Synthesis of 1,3-Benzodioxoles, 1,3-Benzoxathioles and 1,3-Benzodithioles from Allenic Derivatives

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Benzo-condensed five-membered heterocyclic rings containing two heteroatoms have been synthesized starting from disubstituted benzenes and allenic derivatives. The structure of all products was corroborated by elemental analysis and ir and ^{1}H nmr spectroscopy.

It is well known that allenes are versatile reagents in organic syntheses [1]. In particular, cycloaddition reactions of allenes yield carbocyclic and heterocyclic compounds *via* radical or ionic intermediates [2-7]. Allenic compounds react also with equimolar quantities of alcoholates and thiolates to yield ethers and thioethers of enols [8,9]. On the other hand, attempts to add a second molecule of alcoholate or thiolate to the enol ethers or thioethers in a Michael type reaction were unsuccessful [9]. Moreover, reactions of allenes with bifunctionalized benzenes have never been reported in the literature.

Due to the interest in the biological field for benzo-condensed five-membered heterocyclic compounds [10-16] we were prompted to try a new route to the synthesis of such products by attempting the reaction between allenic esters and bifunctionalized benzenes, in view of the fact that an intramolecular reaction would be more facile than an intermolecular one. In fact, a primary reaction of the central electrophilic carbon of the allene with one nucleophilic group of the bifunctionalized benzene could be followed by an intramolecular Michael type addition of the intermediate with the second nucleophilic group to yield the expected five-membered heterocycle. This attempt was successful and the results are reported herewith.

Equimolar amounts of bifunctionalized benzenes **1a-c** and allenic compounds **2a-e** yield heterocyclic compounds **3a-e, 4a-e, 5a,c** in good yields (Scheme 1). All reactions were performed at room temperature, in acetone, in the presence of potassium carbonate with the same ex-
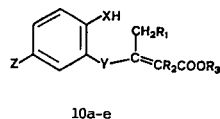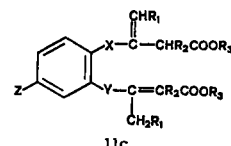
Chart 1
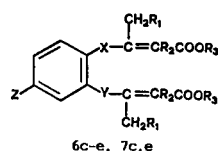
6c: X=Y=O, Z=R$_2$=H, R$_1$=R$_3$=Me
6d: X=Y=O, Z=R$_2$=H, R$_1$=Me, R$_3$=Et
6e: X=Y=O, Z=R$_2$=H, R$_1$=COOMe, R$_3$=Me
7c: X=O, Y=S, Z=R$_2$=H, R$_1$=R$_3$=Me
7e: X=O, Y=S, Z=R$_2$=H, R$_1$=COOMe, R$_3$=Me
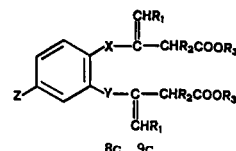
8c: X=Y=O, Z=R$_2$=H, R$_1$=R$_3$=Me
9c: X=Y=S, Z=R$_1$=R$_3$=Me, R$_2$=H

10a: X=O, Y=S, Z=R$_1$=H, R$_2$=R$_3$=Me
10b: X=O, Y=S, Z=R$_1$=H, R$_2$=Me, R$_3$=Et
10c: X=O, Y=S, Z=R$_2$=H, R$_1$=R$_3$=Me
10d: X=O, Y=S, Z=R$_2$=H, R$_1$=Me, R$_3$=Et
10e: X=O, Y=S, Z=R$_2$=H, R$_1$=COOMe, R$_3$=Me

11c: X=O, Y=S, Z=R$_2$=H, R$_1$=R$_3$=Me

Scheme 1
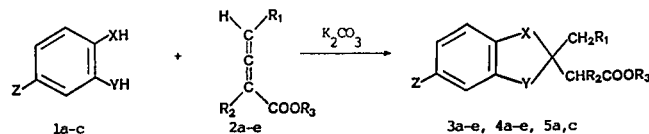
1a: X=Y=O, Z=H
1b: X=O, Y=S, Z=H
1c: X=Y=S, Z=Me

