, $C_{16}H_8O_4$ requires 264.0423, measured 264.0423. Anal. Calcd for $C_{16}H_8O_4$: C, 72.72; H, 3.05. Found: C, 72.54; H, 2.99.

Preparation of β-Keto Ester 8. To a hexane washed suspension of 2.5 g of 50% NaH in 40 mL of dry tetrahydrofuran,

(9) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087.

(10) See Kim, K. S.; Vanotti, E.; Suarato, A.; Johnson, F. *J. Am. Chem. Soc.* **1979**, *101*, 2483 and references therein.

cooled in an ice slush bath, is added a solution of 8.0 g (50 mmol) of diethyl malonate in 10 mL of dry tetrahydrofuran. After hydrogen evolution has ceased, 10.45 g (50 mmol) of *tert*-amyl bromoacetate in 10 mL of dry tetrahydrofuran is added. A white precipitate forms quickly. The mixture is refluxed for 6 h, cooled, and poured into 100 mL of 3 N hydrochloric acid. The aqueous mixture is extracted with ether and the ether extract is washed with brine. After drying and concentration in vacuo, the crude product is subjected to short-path distillation. The yield of a clear oil is 7.6 g (53%): bp 120 °C (1.5 mm); IR (film) 1750 (br) cm^{-1}; NMR ($CDCl_3$) δ 4.2 (t, J = 7 Hz, 4 H), 3.8 (t, J = 6 Hz, 1 H), 2.8 (d, J = 6 Hz, 2 H), 1.75 (q, J = 8 Hz, 2 H), 1.45 (s, 6 H), 1.25 (t, J = 7 Hz, 6 H), 0.9 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.08; H, 8.60.

To a hexane-washed suspension of 1.2 g of 50% NaH in 30 mL of dry tetrahydrofuran is added a solution of 7.2 g (25 mmol) of the above triester in 10 mL of tetrahydrofuran. After hydrogen evolution has ceased, 7 mL of propargyl bromide (20% toluene) is added by syringe. A white precipitate that forms is refluxed for 5 h, cooled, diluted with ether, and washed with 1 N hydrochloric acid and then brine. After drying and concentration in vacuo, the crude product is obtained in 90% yield and is sufficiently pure for the next step. An analytical sample was obtained by bulb-to-bulb distillation, oven temperature 120 °C (1.0 mm): IR (film) 3300, 1745 cm^{-1}; NMR ($CDCl_3$) δ 4.25 (q, J = 7 Hz, 4 H), 3.1 (s, 2 H), 3.0 (d, J = 3 Hz, 2 H), 2.05 (t, J = 3 Hz, 1 H), 1.75 (q, J = 8 Hz, 2 H), 1.45 (s, 6 H), 1.25 (t, J = 7 Hz, 6 H), 0.9 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.30; H, 8.27.

The crude acetylene obtained in the previous reaction is dissolved in 50 mL of benzene and 5 mL of trifluoroacetic acid. The solution is refluxed for 16 h and concentrated in vacuo. The crude product is chromatographed on silica gel (150 g) with hexane–ether (3/1). The purified acid is obtained as a viscous oil in 84% yield from the triester: IR (film) 3600–2600, 3300, 1750 (br), 1200 cm^{-1}; NMR ($CDCl_3$) δ 11.2 (s, 1 H), 4.2 (q, J = 7 Hz, 4 H), 3.25 (s, 2 H), 3.0 (d, J = 3 Hz, 2 H), 2.05 (t, J = 3 Hz, 1 H), 1.25 (t, J = 7 Hz, 6 H); MS, $C_{12}H_{16}O_6$ requires 256.0947, measured 256.0941. An analytical sample was obtained by bulb-to-bulb distillation, oven temperature 135 (1.0 mm). Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.25; H, 6.29. Found: C, 56.22; H, 6.24.

To a solution of 5.1 g (20 mmol) of acid in 100 mL anhydrous ether is added in portions 1.1 g of 50% NaH. After hydrogen evolution had ceased, the mixture is cooled in an ice slush bath and 2.5 mL of oxalyl chloride is added cautiously. A precipitate forms. The mixture is stirred at room temperature for 2 h and filtered. The filtrate is concentrated in vacuo. To a solution of the oily residue in 60 mL of methylene chloride (cold) is added 5 mL of pyridine and then 3.6 g (25 mmol) of Meldrum's acid. Stirring is continued at room temperature for 5 h. The mixture is diluted with ether and washed with 1 N hydrochloric acid (2×) and brine. After drying and concentration in vacuo, the oil is dissolved in 50 mL of methanol and is refluxed for 8 h. After concentration in vacuo the crude product is chromatographed on silica gel (150 g) with hexane–ether (3/1). The pure β-keto ester **8** is obtained as a clear, viscous oil in 50% yield: IR (film) 3300, 1750 (br), 1200 cm^{-1}; NMR ($CDCl_3$) δ 4.2 (q, J = 7 Hz, 4 H), 3.75 (s, 3 H), 3.5 (s, 2 H), 3.4 (s, 2 H), 3.0 (d, J = 3 Hz, 2 H), 2.05 (t, J = 3 Hz, 1 H), 1.25 (t, J = 7 Hz, 6 H); MS, $C_{15}H_{20}O_7$ requires 312.1209, measured 312.1209. Anal. Calcd for $C_{15}H_{20}O_7$: C, 57.68; H, 6.45. Found: C, 57.45; H, 6.64.

