(M, 100), 167 (63), 156 (54), 139 (87), 109 (60), 57 (91).

(*E*)-2-(1-Methoxy-1-phenylmethylidene)-4-methyl-γ-butyrolactone (6g): bp 140 °C (0.2 mmHg); IR (film) 1715 (s), 1695 (sh), 1630 (m), 1255 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (d, J = 6.1 Hz, 3 H), 2.71 (dd, J = 14.9, 7.8 Hz, 1 H), 3.23 (dd, J = 14.9, 10.0 Hz, 1 H), 3.66 (s, 3 H), 4.92 (m, 1 H, coalescing to dd, J = 10.0, 7.8 Hz by irr at 1.46), 7.10-7.84 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 21.5, 38.5, 50.6, 78.1, 127.4 (2 C), 129.1 (2 C), 130.0, 130.2, 164.8, 165.6; HRMS calcd for $C_{13}H_{14}O_3$ 218.0943, found m/z (relative intensity) 218.0935 (M, 27), 185 (72), 105 (100), 77 (66), 59 (53).

(*Z*)-2-(1-(Methoxycarbonyl)ethylidene)-γ-butyrolactone (7). This sample was prepared according to the similar procedure described for **4**, where an equimolar amount of $PdCl_2$ (194 mg, 1.1 mmol) was used in the absence of $CuCl_2$: IR (film) 1755 (s), 1730 (s), 1675 (s), 1150 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05 (t, J = 2.0 Hz, 3 H), 2.92 (tq, J = 7.3, 2.0 Hz, 2 H), 3.85 (s, 3 H), 4.40 (t, J = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.9, 25.5, 51.8, 64.9, 124.1, 138.8, 167.8, 168.9; HRMS calcd for $C_8H_{10}O_4$ 170.0579, found m/z (relative intensity) 170.0587 (M, 15), 139 (100), 112 (11), 85 (27), 83 (42), 67 (10), 43 (17).

Acknowledgment. Partial financial support from the Ministry of Education, Science and Culture, the Japanese Government (Project No. 02231225, 02247217, and 02453095), the Japan Securities Scholarship Foundation, and Yamada Science Foundation is gratefully acknowledged.

Registry No. **1a**, 1123-34-8; **1b**, 624-97-5; **1c**, 60340-28-5; **1d**, 625-31-0; **1e**, 627-27-0; **1f**, 764-37-4; **1g**, 764-38-5; **1h**, 928-97-2; **1i**, 928-96-1; **2a**, 58849-07-3; **2b**, 50598-38-4; *cis*-**2c**, 131067-05-5; *trans*-**2c**, 131067-20-4; *cis*-**2d**, 131067-06-6; *trans*-**2d**, 131067-21-5; **2e**, 19406-00-9; **2f**, 131067-07-7; **2g**, 131067-08-8; **2h**, 131067-09-9; **2i**, 131067-10-2; **3i** (isomer 1), 131067-11-3; **3i** (isomer 2), 131067-12-4; **4a**, 2117-12-6; **4b**, 2117-13-7; **4c**, 10229-10-4; **4d**, 1002-28-4; **4e**, 19781-81-8; **4f**, 131067-13-5; **4g**, 16330-23-7; **5a**, 131078-78-9; **5b**, 131067-18-0; **6c**, 101948-68-9; **6d**, 131067-14-6; **6e**, 131067-15-7; **6f**, 131067-16-8; **6g**, 131067-17-9; **7**, 131067-19-1; acetone, 67-64-1; allylmagnesium bromide, 1730-25-2; cyclohexanone, 108-94-1; dihydrocinnamaldehyde, 104-53-0; 3,3-dimethyl-1-butyne, 917-92-0; 3-pentyn-1-ol, 10229-10-4; propylene oxide, 75-56-9; 1-(1-propenyl)cyclohexanol, 6244-44-6.

Supplementary Material Available: ^{13}C NMR spectra for **2c**, **2i**, **6d-g**, and **7** and ^1H NMR spectra for **5a**, **5b**, and **6c** (10 pages). Ordering information is given on any current masthead page.

Photochemical and Acid-Catalyzed Dienone-Phenol Rearrangements. The Effect of Substituents on the Regioselectivity of 1,4-Sigmatropic Rearrangements of the Type A Intermediate

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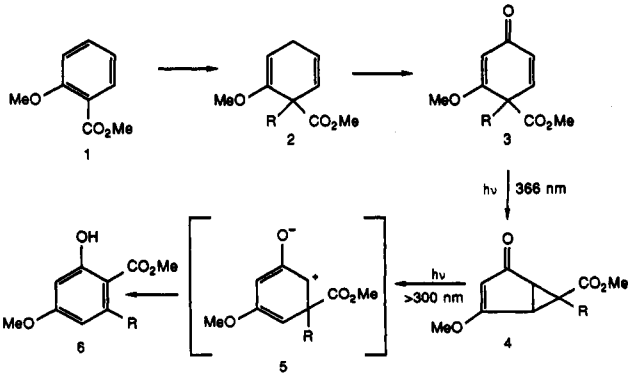
Birch reduction of isophthalic acid and 3-cyanobenzoic acid followed by (1) methylation of the resulting enolate with methyl iodide and (2) esterification with diazomethane provided 2-carbomethoxy- and 2-cyano-6-methyl-6-carbomethoxy-1,4-cyclohexadienes **9** and **25**. Type A photorearrangements of a series of 2-carbomethoxy-, 2-cyano-, 2-methoxy-, and 2-methyl-4-carbomethoxy-4-methyl-2,5-cyclohexadien-1-ones **11**, **26**, **45a**, and **45b** gave 4-carbomethoxy-3-methyl-2-substituted-phenols **12**, **28**, **46**, and **31**. It has been demonstrated that the regioselectivity of type A photorearrangement of C(2) substituted 2,5-cyclohexadien-1-ones is governed by electronic rather than steric effects to give the intermediate C(1) rather than C(3) substituted bicyclo[3.1.0^{1,5}]hex-3-en-2-ones. Regioselectivities of the acid-catalyzed dienone-phenol rearrangements of C(2) substituted 2,5-cyclohexadienones **11**,**45a**, and **45b** appear to be dependent upon the relative stabilities of carbocations resulting from migration of the C(4) carbomethoxy group.

Photorearrangements of 2,5-cyclohexadien-1-ones have attracted the attention of chemists for over 150 years. Outstanding efforts by Zimmerman, Schuster, and many other workers during the last three decades have provided detailed mechanistic understanding of the type A photorearrangement of 2,5-cyclohexadien-1-ones; much of this work already has been reviewed in earlier contributions from this laboratory directed at synthetic aspects of 2,5-cyclohexadien-1-one photochemistry.[1,2]

The type A photorearrangements of 3-methoxy-2,5-cyclohexadien-1-ones **3** give bicyclo[3.1.0]hexenones **4** in excellent yield (Scheme I).[1] While relatively resistant to secondary photorearrangement at 366 nm, bicyclohexenones **4** undergo cyclopropane ring opening when irradiated with light of >300 nm to give zwitterions **5**,[2] from which regioselective 1,2-migrations of the carbomethoxy group give phenols **6**. Cyclohexadienones **3** with a wide variety of alkyl substituents at C(4) are available by alkali metal in ammonia reduction-alkylations[3] of methyl 2-

Scheme I



(1) (a) Schultz, A. G.; Lavieri, F. P.; Macielag, M.; Plummer, M. *J. Am. Chem. Soc.* **1987**, *109*, 3991. (b) Schultz, A. G.; Plummer, M.; Taveras, A. G.; Kullnig, R. K. *Ibid.* **1988**, *110*, 5547. (c) Schultz, A. G.; Taveras, A. G.; Harrington, R. E. *Tetrahedron Lett.* **1988**, *29*, 3907.