2a: R$_1$=H, R$_2$=R$_3$=Me
2b: R$_1$=H, R$_2$=Me, R$_3$=Et
2c: R$_1$=R$_3$=Me, R$_2$=H
2d: R$_1$=Me, R$_2$=H, R$_3$=Et
2e: R$_1$=COOMe, R$_2$=H, R$_3$=Me

3a: X=Y=O, Z=R$_1$=H, R$_2$=R$_3$=Me
3b: X=Y=O, Z=R$_1$=H, R$_2$=Me, R$_3$=Et
3c: X=Y=O, Z=R$_2$=H, R$_1$=R$_3$=Me
3d: X=Y=O, Z=R$_2$=H, R$_1$=Me, R$_3$=Et
3e: X=Y=O, Z=R$_2$=H, R$_1$=COOMe, R$_3$=Me
4a: X=O, Y=S, Z=R$_1$=H, R$_2$=R$_3$=Me
4b: X=O, Y=S, Z=R$_1$=H, R$_2$=Me, R$_3$=Et
4c: X=O, Y=S, Z=R$_2$=H, R$_1$=R$_3$=Me
4d: X=O, Y=S, Z=R$_2$=H, R$_1$=Me R$_3$=Et
4e: X=O, Y=S, Z=R$_2$=H, R$_1$=COOMe, R$_3$=Me
5a: X=Y=S, Z=R$_2$=R$_3$=Me, R$_1$=H
5c: X=Y=S, Z=R$_1$=R$_3$=Me, R$_2$=H

Table 1

Reaction of Bifunctionalized Benzenes with Allenes

Substrate	Allene	Products	Yield %
1a	2a	3a	48
1a	2b	3b	55
1a	2c	3c	49
		6c	4
		8c	26
1a	2d	3d	51
		6d	20
1a	2e	3e	58
		6e	7
1b	2a	4a	25
		10a	50
1b	2b	4b	63
		10b	14
1b	2c	4c	64
		7c	7
		10c	16
		11c	3
1b	2d	4d	68
		10d	3
1d	2e	4e	30
		7e	8
		10e	28
1c	2a	5a	51
1c	2c	5c	55
		9c	15

perimental procedure used in previous, similar reactions [12,17,18].

As shown in Table 1 and in Chart 1, other non cyclic, addition products were obtained together with the heterocyclic compounds.

Analysis of the products obtained in the various reactions reported in the Table 1 suggests the following reaction scheme (Scheme 2) which seems to be in agreement with what is known about the reactivities of the compounds studied [1,8,9].

In fact, the primary nucleophilic attack of the phenoxide or thiophenoxide ion to the central carbon atom of the allene would yield intermediate "A". This in turn would undergo 1,5 or 1,3 hydrogen shifts to yield compounds "B" and "C". "B" would eventually yield the cyclic compound "D" via an intramolecular Michael type addition of the second nucleophilic center to the carbon atom β to the ester moiety. Alternatively, the nucleophilic center of "B" may react with a second molecule of allene forming compounds "E" (with both groups α,β-unsaturated) and "F" (with one group α,β-unsaturated and the other β,γ-unsaturated). This was shown from the isolation:

i) Of Derivatives of the "B" Type in the Reactions Performed with 1b.

These products were transformed in "D" upon further treatment with the potassium carbonate-acetone system (Scheme 3). It is also worth noticing that, in the presence of allene 2c, 10c yields also the addition products 7c and 11c besides the heterocyclic compounds 4c.

ii) Of Derivatives of the "E" and "F" Types.

On the other hand, "C" can only react with a second molecule of allene to yield compounds of the "G" type (e.g. 8c, 9c, where the two aliphatic groups are both β,γ-unsaturated) or of the "H" type (never isolated, where one of the two aliphatic groups is α,β-unsaturated and the other β,γ-unsaturated as in "F" but with the positions inverted; "F" and "H" are identical when X = Y).

