structures is supported by the subsequent radical combination reactions, which afford the 1:1 adducts 3 and the dihydro dimers 5, as well as the 2:1 adducts 6. It is likely that 6 is formed as a secondary product from interaction of CH triplets with 3, but we have no direct evidence to require this mechanism.

There is clearly competition between TEA and ground-state enone for interception of monomeric CH triplets. Increasing the enone concentration favors the photodimerization pathway, while increasing the TEA concentration favors the electron-transfer pathway. Thus, all the primary products formed in this model system arise from monomeric triplet states of cyclohexenone.

Experimental Section

Materials. 2-Cyclohexenone (Aldrich, 99+%) was fractionally distilled under vacuum before use and showed no extraneous peaks in the gas chromatogram. Triethylamine (Aldrich, 99+%) was purified before use by reflux over NaOH and distillation. Acetonitrile (Aldrich, anhydrous, 99+%) was freshly purified before use by heating to reflux over sodium hydride and then distillation from sodium hydride.

Ultraviolet Irradiations. Solutions in Pyrex test tubes sealed with rubber septa were purged with Argon for 8 min and then irradiated in a Rayonet Reactor (New England Ultraviolet Co.) equipped with blacklight lamps whose output is centered at 350 nm. The reactor is equipped with a cooling fan which keeps the temperature at 30–35 °C. When more than one sample needs to be irradiated simultaneously, a rotating turntable ("merry-go-round") is utilized.

Gas Chromatography. All GC analyses were carried out on a Hewlett-Packard Model 5890 gas chromatography equipped with an HP 3396A integrator. Detection was by flame ionization. The capillary column used in all analyses was an Alltech no. 932530 Heliflex RSL-150 column, 30 m × 0.25 mm, with a maximum allowable temperature of 330 °C. The following temperature program was utilized: initial column temperature 100 °C, final column temperature 290 °C, temperature ramp 8 °C/min, injection port 250 °C. Most analyses were carried out in duplicate or triplicate, using dodecane as an internal standard.

Gas chromatography/mass spectral analysis was carried out an HP 5992 GC/MS system equipped with a 20 × 0.25 mm cross-linked methylsilica column. Additional analyses were carried out on a GC/MS system at Columbia University consisting of an HP gas chromatograph, HP5988 mass selective detector, and HP 9216 work station.

Column chromatography of mixtures after irradiation was carried out on silica gel columns using various proportions of hexane and ethyl acetate to isolate the photoproducts.

Preparative-scale thin-layer chromatography of irradiation mixtures after concentration and removal of TEA by extraction was carried out on Alltech silica gel GF plates using a mixture of 95% chloroform/5% ethyl acetate to isolate the photoproducts.

NMR Spectra. ^1H and ^{13}C NMR spectra were obtained on a GE-Nicolet QE-300 300-MHz NMR spectrometer. All spectra were obtained in deuteriochloroform.

Synthesis of 3-(3-Oxocyclohexyl)cyclohexanone (5). The method of Cahiez and Alami was utilizied.[16] Anhydrous tetrahydrofuran (THF) from Aldrich was dried over lithium aluminum hydride and distilled under nitrogen immediately prior to use. Dry THF (10 mL) was added to 1.2 g (0.1 mol) of magnesium turnings. Isopropyl chloride (5.5 mL, 0.06 mol) was dissolved in anhydrous THF, and 3 mL of this soln. was added dropwise to the Mg suspension with stirring. A few drops of 1,2-dibromoethane was added to initiate formation of the Grignard reagent. In a separate apparatus, 3.17 g (0.025 mol) of manganese chloride in 50 mL of THF was stirred for 15 min under nitrogen. The Grignard reagent was added to the $MnCl_2$ suspension using a canula under nitrogen, and the mixture was stirred for 5 min. To this was slowly added 4.96 g (0.05 mol) of 2-cyclohexenone, and the mixture was then stirred at room temperature for 30 min. The reaction mixture was neutralized with 0.5% HCl and then extracted with ether. The extracts were concentrated under vacuum, and the resulting oil was subjected to GC analysis. This analysis demonstrated the presence of only two set of peaks: one peak due to unreacted starting materials and two with retention times identical with the photoproducts concluded to result from reductive dimerization of CH on the basis of MS data.

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A General Synthetic Route to Isobenzofurans Bearing a Functionalized C-1 Substituent

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Aromatic *o*-formyl acetals undergo base-catalyzed Claisen–Schmidt condensation with nitro compounds, ketones, methyl acetate, and acetonitrile to produce functionalized styrenes. Hydrolysis of the acetal and cyclization of the product in methanol provide methoxy phthalans **8** which are used to generate isobenzofurans bearing a functionalized substituent at C-1. The Diels–Alder reactions of these isobenzofurans with several dienophiles have been studied. Conjugated exo-methylene phthalans **20** have been isolated, and an unusual elimination of nitrous acid from nitroalkyl phthalans **8E** and **8F** has been observed.

The last decade has witnessed rapid advances in the chemistry of isobenzofuran (IBF).[1,2] Many versatile routes for IBF generation have been devised, and multisubstituted IBF's have been employed in the synthesis of aromatic and hydroaromatic natural products.[2] Our continuing interest in this area has led us to seek methods that will further broaden the utility of IBF in synthesis. To this end, we have directed our efforts at developing a general procedure for the production of IBF's with C-1 substituents bearing various common functional groups that can be manipulated in a synthetically useful manner. We now report the results of these investigations.

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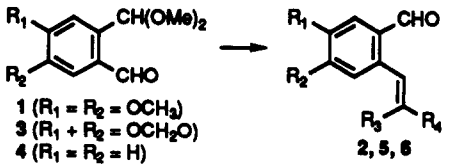
0022-3263/91/1956-1882$02.50/0

Table I. The Claisen-Schmidt Reaction of Aromatic *o*-Formyl Acetals



1 ($R_1 = R_2 = OCH_3$)
3 ($R_1 + R_2 = OCH_2O$)
4 ($R_1 = R_2 = H$)

2, 5, 6

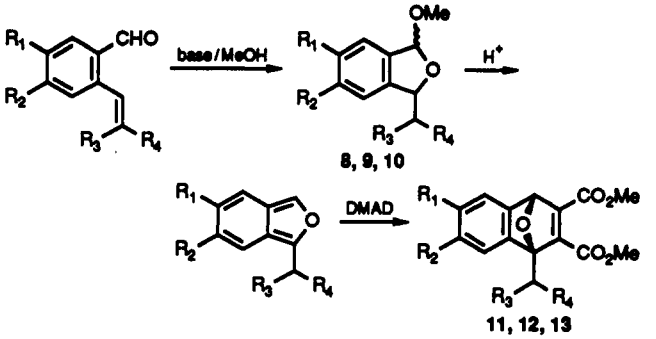
acetal	reagent	product	yield (%)
1	CH_3CO_2Me	**2A**: $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = CO_2Me$	59
3	CH_3CO_2Me	**5**: $R_1 + R_2 = OCH_2O$; $R_3 = H$; $R_4 = CO_2Me$	61
4	CH_3CO_2Me	**6**: $R_1 = R_2 = R_3 = H$; $R_4 = CO_2Me$	65
1	Me_2CO	**2B**: $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = COMe$	51
1	5-hexen-2-one	**2C**: $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = CO(CH_2)_2CH{=}CH_2$	42
1	CH_3CN	**2D**: $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = CN$	73
1	$CH_3CH_2NO_2$	**2E**: $R_1 = R_2 = OMe$; $R_3 = Me$, $R_4 = NO_2$	30

Aromatic *o*-formyl dimethyl acetals, previously used to generate IBF's by Grignard addition to the free aldehyde and subsequent hydrolysis,[3,4] were chosen as the starting materials. Many useful functional groups could not be accommodated in the C-1 substituent of the IBF's prepared by that method because of their incompatibility with the Grignard conditions. Two later methods[5,6] involving reactions of organometallic reagents with the carbonyl group of phthalides also provided similar IBF's, but again their scope was limited in a similar fashion. In the present work we wished to incorporate carbonyl, cyano, and nitro groups in the substituent and therefore planned to react the free aldehyde of the starting material with the requisite substrate in a base-catalyzed Claisen–Schmidt process to produce the respective functionalized styrenes, which could subsequently be cyclized to the methoxy phthalan precursors of the 1-substituted IBF's.