(2) (a) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391. (b) Schultz, A. G. *Pure Appl. Chem.* **1988**, *60*, 981. (c) Schultz, A. G.; Plummer, M. *J. Org. Chem.* **1989**, *54*, 2112.

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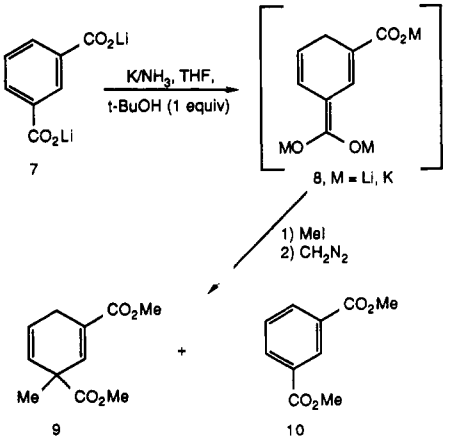
methoxybenzoate (1) to give 1,4-cyclohexadienes 2 followed by bis-allylic oxidations of 2.

Inasmuch as substituted phenols are useful synthetic and biosynthetic substrates, we decided to examine the generality of the dienone–phenol photorearrangement 3 → 6, particularly with regard to the effect of substituents at C(2) on the regioselectivity of phenol formation. Herein, we describe (1) the first Birch reduction–alkylation of isophthalic acid and 3-cyanobenzoic acid, (2) photorearrangements of 2-carbomethoxy-, 2-cyano-, 2-methoxy-, and 2-methyl-4-carbomethoxy-4-methyl-2,5-cyclohexadien-1-ones, and (3) complementary acid-catalyzed dienone–phenol rearrangements of the C(2) substituted 2,5-cyclohexadienones that demonstrate for the first time the regioselectivities of carbomethoxy group 1,2-migration. Of particular mechanistic interest is the elucidation of substituent effects on the regioselectivity of 1,4-sigmatropic rearrangements of the type A intermediate.

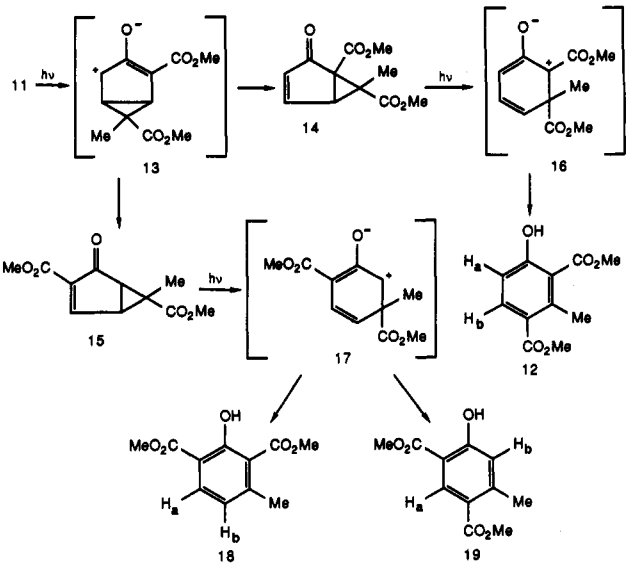
Results and Discussion

The 2-Carbomethoxy Substituent. Attempts to reduce dimethyl isophthalate (10) with lithium or potassium metal, followed by addition of methyl iodide, resulted in complex mixtures of products. The parent carboxylic acid in the form of either the ammonium or alkali metal salt is sometimes the more effective substrate for Birch reduction.[3] The potassium and sodium salts of isophthalic acid were found to be sparingly soluble in NH_3–THF mixtures, while the dilithium salt 7 was completely soluble in a 4:1 distribution of NH_3 and THF. Reductions of 7 with lithium were somewhat difficult to reproduce;[4] however, reduction of 7 with potassium metal in NH_3–THF solution in the presence of 1 equiv of *tert*-butyl alcohol and in situ alkylation of the resulting enolate trianion 8 with methyl iodide, followed by esterification with diazomethane, gave 6-methyl-1,4-cyclohexadiene 9 in 54% isolated yield.[5] A slightly enhanced yield of 9 (57%) was obtained by addition of 1.2 equiv of LiBr to solutions of enolate 7 prior to addition of methyl iodide. This cation

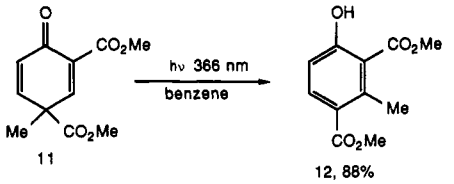


exchange procedure has proven to be especially useful in reactions of 7 and related substrates with homoallylic and other base-sensitive alkyl halides.[1b,5] The high degree of regioselectivity for alkylation of 8 is consistent with (1) the observed reactivity of multiple anions, namely that electrophilic attack generally occurs at the more basic carbon center[6] and (2) the fact that enolates of α,β-unsaturated carbonyl compounds react preferentially at the α- rather than the γ-carbon atom.[7]

Scheme II



Bis-allylic oxidation of 1,4-cyclohexadiene 9 with *tert*-butyl hydroperoxide and pyridinium dichromate (PDC)[1c] provided 2,4-dicarbomethoxy-4-methyl-2,5-cyclohexadien-1-one (11). Irradiation of 11 in benzene solution (0.05 M) at 366 nm gave the crystalline 2,4-dicarbomethoxy-3-methylphenol (12; mp 95.5 °C) in 87% isolated yield.



That the photorearrangement of 11 to 12 does not occur by a direct dienone–phenol rearrangement[8a] of the C(4) methyl substituent was determined by ^1H NMR monitoring of the photoreaction. At early stages of irradiation of 11 (366 nm, C_6D_6), new resonances compatible with the presence of intermediate bicyclo[3.1.0]hexenones were observed; on continued irradiation, the complex spectra eventually simplified to that of phenol 12.[9a] Successful isolation of a bicyclo[3.1.0]hexenone from a related photorearrangement (26 → 27 → 28) provides additional support for the involvement of bicyclohexenone 14 in the photorearrangement of 11 to 12.

Mechanisms for photorearrangement of 11 are considered in Scheme II.[8b] Type A photorearrangement of 11 would give zwitterion 13, which could rearrange to either

(3) Hook, J. M.; Mander, L. N. *Nat. Prod. Rep.* **1986**, *3*, 35.

(4) Irreproducibility may depend on the size, shape, and precise method of addition of the pieces of lithium metal to solutions of 7 in NH_3–THF.

(5) Alkylations of 8 with ethyl iodide, benzyl bromide and allyl bromide or protonation with NH_4Cl provided the 1,4-cyclohexadiene corresponding to 9 in yields ranging from 58 to 65%.