Scheme 2

Scheme 3

$$10a\text{-}e \xrightarrow{K_2CO_3} 4a\text{-}e$$

$$10c + 2c \xrightarrow{K_2CO_3} 4c + 7c + 11c$$
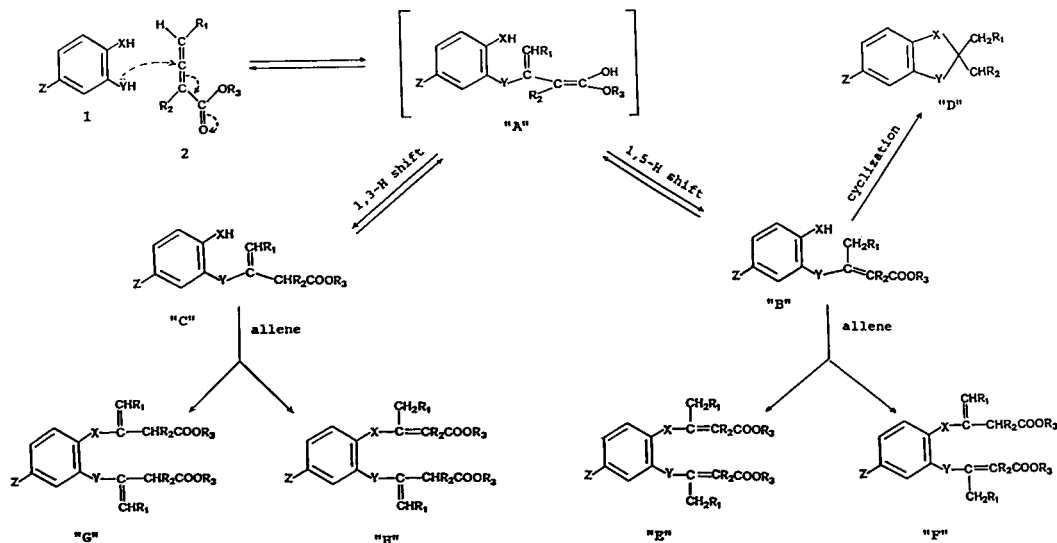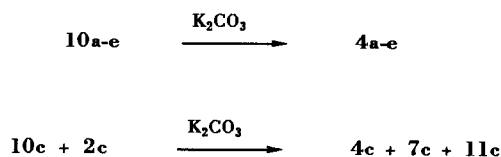
In Table 1 are reported the yields of the reaction products which were actually isolated. It must be pointed out that tlc and/or hplc revealed the presence of other minor reaction products. Many of the unidentified compounds are polymerization products of the allenes; some of them, on the other hand, are most reasonably products reported

Table 2

^{1}H NMR Chemical Shifts and Multiplicities for
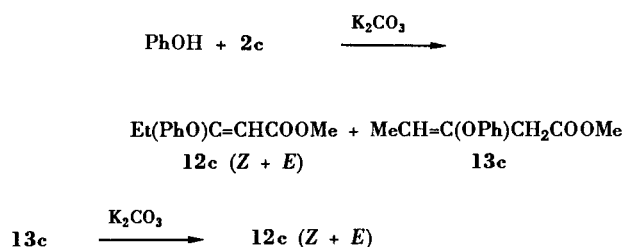Compounds 3a-c, 4a-e, 5a,c [a,b]