In practice, three different acetals (**1**, **3**, and **4**) were used as starting materials, but the bulk of the work was conducted with the dimethoxy derivative **1** prepared in the usual manner[3] from 6-bromoveratraldehyde. These acetals were reacted with the various substrates under base catalysis to provide the *o*-formyl styrenes **2A–E**, **5**, and **6** in moderate yields as shown in Table I. The reaction of **1** with nitroethane was best performed with ammonium acetate.[7] Extensive decomposition resulted under other conditions but nitromethane reacted with **1** in aqueous sodium hydroxide to provide the nitro alcohol **7**. The latter was converted into the IBF precursor, the methoxy phthalan **8F** in 51% overall yield with acetic acid and methanol. Styrenes **2**, **5**, and **6** can also be obtained directly from the *o*-bromo aldehydes by Heck arylation. We have prepared **2A** in this way but find that the two-step procedure through the *o*-formyl acetals is more general and gives better yields.

In the second step, the styrenes **2**, **5**, and **6** in methanol solution were cyclized with a catalytic quantity of base (potassium carbonate for **2A**, **2D**, **5**, and **6**, sodium acetate for the others) at room temperature to provide diastereomeric mixtures of the corresponding methoxy phthalans **8**, **9**, and **10** all bearing a functionalized C-1 substituent and all useable without purification for IBF generation (accomplished in the usual manner[2] with glacial acetic acid in the presence of the dienophile). The efficiency of the IBF synthesis was initially evaluated with dimethyl acetylenedicarboxylate (DMAD) as the dienophile to provide adducts **11**, **12**, and **13** with the results shown in Table II. In two instances the initial adduct suffered aromatization under the conditions of the reaction, and naphthols **14B** and **14F** were the isolated products. The nitro-substituted phthalans were generally poor substrates in this reaction. The primary nitro derivative **8F** only gave a 33% yield of the naphthol while the secondary **8E** and tertiary **15** (vide infra) suffered extensive decomposition under the acidic conditions of IBF generation.

Table II. The Diels–Alder Reactions of C-1 Substituted Isobenzofurans with Dimethyl Acetylenedicarboxylate



8, 9, 10

11, 12, 13

o-formyl-styrene	methoxy phthalan	adduct	overall yield, %
2A	**8A** ($R_1 = R_2 = OMe$; $R_3 = H$; $R_4 = CO_2Me$)	11A	65
5	**9** ($R_1 + R_2 = OCH_2O$; $R_3 = H$; $R_4 = CO_2Me$)	12	67
6	**10** ($R_1 = R_2 = R_3 = H$; $R_4 = CO_2Me$)	13	63
2B	**8B** ($R_1 = R_2 = OMe$; $R_3 = H$, $R_4 = COMe$)	14B[a]	43
2C	**8C** ($R_1 = R_2 = OMe$; $R_3 = H$, $R_4 = CO(CH_2)_2CH{=}CH_2$)	11C	47
2D	**8D** ($R_1 = R_2 = OMe$; $R_3 = H$; $R_4 = CN$)	11D	61
2E	**8E** ($R_1 = R_2 = OMe$; $R_3 = Me$; $R_4 = NO_2$)	–	–
–	**8F** ($R_1 = R_2 = OMe$; $R_3 = H$; $R_4 = NO_2$)	14F[a]	33
–	**8G** ($R_1 = R_2 = OMe$; $R_3 = Me$; $R_4 = CH_2CH_2CO_2Me$)	11G	16

[a] The adduct isomerized to corresponding naphthols **14**.

A possible source of the problem was uncovered with the finding that both **8E** and **8F** were converted to the *o*-formyl ketones **16** and **17** in 22 and 31% yield, respectively, when refluxed in benzene with a catalytic quantity of glacial acetic acid. The products of this reaction, as well as the problems with the Diels–Alder reaction just mentioned, can be accounted for by the elimination of nitrite ion from the isobenzofurans **18**. The resulting oxonium ions lead to the ketones **16** and **17**. The lack of any Diels–Alder adducts from the α-branched examples of **18** (when R_1 and/or R_2 are not hydrogen) implies that they are sufficiently crowded to retard Diels–Alder additions especially when alternative reaction pathways are available. The elimination of nitrous acid evidently requires that the IBF, or at least its cyclic oxonium ion precursor, be formed. The nitro alcohol **19** merely dehydrates to the nitrostyrene

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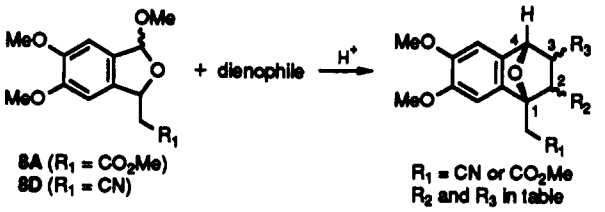
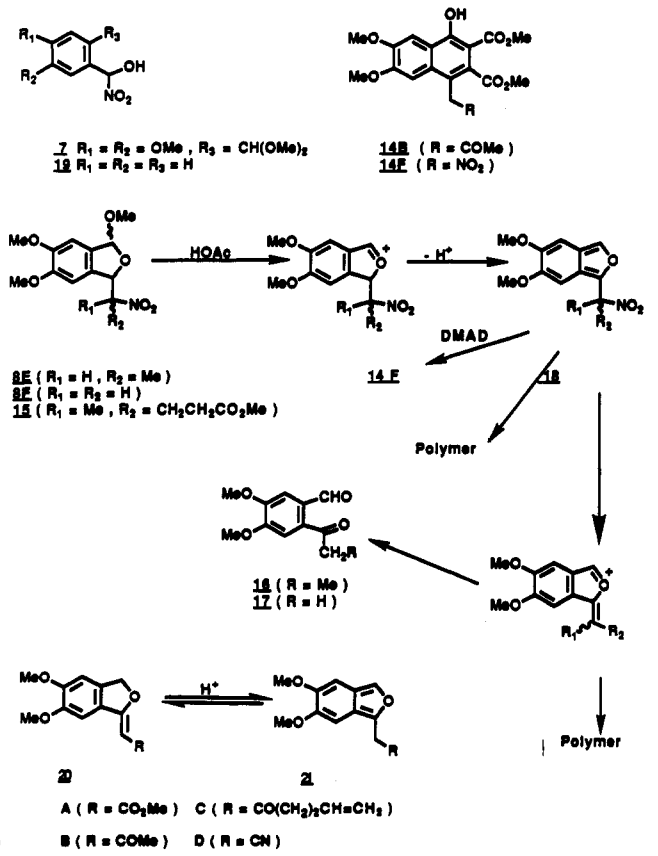
(7) Butterick, J. R.; Unrau, A. M. *J. Chem. Soc., Chem. Commun.* **1974**, 307–8.

Table III. Diels–Alder Reactions with Olefinic Dienophiles



phthalan	dienophile	adduct (ratio) ortho (endo:exo)	adduct (ratio) meta (endo:exo)	total yield, %
8D	dimethyl maleate	(20:1) **22**: $R_2 = R_3 = CO_2Me$	–	59
8D	dimethyl fumarate	(7.8:1) **23**: R_2 = *endo*-CO_2Me; R_3 = *exo*-CO_2Me	–	61
8D	acrolein	(4.5:1.5) **24**: R_2 = CHO; R_3 = H	(1:0) **25**: R_2 = H; R_3 = CHO	56
8D	methyl vinyl ketone	(2.6:2) **26**: R_2 = COMe; R_3 = H	(1:0) **27**: R_2 = H; R_3 = COMe	61
8D	methyl acrylate	(7:3.5) **28**: $R_2 = CO_2Me$; R_3 = H	(2:1) **29**: R_2 = H; $R_3 = CO_2Me$	63
8A	methyl acrylate	(6:3) **30**: $R_2 = CO_2Me$; R_3 = H	(1.5:1) **31**: R_2 = H; $R_3 = CO_2Me$	53
8A	acrylonitrile	(3:1) **32**: R_2 = CN; R_3 = H	–	67
8A	methyl vinyl ketone	(3:1.5) **33**: R_2 = COMe; R_3 = H	(2:0) **34**: R_2 = H; R_3 = COMe	62

and does not form acetophenone when treated with acid. Phthalan **8E** subjected to Michael addition with methyl acrylate and Triton B produced **15**, which was denitrated[8] with tri-*n*-butyltin hydride and AIBN to a complex diastereomeric mixture of phthalans **8G** (Table II). The IBF derived from the latter is α-branched but lacks the nitro group; a low overall yield of the DMAD adduct **11G** was obtained, lending credence to the rationalization above. Furthermore, the modest success of the reaction demonstrates that chemical manipulation of the substituent of an IBF precursor is possible in principle, provided that acidic conditions which affect the methoxy phthalan, are avoided.