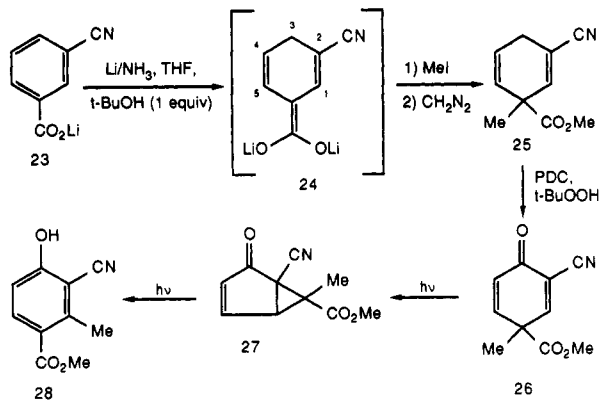
(6) (a) Harris, T. M.; Harris, C. M. *Org. React.* **1969**, *17*, 155. (b) Creger, P. L. *J. Org. Chem.* **1972**, *37*, 1907.

(7) (a) Zimmerman, H. E. In *Molecular Rearrangements*; DeMayo, P., Ed.; Interscience: New York, 1963. (b) Zimmerman, H. E. *Acc. Chem. Res.* **1987**, *20*, 263.

(8) (a) Zimmerman, H. E.; Lynch, D. C. *J. Am. Chem. Soc.* **1985**, *107*, 7745. (b) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, *84*, 4527.

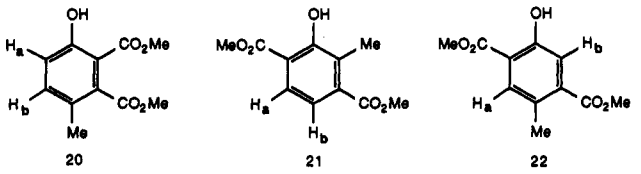
(9) (a) Bicyclohexenones generated by photorearrangements of 4-alkyl-4-carbomethoxy-2,5-cyclohexadien-1-ones are too photoreactive for detection by ^1H NMR spectroscopy; ref 1. (b) It is noteworthy that 4-alkyl-4-cyano-3-methoxy-2,5-cyclohexadien-1-ones have been found to undergo photorearrangement to 6-alkyl-6-cyano-4-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones and *reversible photorearrangement* to 6-alkyl-6-cyano-5-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones: Schultz, A. G.; Reilly, J., manuscript in preparation.

Scheme III



bicyclohexenone **14** or **15**. Photoinitiated cleavage of the internal cyclopropane bond in **14** would give zwitterion **16**; 1,2-migration of the carbomethoxy group in **16** would deliver phenol **12**. However, photorearrangement of the isomeric bicyclohexenone **15** would give the isomeric zwitterion **17**, which could rearrange to phenols **18** and **19**. The available evidence suggests that zwitterion **13** rearranges only to bicyclohexenone **14** and not **15**. However, we presently cannot rigorously exclude the possibility that **15** is formed reversibly and, because of some special effect of the C(3) carbomethoxy substituent, does not undergo a secondary photorearrangement to zwitterion **17**.[9b]

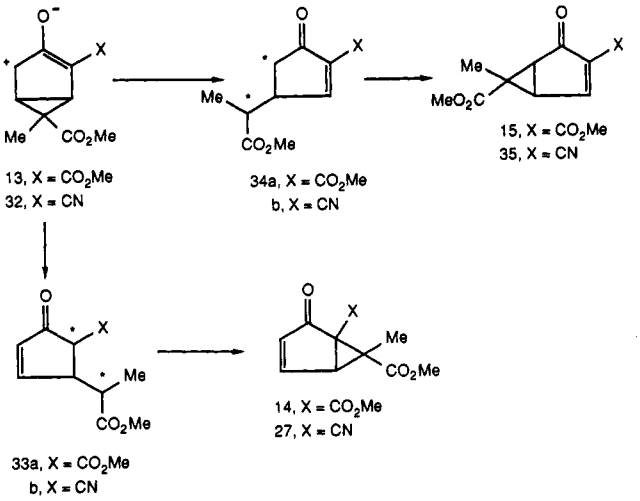
An assignment of structure **12** to the phenol resulting from photorearrangement of **11** rests on ^{1}H NMR spectral data. The photoproduct shows doublets at δ 6.86 (H_a, J = 8.8 Hz) and 7.85 (H_b, J = 8.8 Hz). Thus, phenol **19** was eliminated from further consideration because the aromatic protons would appear as singlets. Phenol **18** (mp 53–4 °C) has been reported[10a] and does not correspond to the photoproduct. Phenols **20–22** are products of methyl rather than carbomethoxy group rearrangement in zwitterions **16** and **17**. Rearrangements of this type were considered improbable on the basis of mechanistic expectations.[1] In any event, the photoproduct is not the previously reported phenol **20**;[10b] in analogy with **19**, phenol **22** was rejected on the basis of coupling constants for H_a and H_b. Phenol **21** was rejected because the chemical shift difference (~1.0 ppm) for H_a and H_b is too large for protons in such similar environments.



The 2-Cyano Substituent. Birch reduction of the lithium salt of 3-cyanobenzoic acid **23** (Scheme III) with lithium metal in NH_3–THF solution in the presence of *tert*-butyl alcohol (1 equiv) presumably generates enolate dianion **24**.[11] Alkylation with methyl iodide followed by esterification with diazomethane and flash chromatography on silica gel gave 6-carbomethoxy-2-cyano-6-methyl-1,4-cyclohexadiene (**25**) in ~45% yield.

The preparation of **25** from **23** in synthetically useful yields is remarkable for several reasons. The nitrile group

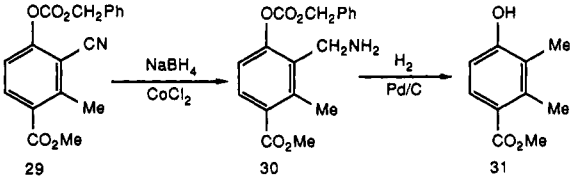
Scheme IV



survives the alkali metal in ammonia reduction of the aryl nucleus,[12] and there is a high degree of regioselectivity for protonation at C(3) to give **24** rather than at C(1) or C(5).[13] Furthermore, alkylation of enolate dianion **24** occurs regioselectively at C(6) rather than adjacent to the nitrile substituent at C(2). It is noteworthy that positional selectivity in alkylations of enolates derived from γ-cyanocrotonic acids appears not to have been explored. Birch reductions of derivatives of 3-cyanobenzoic acid should provide an opportunity to study the effect of substituents and other reaction variables on alkylation regioselectivity.

Bis-allylic oxidation of **25** gave 2,5-cyclohexadienone **26** in 36% overall yield from the starting lithium salt **23**. Irradiation of **26** as described for **11** gave phenol **28** in 77% isolated yield. When the photolysis of **26** was carried out for a brief period of time, bicyclohexenone **27** could be isolated in ~10% yield. Independent irradiation of **27** resulted in rearrangement to phenol **28**.

The structure of **28** was deduced by IR and ^{1}H NMR spectroscopy and chemical conversion to phenol **31**. Thus, protection of the hydroxyl group in **28** as the carbonate **29** was followed by selective reduction of the nitrile group with sodium borohydride–cobalt chloride.[14] Hydrogenolysis of the resulting benzylic amine **30** over palladium on carbon gave methyl 4-hydroxy-2,3-dimethylbenzoate (**31**), which was shown to be identical with **31** prepared by another route (vide infra).