Compounds	Signals
3a	1.29 (3H, d, CH-CH_3), 1.70 (3H, s, CH$_3$), 3.08 (1H, q, CH), 3.68 (3H, s, OCH$_3$), 6.78 (4H, m, Ar-H)
3b	1.35 (3H, t, OCH$_2$-CH_3), 1.50 (3H, d, CH-CH_3), 1.90 (3H, s, CH$_3$), 3.22 (1H, q, CH-CH$_3$), 4.30 (2H, q, OCH_2-CH$_3$), 6.94 (4H, m, Ar-H)
3c	1.01 (3H, t, CH$_2$-CH_3), 2.13 (2H, q, CH_2-CH$_3$), 2.95 (2H, s, CH$_2$-CO), 3.62 (3H, s, OCH$_3$), 6.78 (4H, m, Ar-H)
3d	0.97 (3H, t, CH-CH_3), 1.09 (3H, t, OCH$_2$-CH_3), 2.10 (2H, q, CH_2-CH$_3$), 2.88 (2H, s, CH$_2$-CO), 4.10 (2H, q, OCH_2-CH$_3$), 6.70 (4H, m, Ar-H)
3e	3.26 (4H, s, CH$_2$), 3.65 (6H, s, OCH$_3$), 6.77 (4H, s, Ar-H)
4a	1.36 (3H, d, CH-CH_3), 1.89 (3H, s, CH$_3$), 3.19 (1H, q, CH-CH$_3$), 3.70 (3H, s, OCH$_3$), 6.90 (4H, m, Ar-H)
4b	1.28 (3H, t, OCH$_2$-CH_3), 1.35 (3H, d, CH-CH_3), 1.85 (3H, s, CH$_3$), 3.15 (1H, q, CH-CH$_3$), 4.19 (2H, q, OCH_2-CH$_3$), 6.90 (4H, m, Ar-H)
4c	1.15 (3H, t, CH$_2$-CH_3), 2.23 (2H, q, CH_2-CH$_3$), 3.18 (2H, s, CH$_2$-CO), 3.70 (3H, s, OCH$_3$), 7.00 (4H, m, Ar-H)
4d	1.06 (3H, t, CH$_2$-CH_3), 1.18 (3H, t, OCH$_2$-CH_3), 2.13 (2H, q, CH_2-CH$_3$), 3.08 (2H, s, CH$_2$-CO), 4.10 (2H, q, OCH_2-CH$_3$), 6.90 (4H, q, Ar-H)
4e	3.33 (2H, d, CH_AH$_B$-CO, J$_{AB}$ = 16 Hz), 3.55 (2H, d, CH$_A$H$_B$-CO, J$_{AB}$ = 16 Hz), 3.71 (6H, s, OCH$_3$), 6.95 (4H, m, Ar-H)
5a	1.40 (3H, d, CH-CH_3), 1.90 (3H, s, CH$_3$), 2.30 (3H, s, Ar-CH$_3$), 3.20 (1H, q, CH-CH$_3$), 3.65 (3H, s, OCH$_3$), 6.90 (3H, m, Ar-H)
5c	1.15 (3H, t, CH$_2$-CH_3), 2.30 (3H, s, Ar-CH$_3$), 2.35 (2H, q, CH_2-CH$_3$), 3.22 (2H, s, CH$_2$-CO), 3.68 (3H, s, OCH$_3$), 7.10 (3H, m, Ar-H)

[a] Signals (in parentheses) are expressed: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; long range coupling are not being considered. [b] In deuteriochloroform; δ TMS = 0.00 ppm.

in Scheme 2 which could not be isolated and purified because of their relatively low yield [19].

Scheme 2 does not include all possible reactions and equilibria of the bifunctionalized benzene-allene system. A reasonable product is also the cited derivative "**H**". Moreover, all the unsaturated groups can present either E or Z geometry. Finally, Scheme 2 does not indicate the possible isomerization equilibria between the non cyclic products or intermediates. That some isomerization may occur can be inferred from the results obtained in the reaction of phenol with allene 2c where it was possible to isolate three fractions. One of them was the β,γ-unsaturated compound 13c. The other two fractions were the α,β-unsaturated compound 12c in the two isomeric forms Z and E (Scheme 4) [20]. If the unconjugated product 13c is left for longer periods in the same reaction conditions, it isomerizes to the conjugated one. Thus one cannot exclude that some isomerization occurs also in the reactions of the disubstituted benzenes [21].

Scheme 4

$$PhOH + 2c \xrightarrow{K_2CO_3}$$

$$Et(PhO)C{=}CHCOOMe + MeCH{=}C(OPh)CH_2COOMe$$
$$12c\ (Z + E) \qquad\qquad 13c$$

$$13c \xrightarrow{K_2CO_3} 12c\ (Z + E)$$

In conclusion, kinetic and/or thermodynamic control, which can vary with the nature of the nucleophilic atoms in the bifunctionalized benzene, the substituents in the allene and reaction time, would lead to a different product distribution in the various cases.