When methoxy phthalans **8A–D** were refluxed in benzene with glacial acetic acid in the absence of a dienophile low yields (25–31%) of substituted methylene phthalans **20A–D** were isolated as pure crystalline materials (probably the *Z* isomers as shown). Alkylidene phthalans are notoriously unstable[5] in acid because of equilibration to the corresponding IBF. The stability of these phthalans is probably due to conjugation with the carbonyl and cyano groups and parallels the moderate stability recognized before[9] in the aryl derivatives (R = phenyl, naphthyl). We find, in common with the earlier reports,[5,9] that **20A–D** react with DMAD to provide the expected Diels–Alder adducts of IBF's **21A–D** under catalysis with glacial acetic acid.

Methoxy phthalans **8A** and **8D** were also used to generate IBF's for reaction with doubly bonded dienophiles both symmetrical and unsymmetrical (Table III). With dimethyl maleate and fumarate the cyano phthalan **8D** gave mainly endo adducts. The ratios were estimated by comparison of the H-4 signals in the ^1H NMR spectra of the mixtures (doublet when C-3 ester is endo, singlet when ester is exo). With the unsymmetrical dienophiles regioisomeric mixtures were produced but the ortho adduct predominated in every case and the endo adduct was favored over the exo in each set. The ratios were again estimated from integration of the H-4 signals and in the case of the acrolein adducts **24** and **25** the signals of the aldehyde protons of three isomers were also sufficiently separated for reliable integration. The Diels–Alder reactions of IBF with dienophiles other than maleic anhydride are not reversible[1,2] under the mild conditions used and moreover the results in Table III bear a general similarity to the exo:endo ratios produced[10] with the closely related "stable" IBF's **35** and **36**. The insertion of one methylene group between the furanoid ring and the nitrile (**21D**) or ester (**21A**) function seems to provoke a modest but consistent increase in the proportion of meta regioisomer.

One intramolecular Diels–Alder reaction was attempted with phthalan **8C** which had reacted satisfactorily with DMAD in the intermolecular mode (Table II). When treated under the usual conditions for IBF generation the expected intramolecular adduct **39** was not formed. The only material isolable was **20C** (discussed earlier). This was a disappointing result, and since a very similar phthalan **37** produced the adduct **38** in good yield, the failure of our reaction can only be attributed to the presence of the carbonyl group in **8C**.

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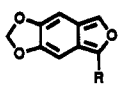
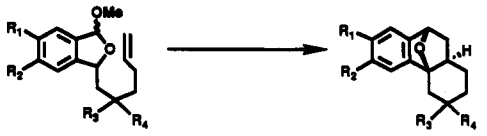


35 (R = CO_2Me)

36 (R = CN)



30 (R_1 = R_2 = OMe, R_3+ R_4 = O) 39 (R_1 = R_2 = OMe, R_3+R_4 = O)

37 (R_1 = OMe, R_2 = R_3 = R_4 = H) 38 (R_1 = OMe, R_2 = R_3 = R_4 = H)

In summary, this study demonstrates that aromatic aldehydes can be converted in reasonable yields to isobenzofurans bearing common functional groups in the C-1 substituent. Interception of these intermediates in situ with acetylenic or olefinic dienophiles leads to multifunctional naphthols, naphthalenes (by direct aromatization[2] of the adducts), or tetralins (by reductive deoxygenation[2]).

Experimental Section

Melting points are uncorrected. Low- and high-resolution mass spectra were obtained at the South-Western Ontario Regional Mass Spectrometry Center at McMaster University, Hamilton, Ontario. ^1H NMR spectra were recorded in $CDCl_3$. Microanalyses were performed by MHW Laboratories of Phoenix, AZ. Silica gel 60 (70–230 mesh) was used for flash chromatography. Preparative TLC was carried out on precoated 1000 μm 20 × 20 mm silica gel GF plates. Acrolein, methyl vinyl ketone, methyl acrylate, and acrylonitrile were distilled prior to use, and 1% hydroquinone was added as the inhibitor. All solvents were distilled and stored over molecular sieves. Many compounds, prepared as diasteromeric mixtures, were oils which could not be distilled without decomposition. In all such instances chromatographic separation, ^1H NMR, and high-resolution mass spectrometry were used to ensure the purity (>95%) and identity of the material.

General Procedure for the Preparation of *o*-Formyl Acetals 1 and 4. A solution of *o*-bromobenzaldehyde dimethyl acetal[3] (22.1 mmol) in dry ether (100 mL) was cooled to −78 °C under N_2, and *n*-BuLi (1.6 M in hexane, 1.1 equiv/mol of acetal) was added dropwise. The resulting mixture was stirred for 1 h and added to DMF (3 equiv mol of acetal). The reaction mixture was allowed to warm to room temperature during 4 h, and water (50 mL) was added. The ether layer was separated, the aqueous layer extracted with ether (2 × 50 mL), and the combined ether extracts were washed with a saturated solution of NaCl, dried over Na_2SO_4, concentrated, and chromatographed with the appropriate solvent system (EtOAc–hexane).

1: flash chromatography (EtOAc–hexane, 1:4) gave a viscous oil **1** (80%); IR (neat) 1670 (CHO) cm^{-1}; ^1H NMR (80 MHz) δ 3.4 (s, 6 H, 2 OMe), 3.99, 4.05 (s, 3 H each, OMe), 5.95 (s, 1 H, CH), 6.18, 6.46 (s, 1 H each, aromatic H); HRMS (EI) m/z 240.0903, M^+, 240.0993 calcd for $C_{12}H_{16}O_5$.

4: flash chromatography (EtOAc–hexane, 1:6) gave a viscous oil **4** (84%); IR (neat) 1672 (CHO) cm^{-1}; ^1H NMR (80 MHz) δ 3.4 (s, 6 H, 2 OMe), 5.62 (s, 1 H, acetal H), 7.2 (m, 2 H, 2 aromatic H), 7.4 (dd, 1 H, J = 2.4, 7 Hz, aromatic H), 7.7 (dd, 1 H, J = 2.4, 7 Hz, aromatic H); HRMS (EI) m/z 180.0757, M^+, 180.0783 calcd for $C_{10}H_{12}O_3$.

General Procedure[11,12] for the Preparation of Styrenes 2A, 5, and 6. In a 100-mL two-necked flask fitted with a short reflux condenser and magnetic stirring bar was placed finely cut sodium (290 mg, 12.6 mmol) under N_2, and dry methyl acetate (3.7 mL) containing absolute ethanol (0.1 mL). The flask was cooled to 0 °C, and the acetal (10 mmol) in methyl acetate (10 mL) was slowly added with stirring, maintaining the temperature at 0–5 °C. Stirring was continued until all the sodium had reacted (ca. 6 h), the reaction mixture was acidified with glacial HOAc, and 2 N HCl (10 mL) was added. The mixture was stirred for 2 h and extracted with EtOAc (3 × 50 mL). The combined EtOAc extracts were dried over Na_2SO_4 and concentrated. The residue was chromatographed with the appropriate EtOAc–hexane mixture, and the product was crystallized from a suitable solvent.

Methyl 3-(4′,5′-Dimethoxy-2′-formylphenyl)propenoate (2A). Flash chromatography (EtOAc–hexane, 1:5) followed by crystallization (EtOAc–hexane) afforded yellow plates (59%): mp 131–132 °C; IR (Nujol) 1730, 1688, 1618 cm^{-1}; ^1H NMR (250 MHz) δ 3.83, 3.97, 3.99 (s, 3 H each, OMe), 6.34, 8.47 (d, 1 H each, J = 15.7 Hz, alkene H), 7.06, 7.40 (s, 1 H each, aromatic H), 10.31 (s, 1 H, CHO); HRMS (EI) m/z 250.0885, M^+, 250.0881 calcd for $C_{13}H_{14}O_5$. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.38, H, 5.59. Found: C, 62.26; H, 5.37.