Regioselectivity of Rearrangement of the Type A Zwitterion. The regioselectivity of photorearrangement of 2,5-cyclohexadienones **11** and **26** appears to be governed by electronic rather than steric effects. Indeed, the favored bicyclohexenones (**14** and **27**) have more severe steric interactions as a result of adjacent quaternary centers than bicyclohexenones **15** and **35** (Scheme IV). Rearrangements of zwitterions such as those presumed to be involved in the type A photorearrangement have been shown to

(10) (a) Takeuchi, N.; Okada, N.; Tobinaga, S. *Chem. Pharm. Bull.* **1983**, *31*, 4355. (b) Kato, T.; Suzuki, T.; Ototani, N.; Maeda, H.; Yamada, K., Kitahara, Y. *J. Chem. Soc., Perkin Trans. 1* **1977**, 206.

(11) For the first examples of Birch reduction and reductive alkylation of benzonitriles, see: Schultz, A. G.; Macielag, M. *J. Org. Chem.* **1986**, *51*, 4983.

(12) Birch, A. J.; Hinde, A. L.; Radom, L. *J. Am. Chem. Soc.* **1980**, *102*, 6430.

(13) Occasionally 5-carbomethoxy-1-cyano-5-methyl-1,3-cyclohexadiene also was observed in crude reaction mixtures containing **25**.

(14) Ganem, B.; Osby, J. O. *Chem. Rev.* **1986**, *86*, 763.

occur with inversion of configuration at the migrating carbon atom.[15] Although this experimental evidence is consistent with a concerted 1,4-sigmatropic rearrangement of the type A intermediate, the transition state for rearrangement might have dipolar or diradical character and, therefore, be subject to substituent effects.[16,17]

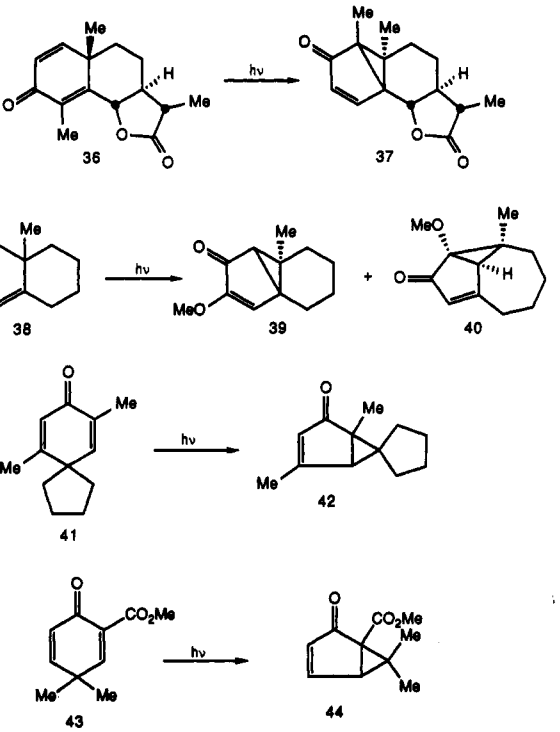
Structures **33** and **34** in Scheme IV are transition-state representations that facilitate an understanding of the effect of substituents at C(2). It is clear that dipolar or diradical character ought to be better stabilized by the C(2) substituent (X) in **33** than in **34**. We wondered what would be the effect on regioselectivity if the electron withdrawing substituents at C(2) were replaced by electron releasing groups.

A search of the photochemical literature uncovered several photorearrangements of 2-substituted 2,5-cyclohexadien-1-ones. Santonin (**36**) has been shown to photorearrange to lumisantonin (**37**) rather than the regioisomer with a methyl group at the double bond of the bicyclohexenone ring system.[18] On the other hand, photorearrangement of the structurally related 2-methoxy-substituted 2,5-cyclohexadien-1-one **38** gave **39** as major and **40** as minor products.[19]

Electronic effects on photorearrangements of **36** and **38** might be overshadowed by effects resulting from the fused cyclohexanone ring. A more relevant example was described by Kropp, who found that the 2,5-dimethyl-2,5-cyclohexadien-1-one **41** photorearranged "predominantly if not exclusively" to bicyclohexenone **42**.[20] However, this example also might be misleading because 3-substituted 2,5-cyclohexadien-1-ones have been shown to photorearrange to the 4-substituted bicyclohexenone (e.g., **3** → **4** and ref 21).

Recently, Broka has reported that irradiation of 2-carbomethoxy-4,4-dimethyl-2,5-cyclohexadien-1-one (**43**) in dioxane solution with a low-pressure mercury-arc lamp (2537 Å) gave bicyclohexenone **44**.[21] The exclusive formation of **44** was thought to be a result of stabilization of the transition state leading to **44** by the carbomethoxy group. Thus, Broka appears to be the first investigator to provide clear evidence suggesting that the 1,4-sigmatropic rearrangement associated with the type A photoreaction is subject to electronic substituent effects. It is noteworthy that **11** with an electron-withdrawing group at C(4) and **43** with two electron-donating groups at C(4) both display the same type of regioselectivity in the type A photorearrangement.

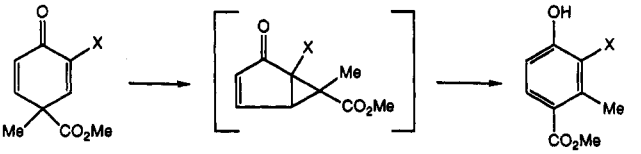
There do not appear to be any reported examples of photorearrangements of 2-cyano-substituted 2,5-cyclohexadien-1-ones.[22] However, the photolysis of 2-formyl-



4,4-dimethyl-2,5-cyclohexadien-1-one in 45% acetic acid in water occurs with incorporation of water; irradiations in aprotic solvents, which might have been expected to produce bicyclo[3.1.0]hexenones, were not reported.[23a] Pirrung and Nunn have suggested that protonated zwitterionic intermediates are responsible for the high regioselectivity observed for photorearrangements of quinone ethylene monoketals in glacial acetic acid.[23b]

The 2-Methoxy and 2-Methyl Substituents. The literature examples do not satisfactorily demonstrate the effect of electron-donating substituents at C(2) of the cyclohexadienone ring. For this reason, we prepared and studied the photochemistry of 2-methoxy- and 2-methyl-2,5-cyclohexadien-1-ones **45a** and **45b**.

Irradiations of **45a** in protic or aprotic solvents resulted in complex product mixtures from which phenol **46** was obtained in low yield. The photorearrangement of 2-methyl-2,5-cyclohexadien-1-one **45b** also was complicated, but phenol **31** could be obtained in 41% isolated yield from irradiation of **45b** in methanol.



45a, X = OMe
b, X = Me

27b, X = OMe
c, X = Me

46, X = OMe
31, X = Me

The formation of phenols **46** and **31** requires the intermediacy of bicyclohexenones **27b** and **27c** (isolated). Thus, electron-releasing substituents at C(2) of the 2,5-cyclohexadien-1-one also facilitate formation of the C(1) substituted bicyclohexenone. The complexity of photoreactions of **45a** and **45b** appears to be the result of the

(15) (a) Zimmerman, H. E.; Crumrine, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 5612. (b) Brennan, T. M.; Hill, R. K. *J. Am. Chem. Soc.* **1968**, *90*, 5614. (c) Zimmerman, H. E.; Crumrine, D. S.; Dopp, D.; Huyffer, P. S. *J. Am. Chem. Soc.* **1969**, *91*, 434.