The structure of compounds 3a-c, 4a-c, 5a-c was unambiguously determined by means of elemental analysis, ir and ^{1}H nmr spectra. Chemical shifts and multiplicities in proton spectra (see Table 2) permitted an easy assignment of all resonance frequences in the aliphatic region. We did not attempt to assign every single peak in the aromatic region of the spectra. It is worthwhile noticing that the ^{1}H nmr spectrum of 4e shows an AB system pattern centered at δ 3.33 and δ 3.55, respectively, due to the geminal protons in the two CH$_2$ groups. The value of the coupling constant J_{AB} = 16 Hz is typical of such a system.

The structure of all non cyclic compounds 6c-e, 7c,e, 8c, 9c, 10a,c-e, Z-12c, E-12c, 13c was also determined by means of elemental analysis, ir and ^{1}H nmr spectra. All ^{1}H nmr parameters are reported in Table 3.

In the reaction of 1a with 2c the chromatographic separation afforded three fractions: the first and the third fractions were identified as the products 3c (see Table 2)

Table 3

¹H-NMR Chemical Shift and Multiplicities for Compounds 6c-e,
7c,e, 8c, 9c, 10a,c-e, Z-12c, E-12c, 13c [a,b]

Compounds	Signals
6c	1.25 (6H, t, CH$_2$-CH$_3$), 2.95 (4H, q, CH$_2$-CH$_3$), 3.60 (6H, s, OCH$_3$), 4.80 (2H, s, CH), 7.10 (4H, m, Ar-H)
6d	1.20 (6H, t, CH$_2$-CH$_3$), 1.22 (6H, t, OCH$_2$-CH$_3$), 2.91 (4H, q, CH$_2$-CH$_3$), 4.09 (4H, q, OCH$_2$-CH$_3$), 4.77 (2H, s, CH), 7.20 (4H, m, Ar-H)
6e	3.60 (6H, s, CH$_2$-COOCH$_3$), 3.75 (6H, s, CH-COOCH$_3$), 4.00 (4H, s, CH$_2$), 4.98 (2H, s, CH), 7.28 (4H, m, Ar-H)
7c	1.22 (6H, t, CH$_2$-CH$_3$), 2.60 (4H, q, CH$_2$-CH$_3$), 3.61 (6H, s, OCH$_3$), 5.15 (2H, s, CH), 7.25 (4H, m, Ar-H)
7e	3.73 (6H, s, CH$_2$-COOCH$_3$), 3.79 (6H, s, CH-COOCH$_3$), 3.89 (4H, s, CH$_2$), 5.42 (2H, s, CH), 6.91 (4H, m, Ar-H)
8c	1.58 (6H, t, CH$_2$-CH$_3$), 3.31 (4H, s, CH$_2$), 3.68 (6H, s, OCH$_3$), 4.78 (2H, q, CH-CH$_3$), 7.06 (4H, m, Ar-H)
9c	1.78 (3H, d, CH-CH$_3$), 1.82 (3H, d, CH-CH$_3$), 2.30 (3H, s, Ar-CH$_3$), 3.22 (2H, s, CH$_2$), 3.25 (2H, s, CH$_2$), 3.64 (6H, s, OCH$_3$), 6.08 (1H, q, CH), 6.19 (1H, q, CH), 7.20 (3H, m, Ar-H)
10a	1.96 (3H, s, CH$_3$-C-S), 2.15 (3H, s, CH$_3$-C-CO), 3.84 (3H, s, OCH$_3$), 7.20 (4H, m, Ar-H)
10c	1.28 (3H, t, CH$_2$-CH$_3$), 2.89 (2H, q, CH$_2$-CH$_3$), 3.61 (3H, s, OCH$_3$), 5.10 (1H, s, CH), 7.05 (4H, m, Ar-H)
10d	0.98 (3H, t, CH$_2$-CH$_3$), 1.33 (3H, t, OCH-CH$_3$), 2.09 (2H, q, CH$_2$-CH$_3$), 4.26 (2H, q, OCH$_2$-CH$_3$), 5.96 (1H, s, CH), 7.20 (4H, m, Ar-H)
10e	3.62 (6H, s, OCH$_3$), 3.86 (2H, s, CH$_2$), 5.44 (1H, s, CH), 7.10 (4H, m, Ar-H)
Z-12c	1.26 (3H, t, CH$_2$-CH$_3$), 2.96 (2H, q, CH$_2$-CH$_3$), 3.62 (3H, s, OCH$_3$), 4.79 (1H, s, CH), 7.20 (5H, m, Ar-H)
E-12c	1.07 (3H, t, CH$_2$-CH$_3$), 2.23 (2H, q, CH$_2$-CH$_3$), 3.63 (3H, s, OCH$_3$), 5.44 (1H, s, CH), 7.10 (5H, m, Ar-H)
13c	1.76 (3H, d, CH-CH$_3$), 3.44 (2H, s, CH$_2$), 3.84 (3H, s, OCH$_3$), 5.12 (1H, q CH-CH$_3$), 7.25 (5H, m, Ar-H)