Methyl 3-(4′,5′-(Methylenedioxy)-2′-formylphenyl)-propenoate (5). Flash chromatography (EtOAc–hexane, 1:5) followed by crystallization ($CHCl_3$, hexane) afforded colorless needles (61%): mp 178–80 °C; IR (Nujol) 1730, 1686, 1620 cm^{-1}; ^1H NMR (250 MHz) δ 3.82 (s, 3 H, CO_2Me), 6.10 (s, 2 H, OCH_2O), 6.31, 8.44 (d, 1 H each, J = 15.7 Hz, alkene H), 7.05, 7.11 (s, 1 H, aromatic H), 10.25 (s, 1 H, CHO); HRMS (EI) m/z 234.0536, M^+, 234.0528 calcd for $C_{12}H_{10}O_5$. Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.52; H, 4.27. Found: C, 61.42; H, 4.20.

Methyl 3-(2′-Formylphenyl)propenoate (6). Flash chromatography (EtOAc–hexane, 1:6) followed by crystallization ($CHCl_3$–hexane) afforded a colorless solid (65%): mp 43–44 °C; IR (Nujol) 1728, 1699, 1621 cm^{-1}; ^1H NMR (250 MHz) δ 3.82 (s, 3 H, CO_2Me), 6.38, 8.53 (d, 1 H each, J = 17 Hz, alkene H), 7.6–7.87 (m, 4 H, aromatic H), 10.29 (s, 1 H, CHO); HRMS (EI) m/z 190.0638, M^+, 190.0630 calcd for $C_{11}H_{10}O_3$. Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.45; H, 5.26. Found: C, 69.42; H, 5.04.

4-(4′,5′-Dimethoxy-2′-formylphenyl)-3-buten-2-one (2B). A solution of acetal **1** (0.923 g, 3.8 mmol), water (3 mL), and acetone (5 mL) was cooled to 0 °C in an ice bath, and 33% NaOH (1 mL) was slowly added. The mixture was stirred at room temperature for 4 h, acidified with 2 N HCl, and further stirred for 2 h. The usual workup followed by flash chromatography (EtOAc–hexane, 1:4) and recrystallization ($CHCl_3$–hexane) afforded **2B** (470 mg, 51%): mp 120–121 °C; IR (Nujol) 1660 (br), 1620 cm^{-1}; ^1H NMR (200 MHz) δ 2.44 (s, 3 H, COMe), 3.99, 4.00 (s, 3 H, each, OMe), 6.59, 8.44 (d, 1 H, J = 16.2 Hz, alkene H), 7.1, 7.37 (s, 1 H each, aromatic H), 10.15 (s, 1 H, CHO); MS (EI) m/z (M^+) 191 (100, $M^+ - CH_3CO$). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 66.21; H, 5.66.

1-(4′,5′-Dimethoxy-2′-formylphenyl)hepta-1,6-dien-3-one (2C). To a solution of acetal **1** (3.2 g, 13 mmol) and 5-hexen-2-one (6.4 mL, 65 mmol) was added 50% NaOH (6 mL) slowly. The mixture was then allowed to reach room temperature, stirred for 5 h, and extracted with EtOAc, and the extracts were concentrated to give a reddish yellow oil. The excess starting ketone was removed by distillation under reduced pressure, and the resulting oil was dissolved in THF (20 mL) and stirred with 2 N HCl (5 mL) for 1 h. The usual workup followed by recrystallization (CH_2Cl_2–hexane) gave **2C** (42%): mp 104–105 °C; IR (Nujol) 1656 (br) cm^{-1}; ^1H NMR (200 MHz) δ 2.46 (dd, 2 H, J = 6.19, 13.9 Hz, CH_2), 2.85 (t, 2 H, J = 7.7 Hz, CH_2), 3.98, 4.0 (s, 3 H each, OMe), 5.06 (m, 2 alkene H), 5.9 (m, 1 H, terminal alkene H), 6.6, 8.4 (d, 1 H each, J = 16 Hz, alkene H), 7.09, 7.38 (s, 1 H each, aromatic H), 10.28 (s, 1 H, CHO); MS (EI) m/z 191 (100, M^+ − CH=CH-$(CH_2)_2CO$). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.07; H, 6.56. Found: C, 69.92; H, 6.42.

2-(4′,5′-Dimethoxy-2′-formylphenyl)-1-cyanoethene (2D). A mixture of powdered 80% KOH (700 mg, 12.5 mmol) and dry acetonitrile[13] (20 mL, freshly distilled from CaH_2) was heated to reflux under N_2, and a solution of acetal **1** (3 g, 12.5 mmol) in acetonitrile (5 mL) was added. The reaction mixture was stirred for 10 min, and the hot solution was poured onto crushed ice and extracted with CH_2Cl_2. The extracts were dried over Na_2SO_4 and

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concentrated, keeping the bath temperature at 30 °C. The resulting yellow viscous oil was then dissolved in THF (20 mL) and stirred with 2 N HCl (10 mL) for 1 h. The usual workup followed by flash chromatography (EtOAc–hexane, 1:5) and two successive crystallizations ($CHCl_3$ and ether) afforded **2D** (73%): mp 150–151 °C; IR (Nujol) 2215 (C≡N), 1678 (CHO), 1612 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.99, 4.00 (s, 3 H each, OMe) 5.81, 8.35 (d, 1 H each, J = 16 Hz, alkene H), 6.98, 7.35 (s, 1 H each, aromatic H), 10.15 (s, 1 H, CHO); HRMS (EI) m/z 217.0752, M^+, 217.0751 calcd for $C_{12}H_{11}O_3N$. Anal. Calcd for $C_{12}H_{11}O_3N$: C, 66.35; H, 5.06; N, 6.45. Found: C, 66.22; H, 5.10; N, 6.21.

2-(4′,5′-Dimethoxy-2′-formylphenyl)-1-methyl-1-nitroethene (2E[7]). A solution of acetal 1 (480 mg, 2 mmol) and NH_4OAc (154 mg 2.5 mmol) in nitroethane (5 mL) was refluxed for 2 min under N_2. The hot solution was cooled in liquid N_2, diluted with EtOAc (25 mL), and filtered. The blackish yellow solution was concentrated, keeping the bath temperature at 30 °C. The resulting black mass was passed through a short column of silica gel (EtOAc–hexane 1:3). The crude product was dissolved in THF (15 mL) and stirred with 2 N HCl (2 mL) for 0.5 h. The usual workup followed by flash chromatography (EtOAc–hexane, 1:9) and crystallization (CH_2Cl_2–hexane) gave **2E** (30%): mp 69–70 °C; IR (Nujol) 1685 (CO), 1647 (C=C), 1525, 1288 (NO_2) cm^{-1}; ^1H NMR (200 MHz) δ 2.28 (d, 3 H, J = 0.8 Hz, CH_3), 3.97, 3.99 (s, 3 H each, OMe), 6.76, 7.45 (s, 1 H each, aromatic H), 8.46 (br, 1 H, alkene H), 10.04 (s, 1 H, CHO); MS (EI) m/z 205 (100, $M^+ - NO_2$). Anal. Calcd for $C_{12}H_{13}O_5N$: C, 57.37; H, 5.17; N, 5.57. Found: C, 57.01; H, 5.02; N, 5.42.

General Procedure for the Preparation of Methoxy Phthalans 8A–E, 9, and 10. To a stirred solution of anhydrous methanol (10 mL), anhydrous K_2CO_3 ($NaOAc$ for **2B, 2C, 2E, 2F**) was added a solution of *o*-formylstyrene (5 mmol) in dry CH_2Cl_2 (5 mL), and stirring at room temperature was continued for 4 h. The usual workup gave a 1:1 cis–trans isomeric mixture of methoxy phthalans together with uncyclized starting material which was separated by crystallization (CH_2Cl_2–hexane) to obtain a viscous oily product. The oil was passed through a short column of silica gel (EtOAc–hexane) to obtain a cis–trans isomeric mixture of methoxy phthalans.