(16) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.

(17) For a recent study of the effect of substituents on rates of Claisen rearrangements with references to earlier work, see: Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.

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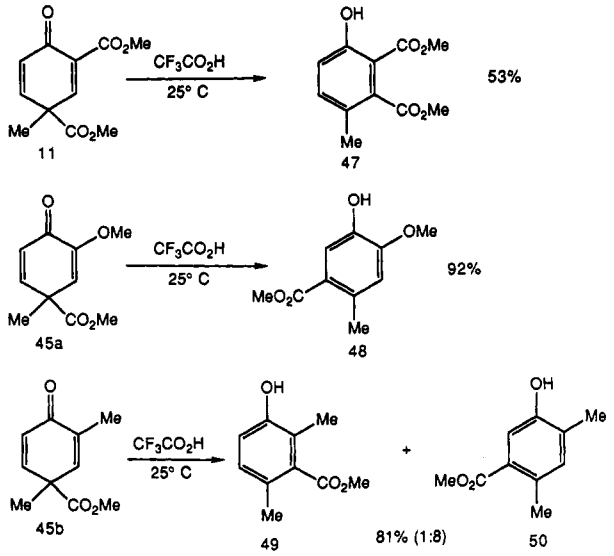
Scheme V



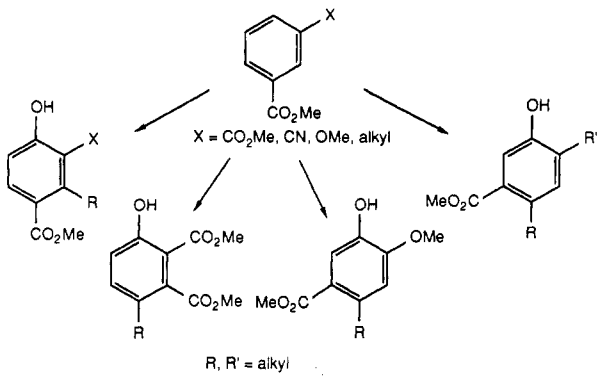
availability of more than one pathway for photorearrangement of intermediate bicyclohexenones **27b** and **27c**.[24] Indeed, 6-carbomethoxy-5,6-dimethyl-2,4-cyclohexadien-1-one was isolated in ~10% yield from irradiation of **45b** in benzene solution. The cyclohexadienone presumably arises from photorearrangement of the intermediate bicyclohexenone **27c** to a diene ketene,[24b] followed by thermal electrocyclization of the diene ketene.

It is noteworthy that the type A intermediate has been assigned both zwitterionic and biradical character.[25] The substituent effects described in this study currently provide no new information that would support one representation over the other. The effect of substituents at C(2) and C(4) of the starting 2,5-cyclohexadienone on the rates of rearrangement of the type A intermediate should be examined; however, photokinetic studies are beyond the scope of the present investigation.

Acid-Catalyzed Dienone–Phenol Rearrangements. Rearrangements of 4-alkyl-4-carboalkoxy-2,5-cyclohexadien-1-ones in trifluoroacetic acid have been shown to result in migration of the carboalkoxy group in preference to simple alkyl substituents.[26] It has been suggested that back-donation of electron density from the π-bond of the carbonyl group is primarily responsible for the high migration tendency of the carboalkoxy group; however, the regioselectivity of the rearrangement has not been investigated.[27].

Treatment of the 2-carbomethoxy-2,5-cyclohexadienone **11** with trifluoroacetic acid at room temperature provided the phthalic diester **47** (Scheme V). By contrast, the 2-methoxy derivative **45a** underwent acid-catalyzed rearrangement of the carbomethoxy group to C(5) to give the benzoic ester **48** in 92% yield. With the less electron releasing methyl substituent at C(2), **45b** rearranged in both directions to give **49** and **50** in a ratio of 1:8. Regioselectivities appear to be dependent upon the relative stabilities of the carbocations generated from carbomethoxy group rearrangement to either C(3) or C(5) of the carbonyl protonated 2,5-cyclohexadienone.

Scheme VI



Conclusion

Methodology for the conversion of 3-substituted benzoic esters to each of the substituted phenols shown in Scheme VI has been described. Although we have reported examples with only methyl groups as alkyl substituents on the target aromatic ring, it is expected that the methodology can be extended to include a wide range of alkyl-substituted analogues. The reductive alkylation step is quite general, and the carbomethoxy group has a considerably greater migration tendency than primary alkyl substituents in both the photochemical and acid-catalyzed dienone–phenol rearrangements.

Experimental Section

General Procedures. Analytical and preparative TLC were performed on silica gel F-254 plates. Ether and THF were distilled from benzophenone sodium ketyl under nitrogen in a standing still. Ethyl acetate and hexane were distilled from CaH_2, while all other solvents were of reagent grade. ^1H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, employing $CDCl_3$ as solvent. Carbon chemical shifts are denoted as "e" (none or two protons) or "o" (one or three protons), as determined from the APT pulse sequence.[28] IR spectra were recorded as $CHCl_3$ solutions unless otherwise noted. Mass spectra were obtained on a GC/MS system using chemical ionization (isobutane). Ultraviolet spectra were recorded in EtOH solvent. Photoreactions were conducted as previously described.[1a]

Dilithium Isophthalate (7). A mixture of isophthalic acid (20.0 g, 120 mmol), $LiOH{\cdot}H_2O$ (10.1 g, 241 mmol), and MeOH (100 mL) was stirred at ambient temperature for 40 min. The MeOH was evaporated, and the residue was dried by benzene azeotrope (3 × 50 mL) and then high vacuum to afford a colorless solid. ^1H NMR (DMSO-d_6): δ 8.44 (s, 1 H), 7.81 (d, J = 7.5 Hz, 2 H), 7.14 (t, J = 7.5 Hz, 1 H).

Dimethyl 1-Methyl-2,5-cyclohexadiene-1,3-dicarboxylate (9). To a mechanically stirred slurry of dilithium isophthalate **7** (0.199 g, 1.18 mmol), t-BuOH (105 μL, 1.11 mmol), and THF (5.0 mL) at −78 °C under N_2 was condensed NH_3 (ca. 20 mL). Potassium (0.121 g, 3.10 mmol) was added to the resultant nearly homogeneous solution; a deep-green coloration formed quickly. After 60 min piperylene was added until the green color turned to yellow. Stirring was continued for an additional 10 min, after which MeI (83 μL, 1.3 mmol) was added. After an additional 60 min, the cooling bath was removed, and the reaction mixture was allowed to warm to ambient temperature while exposed to the atmosphere. After the NH_3 evaporated, the residue was diluted with 5% HCl (50 mL) and extracted with EtOAc (3 × 20 mL).