Coumarin 9. To a mixture of 2.1 g (9 mmol) of hydroxy aldehyde **3** and 3.1 g (10 mmol) β-keto ester **8** in 30 mL of absolute ethanol is added a few drops of piperidine. The mixture is refluxed for 6 h, cooled, diluted with 200 mL of methylene chloride, and washed with 1 N hydrochloric acid and then brine followed by drying and concentrating in vacuo. The crude product is recrystallized from 95% ethanol. The yield is 80%. **9**: mp 153 °C (95% EtOH); IR (mull) 3280 1745, 1690, 1080 cm^{-1}; NMR ($CDCl_3$) δ 8.9 (s, 1 H), 8.2 (m, 2 H), 7.7 (m, 2 H), 4.25 (m, 4 H), 4.15 (s, 3 H), 4.1 (s, 3 H), 3.6 (m, 2 H), 3.1 (d, J = 3 Hz, 2 H), 2.05 (t, J = 3 Hz, 1 H), 1.25 (t, J = 7 Hz, 6 H); MS, $C_{27}H_{26}O_9$ requires 494.1577, measured 494.1576. Anal. Calcd for $C_{27}H_{26}O_9$: C, 65.58; H, 5.30. Found: C, 65.81; H, 5.43.

Quinone 10. To a suspension of 245 mg (0.5 mmol) of **9** in 5 mL of glacial acetic acid is added 1 mL of concentrated nitric acid. The suspension turns to a pale-yellow solution and stirring is continued for 10 min. Water (30 mL) is added. The product precipitates and is filtered, washed with water, and dried. The yield is quantitative. **10**: mp 135–137 °C (95% EtOH); IR (mull) 3290, 1750 (br), 1685 cm^{-1}; NMR ($CDCl_3$) δ 8.75 (s, 1 H), 8.3 (m, 2 H), 7.9 (m, 2 H), 4.2 (m, 4 H), 3.6 (m, 2 H), 3.1 (d, J = 3 Hz, 2 H), 2.05 (t, J = 3 Hz, 1 H), 1.25 (t, J = 7 Hz, 6 H); MS, $C_{25}H_{20}O_9$ requires 464.1107, measured 464.1099. Anal. Calcd for $C_{25}H_{20}O_9$: C, 64.66; H, 4.34. Found: C, 64.89; H, 4.19.

Anthraquinone 11. A suspension of 330 mg of quinone **10** in 5 mL of toluene in a sealed tube is placed in a silicone oil bath heated to 230 °C. Heating is continued for 2 h. After cooling, the product crystallizes and is filtered. The yield of **11** is quantitative. **11**: mp 225–226 °C (acetone–95% EtOH); IR (mull) 1733, 1708, 1682, 1590, 715 cm^{-1}; NMR ($CDCl_3$) δ 8.8 (d, J = 2 Hz, 1 H), 8.25 (m, 3 H), 7.85 (m, 2 H), 4.2 (t, J = 7 Hz, 4 H), 3.7 (s, 2 H), 3.2 (s, 2 H), 1.2 (t, J = 7 Hz, 6 H); MS, $C_{25}H_{20}O_7$ requires 420.1209, measured 420.1218. Anal. Calcd for $C_{24}H_{20}O_7$: C, 68.57; H, 4.80. Found: C, 68.60; H, 5.01.

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Registry No. 2, 70160-54-2; **3**, 82823-28-7; **4** ethyl ester, 70160-53-1; **4** acid, 82823-29-8; **4** acid chloride, 82823-30-1; **5**, 82823-31-2; **6**, 82823-32-3; **7**, 82823-33-4; **8**, 82823-39-0; **9**, 82823-40-3; **10**, 82823-41-4; **11**, 82823-42-5; **11** decarboethoxy, 82823-43-6; **12**, 82823-45-8; **13**, 82823-44-7; 1,4-dimethoxy-2-(methoxymethoxy)naphthalene, 70160-52-0; propargyl alcohol, 107-19-7; diethyl malonate, 105-53-3; *tert*-amyl bromoacetate, 82823-34-5; *tert*-amyl 3,3-bis(ethoxycarbonyl)propionate, 82823-35-6; propargyl bromide, 106-96-7; *tert*-amyl 3,3-bis(ethoxycarbonyl)hex-5-ynoate, 82823-36-7; 3,3-bis(ethoxycarbonyl)hex-5-ynoic acid, 82823-37-8; 3,3-bis(ethoxycarbonyl)-hex-5-ynoyl chloride, 82823-38-9; Meldrum's acid, 2033-24-1.