Methoxy Phthalans 8A. Flash chromatography on silica (EtOAc–hexane, 1:5) gave an isomeric mixture of methoxy phthalans **8A** (71%): IR (neat) 1737 (br) cm^{-1}; ^1H NMR (250 MHz) δ 2.75 (m, 2 H, CH_2) 3.38, 3.45 (s, 3 H, C_3 α- and β-OMe), 3.73, 3.76 (s, 3 H, α- and β-CO_2Me) 3.87, 3.89 (s, 3 H each, OMe), 6.71, 6.74 (s, aromatic H), 6.88 (s, 1 H, aromatic H); HRMS (EI) m/z 282.1097, M^+, 282.1103 calcd for $C_{14}H_{18}O_6$.

Methoxy Phthalans 8B: Flash chromatography (EtOAc–hexane, 1:4) gave an isomeric mixture of methoxy phthalans **8B** (63%): IR (neat) 1710 (br) cm^{-1}; ^1H NMR (250 MHz) δ 2.24 (s, 3 H, $COCH_3$), 2.85 (m, 2 H, CH_2) 3.38, 3.48 (s, C_3 α- and β-OMe), 3.87, 3.89 (s, 3 H each, OMe), 5.55 (t, J = 5.7 Hz, C_1-H), 5.17 (dd, J = 2.2, 5.7 Hz, C_1-H) 6.70, 6.73 (s, aromatic H), 6.86 (s, aromatic H); HRMS (EI) m/z 266.1149, M^+, 266.1154 calcd for $C_{14}H_{18}O_5$.

Methoxy Phthalans 8C. Flash chromatography (EtOAc–hexane, 1:5) gave an isomeric mixture of methoxy phthalans **8C** (65%): IR (neat) 1709 (C=O), 1640 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 2.45 (dd, 2 H, J = 6.8, 13 Hz, CH_2), 2.60, 2.86 (m, 2 H each, 2 CH_2), 3.37, 3.47 (s, C_3, α- and β-OMe), 3.86, 3.88 (s, 3 H each, OMe), 5.01 (m, 2 H, alkene H), 5.55 (t, J = 5.7 Hz, C_1-H), 5.8 (m, alkene H + C_1-H), 5.99 (s, C_3-H), 6.12 (d, J = 2.3 Hz, C_3-H), 6.70, 6.72 (s, aromatic H), 6.86 (s, 1 H, aromatic H); HRMS (EI) m/z 306.1462, M^+, 306.1467 calcd for $C_{17}H_{22}O_5$.

Methoxy Phthalans 8D. Flash chromatography (EtOAc–hexane, 1:6) gave an isomeric mixture of methoxy phthalans **8D** (80%): IR (neat) 2216, 2204 (C≡N) cm^{-1}; ^1H NMR (250 MHz) δ 2.79 (m, 2 H, CH_2), 3.43, 3.51 (s, 3 H, C_3 α- and β-OMe), 3.89 (s, 6 H, 2 OMe), 5.28 (t, J = 6.7 Hz, C_1-H), 5.50 (m, C_1-H), 6.01 (s, C_3-H), 6.2 (d, J = 2.3 Hz C_3-H), 6.8 (s, aromatic H), 6.88, 6.89 (s, each, aromatic H); HRMS (EI) m/z 249.0870, M^+, 249.0877 calcd for $C_{13}H_{15}O_4N$.

Methoxy Phthalans 8E. Flash chromatography (EtOAc–hexane, 1:7) gave an isomeric mixture of methoxy phthalans **8E** (32%): IR (neat) 1545, 1283 cm^{-1}; ^1H NMR (250 MHz) δ 1.41, 1.50 (d, 3 H, J = 6.7 Hz, CH_3) 3.39, 3.56 (s, 3 H, C_3 α- and β-OMe) 3.0 (s, 6 H, 2 OMe), 4.64 (m, 2 H, $CHNO_2$), 5.63 (d, J = 5.1 Hz, C_1-H), 5.89 (m, C_1-H), 6.2 (d, J = 2.7 Hz, C_3-H), 6.61, 6.63 (s, aromatic H), 6.88 (s, aromatic H); HRMS (EI) m/z 283.1071, M^+, 283.1056 calcd for $C_{13}H_{17}O_6N$.

Methoxy Phthalans 9. Flash chromatography (EtOAc–hexane, 1:5) gave an isomer mixture of methoxy phthalans **9** (73%): IR (neat) 1740 (br, CO_2Me) cm^{-1}; ^1H NMR (200 MHz) δ 2.74 (m, 2 H, CH_2), 3.37, 3.43 (s, 3 H, C_3 α- and β-OMe), 3.74, 3.75 (s, α- and β-CO_2Me), 5.46 (t, J = 6.1 Hz, C_1-H), 5.59 (dd, J = 2.5, 6.1 Hz, C_1-H), 6.01 (m, OCH_2O + C_1-H), 6.09 (d, J = 2.5 Hz, C_1-H), 6.64, 6.65 (s, aromatic H), 6.77 (s, aromatic H); HRMS (EI) m/z 266.0799, M^+, 266.0790 calcd for $C_{13}H_{14}O_6$.

Methoxy Phthalans 10. Flash chromatography on silica (EtOAc–hexane, 1:7) gave an isomeric mixture of methoxy phthalans **10** (82% by NMR) together with unreacted starting material which was not separable: IR (neat) 2738 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) δ 2.77 (m, 2 H, CH_2), 3.42, 3.47 (s, 3 H, C_3 α- and β-OMe), 3.74, 3.76 (s, 3 H, α- and β-CO_2Me), 5.6 (t, J = 6.6 Hz, C_1-H), 5.7 (dd, J = 2, 6.6 Hz, C_1-H), 6.07 (s, C_1-H), 6.18 (d, J = 2 Hz, C_1-H), 7.36, 7.37 (m, 4 H, aromatic H); HRMS (EI) m/z 221.0823, $M^+ - 1$, 221.0814 calcd for $C_{12}H_{13}O_4$.

Methoxy Phthalans 8F. To mixture of nitromethane (4.0 mL, 6.5 mmol), acetal 1 (1.6 g, 6.5 mmol), and methanol (1.3 mL) was added NaOH (276 mg, 6.9 mmol) in H_2O (1 mL) with stirring at such a rate that the temperature was kept at 10–15 °C. After 15 min of stirring, ice water (5 mL) was added and the reaction mixture was allowed to warm to room temperature. The mixture was acidified with NH_4Cl and extracted with CH_2Cl_2. The extracts were dried over Na_2SO_4, concentrated, keeping the bath temperature at 30 °C, and vacuum dried. The resulting hydroxy acetal **7** was then dissolved in anhydrous MeOH (25 mL) and reflux under N_2 with glacial acetic acid (0.4 mL) for 10 h. The reaction mixture was neutralized with Na_2CO_3, extracted with EtOAc, dried, concentrated, and chromatographed (EtOAc–hexane, 1:6) to afford an isomeric mixture of methoxy phthalans **8F** (51%): IR (neat) 1549, 1243 cm^{-1}; ^1H NMR (200 MHz) δ 3.43, 3.53 (s, 3 H, C_3 α- and β-OMe), 3.89, 3.90 (s, 3 H each, OMe), 4.6 (m, 2 H, CH_2), 5.75 (dd, J = 4.9, 7.85 Hz, C_1-H), 5.92 (m, C_1-H), 6.01 (s, C_3-H), 6.18 (d, J = 2.4 Hz, C_3-H), 6.69, 6.72 (s, aromatic H), 6.89, 6.91 (s, aromatic H); HRMS (EI) m/z 269.0895, M^+, 269.0899 calcd for $C_{12}H_{15}O_6N$.