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The combined organic extracts were dried ($MgSO_4$), and ethereal CH_2N_2 was added until N_2 evolution ceased and the yellow coloration persisted. Excess CH_2N_2 was quenched by addition of glacial HOAc. Evaporation of solvents afforded **9** as an oil. Chromatography (4 g of silica gel, 10% EtOAc/hexanes) gave **9**, 0.336 g, 0.636 mmol, 54%, containing ~5% of **10**. IR (film): 1770 (ester C=O), 1720 (vinyl ester C=O), 1677 (C=C), 1638 (vinyl ester C=C). ^1H NMR: δ 6.98 (m, 1 H), 5.88 (m, 1 H), 5.70 (m, 1 H), 3.78 (s, 3 H), 3.72 (s, 3 H), 2.92 (m, 2 H), 1.41 (s, 3 H). ^{13}C NMR: δ 173.50 (e), 166.29 (e), 138.08 (o), 127.02 (e), 126.79 (o), 123.68 (o), 51.82 (o), 51.15 (o), 44.83 (e), 26.24 (o), 24.93 (e). CIMS: 211 ($M^+ + 1$). An acceptable combustion analysis for **9** could not be obtained.

Dimethyl 1-Methyl-4-oxo-2,5-cyclohexadiene-1,3-dicarboxylate (11). To a vigorously stirred slurry of **9** (2.92 g, 13.9 mmol), PDC (20.9 g, 55.6 mmol), Celite (2.9 g), and benzene (65 mL) was added *t*-BuOOH (6.2 mL of a 90% solution in 1:1 *t*-BuOH/H_2O, 56 mmol). After stirring for 22 h, the mixture was filtered, and the filter cake was washed with ether (3 × 60 mL). The combined filtrates were evaporated to afford **11** as a dark oil. Chromatography (100 g silica gel, 30% to 40% EtOAc/hexanes gradient) gave **11** as an oil, 0.89 g (3.9 mmol, 29%). IR: 1735 (esters), 1670 (dienone C=O), 1640 (vinyl ester C=C). ^1H NMR: δ 7.71 (d, J = 3.0 Hz, 1 H), 7.04 (dd, J = 3.0, 10.2 Hz, 1 H), 6.35 (d, J = 10.2 Hz, 1 H), 3.87 (s, 3 H), 3.78 (s, 3 H), 1.63 (s, 3 H). ^{13}C NMR: δ 180.18 (e), 169.97 (e), 164.38 (e) 153.12 (o), 147.25 (o), 131.46 (e), 129.35 (o), 53.26 (o), 52.24 (o), 48.10 (e), 24.54 (o). UV: 237 nm (ε = 9400). CIMS: 225 ($M^+ + 1$). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 58.78; H, 5.47.

Dimethyl 4-Hydroxy-2-methylbenzene-1,3-dicarboxylate (12). A degassed solution of **11** (33.6 mg, 0.150 mmol) in benzene (3.0 mL) was irradiated through Uranyl glass for 3 h. Evaporation of solvent afforded **12** (33.9 mg) as a solid. Preparative TLC (2.0 mm silica gel, 30% EtOAc/hexane) gave **12** (29.4 mg, 0.131 mmol, 87%). Recrystallization from hexane gave colorless needles, mp 95.5 °C. IR: 3080 (br, OH), 1725 (C=O). ^1H NMR: δ 7.85 (d, J = 8.8 Hz, 1 H), 6.86 (d, J = 8.8 Hz, 1 H), 3.99 (s, 3 H), 3.87 (s, 3 H), 2.71 (s, 3 H). UV: 256 nm (ε = 11 700). CIMS: 225 ($M^+ + 1$). Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.04; H, 5.47.

Lithium 3-Cyanobenzene-1-carboxylate (23). A slurry of 3-cyanobenzoic acid (10.0 g, 68.0 mmol), $LiOH·H_2O$ (2.85 g, 67.9 mmol), and MeOH (50 mL) was stirred until homogeneous (15 min). Solvent evaporation gave a residue that was dried via benzene azeotrope (3 × 20 mL) and then high vacuum to afford **23** as a colorless solid. ^1H NMR (DMSO-d_6): δ 8.38 (d, J = 7.7 Hz, 1 H), 7.66 (d, J = 7.7 Hz, 1 H), 7.45 (t, J = 7.7 Hz, 1 H).

Methyl 3-Cyano-1-methyl-2,5-cyclohexadiene-1-carboxylate (25). To a mechanically stirred solution of Li (0.217 g, 34.0 mmol) in THF (50 mL) and NH_3 (ca. 200 mL) at −78 °C under Ar was added **23** (2.175 g, 14.2 mmol). The mixture rapidly became homogeneous, and a deep green coloration developed. After 10 min *t*-BuOH (1.34 mL, 14.2 mmol) was added. Stirring was continued for 60 min, while Li was added as needed to maintain a deep green coloration. On addition of MeI (1.06 mL, 17.0 mmol) the color faded rapidly. After 60 min of stirring, the cooling bath was removed and the reaction mixture was allowed to warm to ambient temperature while exposed to the atmosphere. The residue was diluted with 5% HCl (100 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and treated with ethereal CH_2N_2. Excess CH_2N_2 was quenched with glacial HOAc. Evaporation of the solvents gave **25** as a dark oil, 2.31 g, which was used without further purification. IR (film): 2220 (CN), 1730 (C=O), 1630 (C=C). ^1H NMR: δ 6.67 (m, 1 H), 5.82 (br s, 2 H), 3.73 (s, 3 H), 2.85 (br s, 2 H), 1.41 (s, 3 H). CIMS: 178 ($M^+ + 1$). Acceptable combustion analysis for **25** could not be obtained. Attempted reduction of **23** with potassium metal followed by treatment with CH_2N_2 gave esterified **23**.

Methyl 1-Methyl-3-cyano-4-oxo-2,5-cyclohexadiene-1-carboxylate (26). Oxidation of **25** as described for the preparation of **11** and chromatography of the product (80 g of silica gel, 20% to 50% EtOAc/hexanes gradient) gave **26** as an oil which solidified on standing (0.966 g, 5.05 mmol, 36% from **23**). Recrystallization from ether/hexanes afforded **26** as prisms, mp 59–60 °C. IR (film): 2240 (CN), 1735 (ester), 1670 (dienone C=O). ^1H NMR: δ 7.82 (d, J = 2.9 Hz, 1 H), 7.19 (dd, J = 2.9, 10.2 Hz, 1 H), 6.40 (d, J = 10.2 Hz, 1 H), 3.82 (s, 3 H), 1.69 (s, 3 H). UV: 240 (ε = 9100), 366 nm (ε = 16.8). CIMS: 192 (89, $M^+ + 1$), 148 (100, $M - CO_2$). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.78; H, 4.75; N, 7.39.

Methyl 3-Cyano-4-hydroxy-2-methylbenzene-1-carboxylate (28). A degassed solution of **26** (0.709 g, 3.71 mmol) in benzene (37.0 mL) was irradiated through Uranyl glass for 21 h, during which time **28** crystallized from the reaction solution. Filtration afforded **28** (0.525 g). Evaporation of the filtrate and chromatography of the residue (8 g of silica gel, 10% to 50% EtOAc/hexanes) afforded additional **28** (17.9 mg; total 0.543 g, 2.84 mmol, 77%). Recrystallization from EtOAc provided analytically pure **28**, mp 250 °C (sealed tube). IR (KBr): 3310 (OH), 2212 (CN), 1676 (C=O). ^1H NMR (DMSO-d_6): δ 11.57 (br s, 1 H), 7.94 (d, J = 8.9 Hz, 1 H), 6.90 (d, J = 8.9 Hz, 1 H), 3.83 (s, 3 H), 2.70 (s, 3 H). UV: 257 (ε = 11 000), 294 nm (ε = 6000). CIMS: 192 ($M^+ + 1$). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.67; H, 4.68; N, 7.24.