[a] Signals (in parentheses) are expressed: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; long range coupling are not being considered. [b] In deuteriochloroform; δ TMS = 0.00 ppm.

and 8c (see Table 3), respectively. The second fraction was an inseparable mixture of three products. A number of signals in the aliphatic region of its ¹H nmr spectrum could be easily assigned by comparison with the spectra of the pure compounds to 3c (one triplet centered at δ 1.01, one quartet centered at δ 2.13, two singlets centered at δ 2.95 and δ 3.62) and to 8c (one doublet centered at δ 1.58, one quartet centered at δ 4.78, two singlets centered at δ 3.31 and δ 3.68). The remaining signals of the aliphatic

region (one triplet centered at δ 1.25, one quartet centered at δ 2.95, two singlets centered at δ 3.60 and δ 4.80) were easily assigned to the α,β-unsaturated ester 6c (see Table 3). It must be pointed out that the aromatic region is too complex to isolate the signals of the three products 3c, 6c, 8c. Further evidence of this was obtained by 2D-¹H nmr analysis (COSY-90). The percentage of the three compounds, 3c, 6c, 8c, calculated from the integrals of the assigned peaks, was 29%, 43%, 28%, respectively.

The reaction of 1b with 2c yields three chromatographic fractions. The first fractions was identified as pure (hplc) 4c by its ¹H nmr spectrum (see Table 2). The second fraction is a mixture (hplc) of two components. One of them is 4c (hplc). The ¹H nmr spectrum shows two triplets centered at δ 1.15 and δ 1.22, two quadruplets centered at δ 2.23 and δ 2.60, four singlets centered at δ 3.18, δ 3.61, δ 3.70, δ 5.15 and several multiplets in the aromatic region between δ 6.81 and δ 7.60. Comparison with ¹H nmr spectrum of 4c permits the elimination of a number of aliphatic signals of 4c (the aromatic region is too complex to isolate the signals of 4c). The remaining signals (δ 1.22, δ 2.60, δ 3.61, δ 5.15) have been attributed to compound 7c (see Table 3). The percentage of the two compounds 4c and 7c are 30% and 70%, respectively, as calculated by the values of the integrals in the ¹H nmr spectrum relative to the peaks assigned to the two compounds.

The third fraction is a mixture (hplc) of two major components and several minor unidentified products. The ¹H nmr spectrum of the mixture, disregarding the signal of minor intensity shows several peaks (one triplet centered at δ 1.25, one quartet centered at δ 2.95, two singlets centered at δ 3.60 and δ 4.80 and several multiplets in the aromatic region between δ 6.88 and δ 7.40) which indicate the presence of 7c (see Table 3). A number of the signals (one doublet centered at δ 1.56, one singlet centered at δ 3.20 and one quartet centered at δ 4.80) can be attributed to a β,γ-unsaturated moiety as indicated by comparison with the ¹H nmr spectrum of 8c. We attribute these signals to the formation of compound 11c which has one α,β- and one β,γ-unsaturated moiety. This is in accord also with the results obtained in the reaction of 10c with 2c (see above and experimental). Calculation of the integral values of the assigned peaks showed that the percentage ratio of the two compounds of the mixture was 55:45.