Methoxy Phthalans 15. To a solution of methoxy phthalans **4E** (253 mg, 1 mmol), 35% solution Triton B in methanol (0.04 mL), and *tert*-butyl alcohol (0.2 mL) in THF (1 mL) was added methyl acrylate (0.45 mL, 5 mmol) under N_2, and the mixture was stirred at room temperature for 18 h.[14] The usual workup followed by flash chromatography (EtOAc–hexane, 1:6) gave the methoxy phthalans **15** (265 mg, 72%): IR (neat) 1738 (br, CO_2Me), 1534, 1255 (NO_2) cm^{-1}; ^1H NMR (250 MHz) δ 1.25, 1.3 (s, 3 H, CH_3), 2.5 (m, 4 H, 2 CH_2), 3.38, 3.6 (s, 3 H, C_3 α- and β-OMe), 3.63, 3.69 (s, 3 H, CO_2Me), 3.83, 3.9 (s, 3 H each, OMe), 5.65 (s, C_1-H), 5.8 (d, J = 2.6 Hz, C_1-H), 5.98 (s, C_2-H), 6.2 (d, J = 2.6 Hz, C_3-H), 6.42, 6.44 (s, 1 H, aromatic H), 6.87 (s, 1 H, aromatic H); HRMS (EI) m/z 369.1424, M^+, 369.1424 calcd for $C_{17}H_{23}O_8N$.

Methoxy Phthalans 8G. A solution of methoxy phthalans **15** (369 mg, 1 mmol), Bu_3SnH (1.89 mL, 5 mmol), and AIBN (49.26 mg, 0.3 mmol) in benzene (2 mL) was refluxed under N_2 for 2 h.[8] The reaction mixture was cooled to room temperature, diluted with acetonitrile (25 mL), filtered through a thin pad of Celite which was washed with hexane (5 × 25 mL), and chromatographed (EtOAc–hexane, 1:8) to obtain partially pure methoxy phthalans **8G** which were directly used for the next reaction without further purification.

General Procedure for the Preparation of DMAD Adducts 11–14. The methoxy phthalan (100 mg) was dissolved in excess DMAD (3 mL) and a catalytic amount (ca. 0.1 mL) of glacial HOAc, and the mixture was heated at 80 °C for 2 h. Excess DMAD was removed by vacuum distillation, and the product was purified by flash chromatography followed by crystallization from an appropriate solvent.

Adduct 11A. Flash chromatography on silica (EtOAc–hexane, 1:3) followed by crystallization (Et_2O–CH_2Cl_2–hexane) gave the adduct **11A** (65%): mp 125–126 °C; IR (Nujol) 1726 (br, CO_2Me), 1633 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.23, 3.71 (d, 1 H each,

(14) Hill, D. K.; Sawada, S.; Bock, M. G.; Green, J. R. *Heterocycles* **1987**, *25*, 515–520.

J = 16 Hz, CH_2), 3.72, 3.78, 3.81, 3.86 (s, 3 H each, OMe), 5.9 (s, 1 H, C_4-H), 6.96, 7.04 (s, 1 H each, aromatic H); HRMS (EI) m/z 392.1108, M^+, 392.1107 calcd for $C_{19}H_{20}O_9$. Anal. Calcd for $C_{19}H_{20}O_9$: C, 58.14; H, 5.70. Found: C, 58.06; H, 5.68.

Adduct 14B. Flash chromatography (EtOAc–hexane, 1:3) followed by crystallization ($CHCl_3$–hexane) gave the adduct **14B** (43%): mp 160–161 °C; IR (Nujol) 1718 (br), 1620 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 2.06 (s, 3 H, $COCH_3$), 3.85 (s, 2 H, CH_2), 3.94, 3.97, 3.99, 4.04 (s, 3 H each, OMe), 7.10, 7.71 (s, 1 H each, aromatic H), 12.25 (s, 1 H, D_2O exchangeable, C_4-OH); HRMS (EI) m/z 376.1149, M^+, 376.1158 calcd for $C_{19}H_{20}O_8$. Anal. Calcd for $C_{19}H_{20}O_8$: C, 60.63; H, 5.31. Found: C, 60.61; H, 5.21.

Adduct 11C. Flash chromatography (EtOAc–hexane, 1:5) gave the adduct **11C** (oil) (47%): IR (neat) 1702 (br), 1630 (br) cm^{-1}; ^1H NMR (250 MHz) δ 2.34 (dd, 2 H, J = 6.7, 13.6 Hz, allylic CH_2), 2.64 (t, 2 H, J = 6.7 Hz, CH_2CO), 3.4, 3.66 (d, 1 H each, J = 16.6 Hz, CH_2), 377, 3.78, 3.86, 3.87 (s, 3 H each, OMe), 5.01 (m, 2 H, alkene H), 5.84 (m, 1 H, alkene H), 5.88 (s, 1 H, C_4-H), 6.94, 7.05 (s, 1 H each, aromatic H); HRMS (EI) m/z 416.1475, M^+, 416.1471 calcd for $C_{22}H_{24}O_8$.

Adduct 11D. Flash chromatography (EtOAc–hexane, 1:6) followed by crystallization (ether) gave the adduct **11D** (61%): mp 109–110 °C; IR (Nujol) 2249 (C≡N), 1716 (br, CO_2Me) 1640 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.55 (AB q, 2 H, J = 13 Hz, CH_2), 3.81, 3.82, 3.87, 3.88 (s, 3 H each, OMe), 5.92 (s, 1 H, C_4-H) 6.99, 6.07 (s, 1 H each, aromatic H); HRMS (EI) m/z 359.0094, M^+, 359.1005 calcd for $C_{18}H_{17}O_7N$. Anal. Calcd for $C_{18}H_{17}O_7N$: C, 60.16; H, 4.73. Found: C, 59.82; H, 4.41.

Adduct 14F. Flash chromatography (EtOAc–hexane, 1:3) followed by crystallization (CH_2Cl_2–hexane) gave the adduct **14F** (33%): mp 190–191 °C; IR (Nujol) 1722 (br) cm^{-1}; ^1H NMR (250 MHz) δ 3.95, 3.97 (s, 3 H each, 2 CO_2Me), 4.07, 4.05 (s, 3 H each, 2 OMe), 5.8 (s, 2 H, CH_2NO_2), 7.16, 7.74 (s, 1 H each, 2 aromatic H), 12.38 (s, 1 H, C_4-OH); HRMS (EI) m/z 379.0901, M^+, 379.0903 calcd for $C_{17}H_{17}O_9N$. Anal. Calcd for $C_{17}H_{17}O_9N$: C, 53.82; H, 4.48. Found: C, 53.63; H, 4.31.

Adduct 12. Flash chromatography (EtOAc–hexane, 1:4) followed by crystallization (ether–CH_2Cl_2–hexane) gave the adduct **12** (63%): mp 103–104 °C; IR (Nujol) 1723 (br, CO_2Me), 1642 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 3.2, 3.65 (d, 1 H each, J = 16 Hz, CH_2), 3.71, 3.77, 3.80 (s, 3 H each, OMe), 5.86 (s, 1 H, C_4-H), 5.91, 5.95 (d, 1 H each, J = 1.4 Hz, OCH_2O), 6.86, 6.91 (s, 1 H each, aromatic H); HRMS (EI) m/z 376.0802, M^+, 376.0794 calcd for $C_{18}H_{16}O_9$. Anal. Calcd for $C_{18}H_{16}O_9$: C, 57.44; H. 4.25. Found: C, 57.24; H, 4.58.

Adduct 13. Flash chromatography (EtOAc–hexane, 1:6.5) gave **13** (oil) (67%): IR (neat) 1733 (br, CO_2Me), 1640 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.23, 3.75 (d, 1 H, J = 16.2 Hz, CH_2), 3.73, 3.77, 3.80 (s, 3 H each, OMe), 5.95 (s, 1 H, C_4-H), 7.05–7.35 (m, 4 H, aromatic H); HRMS (EI) m/z 332.0901, M^+, 332.0896 calcd for $C_{17}H_{16}O_7$.

Adduct 11G. Flash chromatography (EtOAc–hexane, 1:5) followed by crystallization (ether–CH_2Cl_2–hexane) gave the adduct **11G** (16% overall): mp 115–116 °C; IR (Nujol) 1732 (br, CO_2Me), 1703 (COMe), 1626 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 1.05 (d, 3 H, J = 6.9 Hz, CH_3), 1.74, 1.93 (m, 1 H each, CH_2), 2.45 (m, 2 H, CH_2CO), 2.78 (m, 1 H, CH), 3.69, 3.75, 3.83, 3.85, 3.87 (s, 3 H each, OMe), 5.89 (s, 1 H, C_4-H), 6.95, 7.02 (s, 1 H each, aromatic H); HRMS (EI) m/z 434.1582, M^+, 434.1577 calcd for $C_{22}H_{26}O_9$. Anal. Calcd for $C_{22}H_{26}O_9$: C, 60.80; H, 5.98. Found: C, 60.51; H, 5.62.