When the photolysis of **26** was carried out for shorter periods of time, bicyclohexenone **27** could be isolated as a mixture of diastereomers by chromatography on silica gel. IR: 2258 (CN), 1737 (C=O). ^1H NMR: 7.48 (dd, J = 2.9, 7.8 Hz, 1 H, minor diastereomer), 7.40 (dd, J = 2.8, 5.8 Hz, 1 H, major diastereomer), 6.15 (d, J = 7.8 Hz, 1 H, minor), 5.95 (d, J = 5.8 Hz, 1 H, major), 3.86 (s, 3 H, minor), 3.67 (s, 3 H, major), 3.16 (d, 2 H, both diastereomers), 1.73 (s, 3 H, major), 1.44 (s, 3 H, minor).

Methyl 4-(((Benzyloxy)carbonyl)oxy)-3-cyano-2-methylbenzene-1-carboxylate (29). To a vigorously stirred mixture of **28** (72.0 mg, 0.377 mmol), K_2CO_3 (0.211 g, 1.53 mmol), CH_2Cl_2 (2.0 mL), and water (2.0 mL) was added benzyl chloroformate (1.08 mL, 7.57 mmol). After 22 h the mixture was diluted with CH_2Cl_2 (50 mL), washed with 10% Na_2CO_3 (20 mL), and dried ($MgSO_4$), and the solvents were evaporated to afford 0.12 g of **29**. Chromatography (4 g of silica gel, 30% EtOAc/hexanes) gave pure **29** as a glass (92.7 mg, 0.285 mmol, 76%). Crystallization from CCl_4/hexanes gave plates, mp 79–79.5 °C. IR: 2245 (CN), 1782 (carbonate), 1740 (ester). ^1H NMR: δ 8.06 (d, J = 8.9 Hz, 1 H), 7.39 (m, 5 H), 6.86 (d, J = 8.9 Hz, 1 H), 5.25 (s, 2 H), 3.87 (s, 3 H), 2.81 (s, 3 H). CIMS: 326 (31, $M^+ + 1$), 248 (28, $M - C_6H_6$), 192 (100, $M - PhCH_2OCO$). Anal. Calcd for $C_{18}H_{15}NO_5$: C, 66.45; H, 4.65; N, 4.31. Found: C, 66.42; H, 4.69; N, 4.23.

Methyl 3-(Aminomethyl)-4-(((benyloxy)carbonyl)oxy)-2-methylbenzene-1-carboxylate (30). To a vigorously stirred slurry of **29** (0.105 g, 0.324 mmol) and $CoCl_2·6H_2O$ (0.154 g, 0.647 mmol) in MeOH (5.0 mL) under Ar was added $NaBH_4$ (0.1218 g, 3.22 mmol); vigorous gas evolution, a mild exotherm, and black precipitate resulted. After being stirred for 20 min, the reaction mixture was quenched by addition of 5% HCl (5 mL), followed by dilution with water (50 mL) and concentrated NH_4OH (3 mL) and then extraction with EtOAc (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), and the solvents were evaporated to afford 68 mg of **30**. Chromatography (4 g silica gel, 30% EtOAc/hexanes) gave **30** as a solid (41.5 mg, 0.126 mmol, 39%). Recrystallization from EtOAc/hexanes gave tiny needles, mp 171.5–172 °C. IR (KBr): 3330 (NH), 1705 (C=O). ^1H NMR: δ 9.28 (br s, 1 H), 7.78 (d, J = 8.8 Hz, 1 H), 7.34 (s, 5 H), 6.85 (d, J = 8.8 Hz, 1 H), 5.56 (br s, 1 H), 5.12 (s, 2 H), 4.40 (d, J = 6.6 Hz, 2 H), 3.84 (s, 3 H), 2.57 (s, 3 H). CIMS: 330 (100, $M^+ + 1$), 222 (83, $M - PhCH_2OH$), 91 (64, C_7H_7). Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.71; H, 5.85; N, 4.26.

Methyl 2,3-Dimethyl-4-hydroxybenzene-1-carboxylate (31). A stirred slurry of **30** (33.7 mg, 0.102 mmol) and 5% Pd/C (16.1 mg) in EtOH (2.0 mL) was hydrogenated at 1 atm for 19 h. Filtration and evaporation of the filtrate afforded **30**, which was purified by chromatography (4 g silica gel, 30% EtOAc/hexanes) to give **30** as a solid (5.5 mg, 30 μmol, 30%). Recrystallization from toluene afforded needles, mp 155–156 °C. IR: 3315 (br, OH), 1710 (C=O). ^1H NMR: δ 7.64 (d, J = 8.5 Hz, 1 H), 6.65 (dd, J = 8.5 Hz, 1 H), 5.28 (br s, 1 H), 3.86 (s, 3 H), 2.52 (s, 3 H), 2.20 (s, 3 H). UV: 261 nm (ε = 11 000). CIMS: 181 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.71; H, 6.75.

Methyl 3-Methoxy-1-methyl-4-oxo-2,5-cyclohexadiene-1-carboxylate (45a). To a stirred solution of methyl 3-methoxy-

benzene-1-carboxylate (5.00 g, 30.0 mmol) and *t*-BuOH (2.85 mL, 30.2 mmol) in THF (50 mL) and NH_3 (ca. 200 mL) at −78 °C under N_2 was added potassium as needed to maintain a deep-blue coloration for 15 min. MeI (5.6 mL, 90 mmol) was added; stirring was continued for an additional 45 min, after which the cooling bath was removed and the reaction mixture was allowed to warm to ambient temperature while exposed to the atmosphere. The residue was diluted with ether (100 mL), washed with water (20 mL) and saturated Na_2CO_3 (20 mL), and then dried ($MgSO_4$). Evaporation of the solvents afforded an oil (4.89 g, 26.8 mmol, 89%), sufficiently pure for further use. ^1H NMR: δ 5.75 (m, 2 H), 4.73 (s, 1 H), 3.68 (s, 3 H), 3.58 (s, 3 H), 2.70 (m, 2 H), 1.37 (s, 3 H).

To a vigorously stirred slurry of the oil (2.92 g, 13.9 mmol) in benzene (65 mL) was added PDC (20.9 g, 56 mmol), Celite (2.9 g), and *t*-BuOOH (6.2 mL of a 90% solution in 1:1 *t*-BuOH/H_2O, 55.8 mmol). After being stirred for 22 h the mixture was filtered through Celite, and the filter cake was washed with ether (3 × 60 mL). The combined filtrates were evaporated to afford **45a** as a dark oil, 3.08 g. Chromatography (100 g silica gel, 30% to 40% EtOAc/hexanes gradient) gave an oil (0.89 g, 4.0 mmol, 29%), which was further purified by Kugelrohr distillation at 45 °C (0.7 mmHg). IR (film): 1745 (ester), 1672 (dienone C=O), 1642 (C=C), 1612 (C=$COCH_3$). ^1H NMR: δ 7.08 (dd, *J* = 2.6, 10.0 Hz, 1 H), 6.34 (d, *J* = 10.0 Hz, 1 H), 5.97 (d, *J* = 2.6 Hz, 1 H), 3.75 (s, 3 H), 3.72 (s, 3 H), 1.61 (s, 3 H). ^{13}C NMR: δ 179.33 (e), 171.84 (e), 151.72 (e), 148.70 (o), 128.78 (o), 116.22 (o), 54.42 (o), 52.62 (o), 48.61 (e), 25.53 (o). UV: 242 (ε = 9500), 366 nm (ε = 5.0). CIMS: 197 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 60.98; H, 6.01.