Preparation of Keto–Aldehydes 16 and 17. The solutions of methoxy phthalans **8E** and **F** (100 mg) in benzene (5 mL) were refluxed under N_2 with glacial acetic acid (ca. 0.1 mL) for 12 h. The usual workup followed by flash chromatography (EtOAc–hexane) and crystallization (CH_2Cl_2–hexane) afforded **16** and **17**.

2-Propionyl-4,5-dimethoxybenzaldehyde (16): yield 22%; mp 114–116 °C; IR (Nujol) 1722 (CHO), 1676 (CO) cm^{-1}; ^1H NMR (80 MHz) δ 1.23 (t, 3 H, J = 8.5 Hz, CH_3), 2.95 (q, 2 H, J = 8.5 Hz, CH_2), 3.99, 4.02 (s, 3 H each, OMe), 7.17, 7.43 (s, 1 H each, aromatic H), 10.22 (s, 1 H, CHO); HRMS (EI) m/z 222.0895, M^+, 222.0892 calcd for $C_{12}H_{14}O_4$. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.83; H, 6.30. Found: C, 64.51; H, 6.27.

2-Acetyl-4,5-dimethoxybenzaldehyde (17): yield 31%; mp 98–100 °C; IR (Nujol) 1726 (CHO) 1679 (CO) cm^{-1}; ^1H NMR (80 MHz) δ 2.65 (s, 3 H, $COCH_3$), 4.01 (s, 6 H, 2 OMe), 7.18, 7.45 (s, 1 H each aromatic H), 10.21 (s, 1 H, CHO); HRMS (EI) m/z 208.0729, M^+, 208.0722 calcd for $C_{11}H_{12}O_4$. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.44; H, 5.76. Found: C, 63.11; H, 5.66.

General Procedure for the Preparation of Alkylidene Phthalans 20A–D. A solution of methoxy phthalans **8A–D** (1 mmol) and glacial HOAc (0.5 mL) in dry benzene (10 mL) was refluxed under N_2 for 8 h. The usual workup followed by preparative TLC (EtOAc–hexane) and crystallization (CH_2Cl_2, hexane) gave alkylidene phthalans **20A–D**.

Alkylidene Phthalan 20A. Preparative TLC on silica (EtOAc–hexane, 1:4) and crystallization (CH_2Cl_2–hexane) gave unstable alkylidene phthalan **20A** (23%): mp 148–150 °C; IR (Nujol) 1759 (CO_2Me), 1624 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.75 (s, 3 H, CO_2Me), 3.92, 3.93 (s, 3 H each, OMe), 5.36 (s, 1 H, alkene H), 5.50 (s, 2 H, CH_2), 6.85, 6.97 (s, 1 H each, aromatic H); HRMS (EI) m/z 250.0829, M^+, 250.0817 calcd for $C_{13}H_{14}O_5$.

Alkylidene Phthalan 20B. Preparative TLC (EtOAc–hexane, 1:5) and crystallization (CH_2Cl_2–hexane) gave unstable alkylidene phthalan **20B** (28%); mp 176–178 °C; IR (Nujol) 1605 (C=C), 1660 (CO) cm^{-1}; ^1H NMR (250 MHz) δ 2.42 (s, 3 H, $COCH_3$), 3.93, 3.95 (s, 3 H each, OMe), 5.48 (s, 2 H, CH_2), 5.66 (s, 1 H, alkene H), 6.88, 6.98 (s, 1 H each, aromatic H); HRMS (EI) m/z 234.0887, M^+, 234.0880 calcd for $C_{13}H_{14}O_4$.

Alkylidene Phthalan 20C. Preparative TLC (EtOAc–hexane, 1:5) and crystallization (CH_2Cl_2–hexane) gave unstable alkylidene phthalan **20C** (27%): mp 142–144 °C; IR (Nujol) 1650 (CO), 1640 (C=C terminal), 1609 (C=C conj) cm^{-1}; ^1H NMR (250 MHz) δ 2.42 (q, 2 H, J = 7, 13 Hz, CH_2), 2.81 (t, 2 H, J = 7 Hz, CH_2CO), 3.93, 3.94 (s, 3 H each, OMe), 5.01 (m, 2 H, alkene H), 5.46 (s, 2 H, CH_2), 5.68 (s, 1 H, alkene H), 5.84 (m, 1 H, alkene H), 6.88, 6.99 (s, 1 H each, aromatic H); HRMS (EI) m/z 274.1213, M^+, 274.1205 calcd for $C_{16}H_{18}O_4$.

Alkylidene Phthalan 20D. Preparative TLC (EtOAc–hexane, 1:6) followed by crystallization ($CHCl_3$–hexane) gave unstable alkylidene phthalan **20D** (31%): mp 129–130 °C; IR (Nujol) 2198 (C≡N) 1613 (C=C) cm^{-1}; ^1H NMR (250 MHz) δ 3.93, 3.94 (s, 3 H each, OMe), 5.34 (s, 1 H, alkene H), 5.44 (s, 2 H, CH_2), 6.86, 6.92 (s, 1 H each, aromatic H); HRMS (EI) m/z 217.0732, M^+, 217.0698 calcd for $C_{12}H_{11}O_3N$.

Preparation of Adduct 22. The methoxy phthalan **8D** (240 mg, 1 mmol) was dissolved in dimethyl maleate (5 mL) and glacial acetic acid (0.4 mL) and heated at 100 °C for 3 h. The reaction mixture was neutralized with Na_2CO_3, extracted with EtOAc (3 × 20 mL), and chromatographed (EtOAc–hexane, 3:7) to give a partially pure yellow oil. The yellow oil was subjected to preparative TLC (EtOAc–hexane, 3:7, double elution) followed by recrystallization (ether) to afford colorless crystals of adduct **22** (213 mg, 50%) (ortho endo:exo = 20:1): mp 139–140 °C; IR (Nujol) 2254 (C≡N), 1733 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) 3.41 (AB q, 2 H, J = 16 Hz, CH_2CN), 3.5 (d, 1 H, J = 4 Hz, $H_{2\beta}$), 3.85 (dd, 1 H, J = 4, 4.9 Hz, $H_{3\beta}$), 3.5, 3.52, 3.86, 3.89 (s, 3 H each, OMe), 5.45 (d, 1 H, J = 4.9 Hz, H-4), 6.84, 6.87 (s, 1 H each, aromatic H); HRMS (EI) m/z 361.1163, M^+, 361.1164 calcd for $C_{18}H_{19}O_7N$. Anal. Calcd for $C_{18}H_{19}O_7N$: C, 59.83; H, 5.26; N, 3.87. Found: C, 59.67; H, 5.03; N, 3.92.

General Procedure for the Preparation of Adducts 23–34 (Table III). The methoxy phthalan (**8A** or **8D**, 1 mmol) mixed with excess dienophile (3 or 4 mmol) was refluxed in $CHCl_3$ or CCl_4 with glacial acetic (0.3 mL) for 7–10 h. A similar workup as for **22** was used to isolate the adducts.

Adducts 23 was chromatographed (EtOAc–hexane, 2:7) and crystallized to give an inseparable isomeric mixture of the adducts **23** (220 mg, 61%) (ortho endo:exo = 7.8:1): mp mixture 143–144 °C; IR (Nujol) 2247 (C≡N), 1728 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) ortho endo, δ 3.13 (d, 1 H, J = 4 Hz, $H_{2\alpha}$), 3.57 (AB q, 2 H, J = 16 Hz, CH_2CN), 3.72 (d, 1 H, J = 4 Hz, $H_{3\beta}$), 3.54, 3.81, 3.86, 3.89 (s, 3 H each, OMe), 5.64 (s, 1 H, C_4-H), 6.72, 6.95 (s, 1 H each, aromatic H); HRMS (EI) m/z 361.1163, M^+, 361.1164 calcd for $C_{18}H_{19}O_7N$.