Methyl 1,3-Dimethyl-4-oxo-2,5-cyclohexadiene-1-carboxylate (45b). To a mechanically stirred solution of *m*-toluic acid (4.00 g, 29.4 mmol) in NH_3 (ca. 200 mL) at −78 °C under Ar was added lithium (0.75 g, 120 mmol). After 20 min MeI (7.3 mL, 120 mmol) was added, and stirring was continued for an additional 10 min. The cooling bath was removed, and the NH_3 was allowed to evaporate. The residue was diluted with 5% HCl (200 mL), concentrated HCl until pH ~2, and then extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with saturated Na_2SO_3 (50 mL) and dried ($MgSO_4$), and the solvents were evaporated to afford a pale yellow oil (3.74 g, 22.5 mmol, 77%). IR (film): 1735 (C=O). ^1H NMR: δ 5.70 (m, 2 H), 5.47 (m, 1 H), 3.68 (s, 3 H), 2.57 (m, 2 H), 1.74 (s, 3 H), 1.30 (s, 3 H).

To a vigorously stirred slurry of the oil (3.60 g, 21.7 mmol) in benzene (110 mL) was added PDC (32.6 g, 87 mmol), Celite (7.2 g), and *t*-BuOOH (9.6 mL of a 90% solution in 1:1 *t*-BuOH/H_2O, 86.3 mmol). Workup as described for **45a** gave **45b** as a yellow oil (2.84 g, 15.8 mmol, 73%). The analytical sample was obtained by Kugelrohr distillation at 40 °C (3.5 mmHg). IR (film): 1735 (C=O). ^1H NMR: δ 5.70 (m, 2 H), 5.47 (m, 1 H), 3.68 (s, 3 H), 2.57 (m, 2 H), 1.74 (s, 3 H), 1.30 (s, 3 H). UV: 243 (ε = 12000), 366 nm (ε = 10.0). CIMS: 181 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.61; H, 6.75.

Methyl 4-Hydroxy-3-methoxy-2-methylbenzene-1-carboxylate (46). A solution of **45a** (39.9 mg, 0.203 mmol) in benzene (4.1 mL) was degassed with N_2 for 10 min and irradiated through Uranyl glass for 19 h. Evaporation of the solvent and preparative TLC of the residue (0.5 mm silica gel, 50% EtOAc/hexanes) afforded **46** (2.8 mg, 14 mmol, 7%). ^1H NMR: δ 7.71 (d, *J* = 8.4 Hz, 1 H), 6.83 (d, *J* = 8.4 Hz, 1 H), 6.02 (s, 1 H), 3.88 (s, 3 H), 3.80 (s, 3 H), 2.67 (s, 3 H).

Irradiation of 45b. A degassed solution of **45b** (55.8 mg, 0.310 mmol) in benzene (6.2 mL) was irradiated through Uranyl glass for 2 h. Evaporation of the solvent and preparative TLC of the residue (0.5 mm silica gel, 30% EtOAc/hexanes, developed twice) afforded two compounds.

The most mobile material was **31** (7.2 mg, 40 μmol, 13%), identical (NMR, TLC) with material prepared from **30**.

The least mobile fraction contained **27c** (obtained as a single diastereomer, 4.1 mg, 23 μmol, 7.3%). ^1H NMR: δ 7.43 (dd, *J* = 5.7, 2.6 Hz, 1 H), 5.80 (d, *J* = 5.7 Hz, 1 H), 3.61 (s, 3 H), 2.30 (d, *J* = 2.6 Hz, 1 H), 1.46 (s, 3 H), 1.43 (s, 3 H).

A degassed solution of **45b** (50.5 mg, 0.280 mmol) in MeOH (5.6 mL) when irradiated through Uranyl glass for 22 h followed by preparative TLC (0.5 mm silica gel, 30% EtOAc/hexanes) gave **31** (20.7 mg, 0.115 mmol, 41%).

Dimethyl 3-Hydroxy-6-methylbenzene-1,2-dicarboxylate (47). A solution of **11** (15.6 mg, 69.5 μmol) in CF_3CO_2H (1.0 mL) under Drierite was stirred for 22 h at ambient temperature. Evaporation of the solvent and preparative TLC of the residue (2.0 mm silica gel, 50% EtOAc/hexane) gave **47** (10.6 mg, 53%). Crystallization (hexanes) afforded **47** as tiny prisms, mp 66 °C. IR: 1738 (ester). ^1H NMR: δ 10.78 (s, 1 H), 7.30 (d, *J* = 8.4 Hz, 1 H), 6.97 (d, *J* = 8.4 Hz, 1 H), 3.92 (s, 3 H), 3.90 (s, 3 H), 2.21 (s, 3 H). UV: 219 (ε = 14000), 318 nm (ε = 4900). CIMS: 225 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 60.98; H, 6.01.

Methyl 5-Hydroxy-4-methoxy-2-methylbenzene-1-carboxylate (48). Dienone–phenol rearrangement (CF_3CO_2H, 3 h) of **45b** gave **48** as a colorless solid (31.5 mg, 0.161 mmol, 92%). Recrystallization from benzene/hexanes afforded tiny prisms, mp 104 °C. IR: 3542 (OH), 1708 (C=O). ^1H NMR: δ 7.53 (s, 1 H), 6.68 (s, 1 H), 5.52 (s, 1 H), 3.92 (s, 3 H), 3.85 (s, 3 H), 2.56 (s, 3 H). CIMS: 197 (100, $M^+ + 1$), 165 (17, $M^+ + 1 - CH_3OH$). Anal. Calcd for $C_{10}H_{12}O_3$: C, 61.21; H, 6.17. Found: C, 60.91; H, 6.25.

Methyl 2,6-Dimethyl-3-hydroxybenzene-1-carboxylate (49) and Methyl 2,4-Dimethyl-5-hydroxybenzene-1-carboxylate (50). Dienone–phenol rearrangement (CF_3CO_2H, 17 h) of **45b** gave a mixture of **49** and **50**. This mixture was subjected to chromatography (4 g of silica gel, 10% to 20% EtOAc/hexanes gradient) to afford 40.1 mg (0.223 mmol, 81%) of **49** and **50** (1:8 by ^1H NMR spectroscopy). Separation was achieved by fractional crystallization from hexane, which afforded **50** (mp, IR, ^1H NMR agreed with previously reported values).[29] The mother liquor was enriched in **49**, but could not be obtained free of **50**. ^1H NMR: δ 6.88 (d, *J* = 8.0 Hz, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 3.92 (s, 3 H), 2.21 (s, 3 H), 2.18 (s, 3 H).

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Supplementary Material Available: ^1H NMR spectra of **7**, **23**, **27**, **27c**, **46**, **49**, and **50** (7 pages). Ordering information is given on any current masthead page.

(29) Newman, M. S.; Chung, H. M. *J. Org. Chem.* **1974**, *39*, 1036.