Adducts 24 and 25. Chromatography (EtOAc–hexane, 1:5) gave an oily inseparable mixture of isomeric adducts (153 mg, 56%) (ortho endo:exo:meta endo 4.5:1.5:1): IR (neat) 2202 (C≡N), 2252 (C≡N), 1717 (br, CHO) cm^{-1}; ^1H NMR (200 MHz) complex 8.91, 9.01, 9.7 (d, J = 2.4 Hz, CHO, ortho endo, meta endo, ortho exo, respectively); HRMS (EI) m/z 273.1001, M^+, 273.0974 calcd for $C_{15}H_{15}O_4N$.

Adducts 26 and 27. Chromatography (EtOAc–hexane, 1:5) gave an oily inseparable mixture of isomeric adducts (175 mg 61%) (ortho endo:exo:meta endo 2.6:2:1): IR (neat) 2203 (CN), 2253 (CN), 1633 (CO) cm^{-1}; ^1H NMR (200 MHz) complex 5.39, 5.45 (d, J = 4.8 Hz ortho endo:exo C_4-H, respectively), 5.51 (s, meta exo C_4-H); HRMS (EI) m/z 287.1159, M^+, 287.1158 calcd for $C_{16}H_{17}O_4N$.

Adducts 28 and 29. Flash chromatography (EtOAc–hexane, 1:4) gave an oily inseparable isomeric mixture of the adducts (190 mg, 63%) (ortho endo:exo:meta endo:exo 7:3.5:2:1): IR (neat) 2203 (br, C≡N), 2255 (br, C≡N), 1746 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) complex δ 5.38, 5.46, 5.31 (d, J = 4.8 Hz, ortho endo:exo:meta endo C_4-H, respectively), 5.59 (s, 1 H, meta exo); HRMS (EI) m/z 303.1101, M^+, 303.1095 calcd for $C_{16}H_{17}O_5N$.

Adducts 30 and 31. Flash chromatography (EtOAc–hexane, 3:7) gave an oily inseparable isomeric mixture of the adducts (178 mg 53%) (ortho endo:exo:meta endo:exo 6:3:1.5:1): IR (neat) 1755 (br CO_2Me) cm^{-1}; ^1H NMR (250 MHz) complex δ 5.34, 3.4, 5.48 (d, J = 4.5 Hz, ortho endo, exo, meta endo C_4-H, respectively), 5.55 (s, meta exo C_4-H); HRMS (EI) m/z 336.1200, M^+, 366.1203 calcd for $C_{17}H_{20}O_7$.

Adducts 32. Flash chromatography (EtOAc–hexane, 1:5) gave an isomeric mixture of adducts **32** (203 mg, 67%) (ortho endo:exo 3:1) which afforded, on crystallization (ether–CH_2Cl_2–hexane), colorless crystals of the ortho endo isomer: mp 163–164 °C; IR (Nujol) 2319 (C≡N), 1746 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) δ 1.98 (dd, 1 H, $J_{H3\alpha-2\beta}$ = 6, $J_{H3\beta-3\alpha}$ = 12 Hz, H3α), 2.47 (ddd, 1 H, $J_{H3\beta-2\beta}$ = 4.5, $J_{H3\beta-H4}$ = 4.8 Hz, $J_{H3\beta-3\alpha}$ = 12 Hz, H3β), 2.93 (dd, 1 H, $J_{H2\beta-3\beta}$ = 4.5, $J_{H2\beta-3\alpha}$ = 6 Hz, H2β), 3.46 (AB q, 2 H, J = 17 Hz, CH_2), 3.83, 3.86, 3.87 (s, 3 H each, OMe), 5.43 (d, 1 H, J = 4.8 Hz, H4), 6.82, 6.85 (s, 1 H each, aromatic H); HRMS (EI) m/z 303.1101, M^+, 303.1107 calcd for $C_{16}H_{17}O_5N$. Anal. Calcd for $C_{16}H_{17}O_5N$: C, 63.36; H, 5.61. Found: C, 63.13; H, 5.69.

Exo isomer (oil): IR (neat) 2241 (C≡N), 1736 (br, CO_2Me) cm^{-1}; ^1H NMR (250 MHz) δ 1.69 (dd, 1 H, $J_{H3\alpha-2\alpha}$ = 10, $J_{H3\alpha-3\beta}$ = 12 Hz, H3α), 2.65 (ddd, 1 H, $J_{H2\alpha-3\beta}$ = 4.5 Hz, $J_{H4-3\beta}$ = 4.7 Hz, $J_{H3\beta-3\alpha}$ = 12 Hz, H3β), 3.43 (dd, 1 H, $J_{H2\alpha-3\beta}$ = 4.5 Hz, $J_{H2\alpha-3\alpha}$ = 10 Hz, $H_{2\alpha}$) 3.32 (AB q, 2 H, J = 17 Hz, CH_2) 3.75, 3.88, 3.91 (s, 3 H each, OMe), 5.42 (d, 1 H, J = 4.7 Hz, H4), 6.87, 6.98 (s, 1 H each, aromatic H); HRMS (EI) m/z 303.1101, M^+, 303.1107 calcd for $C_{16}H_{17}O_5N$.

Adducts 33 and 34. Preparative TLC on silica (EtOAc–hexane, 1:5, triple elution) gave a mixture of endo/exo isomers of ortho and endo isomer of meta (3:1.5:2, respectively) (198 mg, 62%). Meta endo isomer **34** (oil): IR (neat) 1733 (CO_2Me), 1707 ($COCH_3$) cm^{-1}; ^1H NMR (250 MHz) δ 1.87 (dd, 1 H, $J_{H2\alpha-3\alpha}$ = 8.7, $J_{H2\alpha-2\beta}$ = 10.8 Hz, H2α), 2.18 (dd, 1 H, $J_{H2\beta-3\alpha}$ = 4.3, $J_{H2\beta-2\alpha}$ = 10.8 Hz, H2β), 2.29 (s, 3 H, $COCH_3$), 2.65 (dd, 1 H, $J_{H3\alpha-2\beta}$ = 4.31, $J_{H3\alpha-2\alpha}$ = 8.7 Hz, H3α), 3.21, 3.3 (d, 1 H each, J = 15.2 Hz, CH_2), 3.75, 3.86, 3.88 (s, 3 H each, OMe), 5.46 (s, 1 H, H4), 6.86, 6.90 (s, 1 H each, aromatic H); HRMS (EI) m/z 320.1256, M^+, 320.1260 calcd for $C_{17}H_{20}O_6$.

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Diels–Alder Reactions of 1,2-(1,1′-Binaphthalene-2,2′-diyldisulfonyl)ethylene with Symmetrical and Unsymmetrical Dienes[1]

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The C_2-symmetrical chiral reagent 1,2-(1,1′-binaphthalene-2,2′-diyldisulfonyl)ethylene (1) is a reactive dienophile and forms Diels–Alder adducts with symmetrical and unsymmetrical dienes. In the case of unsymmetrical dienes the reaction affords, in most cases, a single diastereomeric adduct whose stereochemistry has been determined by NMR spectroscopy and confirmed by X-ray structure determination of selected adducts. The arylsulfonyl groups can be removed with formation of a double bond, making 1 a chiral synthetic equivalent of acetylene in [4 + 2]-cycloaddition reactions. The binaphthyl auxiliary can be recovered and recycled.

Among the electron-withdrawing groups which most commonly activate the standard Diels–Alder reaction (e.g. COR, COOR, CN, NO_2, SOR, SO_2R) only a few (e.g. COR, CO_2R, SOR, SO_2R) are amenable to the introduction of a chiral auxiliary, and even fewer (e.g. SOR, SO_2R) allow the facile removal of both the activating functionality and the chiral auxiliary. We have developed the sulfonyl activated, C_2-symmetrical chiral dienophile **1**, and we now report its preparation and reactivity, as well as a discussion on the stereochemistry and the factors influencing diastereoselectivity in its [4 + 2]-cycloadditions. Synthetic applications, which are dependent on the availability of quantities of the reagent in optically pure form, will be reported in due course.

Dienophile **1** is structurally similar to (*Z*)- and (*E*)-1,2-bis(phenylsulfonyl)ethylenes ($PhSO_2CH{=}CHSO_2Ph$), thus maintaining the chemical properties associated with these achiral reagents, which have been reported as synthetic equivalents of acetylene in [4 + 2]-cycloaddition reactions.[3-5]

Results and Discussion

Preparation of Dienophile 1. Dienophile **1** is readily available from dithiol **2**[6] by the methodology used for ob-

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