The reaction of phenol with allene 2c was the only case where Z and E isomers could be separated by column chromatography so that it became possible to use ¹H nmr spectra for the assignment of the precise geometry. The signals centered at δ 2.96 and δ 4.79 of one of the two isomers of 12c, compared [9] with the signals centered at δ 2.23 and δ 5.54 of the other isomers, permitted the assignment of the Z and E configuration (see Table 3).

EXPERIMENTAL

The ^{1}H nmr spectra were recorded on a Varian VXR-300 spectrometer. The ir spectra were recorded using sodium chloride plates on a Perkin-Elmer 1310 grating spectrophotometer. The hplc analyses were performed by using a Waters 600 apparatus with an ODS column (4.6 x 250 mm) and uv detector. The preparative hplc was performed by using an ODS column (10 x 250 mm). All flash-chromatographies were performed on silica G60 (Merck) columns. The tlc analyses were carried out on a silica gel 60 F_{254} plates (Merck); the location of spots was detected by illumination with a uv lamp. Melting points were determined on a Kofler hot stage microscope and are uncorrected. Elemental analyses were carried out on a Carlo Erba Model 1106 Elemental Analyzer.

1,2-Benzenediol (1a) and 4-methyl-1,2-benzenedithiol (1c) were purchased from Fluka and were used directly. 2-Hydroxybenzenethiol (1b) [22], methyl 2-methyl-2,3-butadienoate (2a) [23], ethyl 2-methyl-2,3-butadienoate (2b) [24], methyl 2,3-pentadienoate (2c) [24], ethyl 2,3-pentadienoate (2d) [24] and dimethyl 2,3-pentadienedioate (2e) [25] were prepared by literature procedures. Acetone was purchased from Fluka and was distilled over calcium chloride before use.

Reaction of 1a with 2a. General Procedure.

A mixture of 1a (48 mmoles), anhydrous potassium carbonate (96 mmoles) and dry acetone (50 ml) was stirred and flushed with nitrogen for 2 hours at room temperature. A solution of 2a (48 mmoles) in acetone (10 ml) was added dropwise and the stirring was continued for 2 days. The mixture was poured into water and then extracted with ether. The organic layer was washed with 10% aqueous sodium hydroxide and then dried over anhydrous calcium chloride. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a residue which was purified by flash-chromatography. On elution with hexane-ethyl acetate (10:1), methyl 2-(2-methyl-1,3-benzodioxol-2-yl)propanoate (3a) was obtained as a yellow viscous oil, yield 48%; ir (neat): 1745 cm^{-1} (C = O).

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.71; H, 6.2.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted 1a.

Reaction of 1a with 2b.

The reaction was performed according to the method described above. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a product which was flash-chromatographed. On elution with hexane-ethyl acetate (20:1), ethyl 2-(2-methyl-1,3-benzodioxol-2-yl)propanoate (3b) was obtained as a yellow viscous oil, yield 55%; ir (neat): 1740 cm^{-1} (C = O).

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 65.97; H, 6.74.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted 1a.

Reaction of 1a with 2c.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed three significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl

acetate (5:1) as eluent. Elution of the crude product gave three fractions. The first fraction was methyl 2-ethyl-1,3-benzodioxol-2-ylacetate (3c), a colourless oil, yield 45%; ir (neat): 1740 cm^{-1} (C = O).

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.69; H, 6.31.

The second fraction was an oil (1.5 g), which by hplc analysis turned out to be a mixture of three compounds. By ^{1}H nmr spectra these compounds were identified as 3c (29%), dimethyl 3,3'-(1,2-phenylenedioxy)di-3-pentenoate (8c) (28%) and dimethyl 3,3'-(1,2-phenylenedioxy)di-2-pentenoate (6c) (43%), respectively (see Discussion).

The third fraction was 8c, a pale yellow viscous oil, yield 24%; ir (neat): 1745 cm^{-1} (C = O).

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 64.65; H, 6.63. Found: C, 64.52; H, 6.57.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted 1a.

Reaction of 1a with 2d.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction was ethyl 2-ethyl-1,3-benzodioxol-2-ylacetate (3d), a pale yellow oil, yield 51%; ir (neat): 1740 cm^{-1} (C = O).

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 66.01; H, 6.73.

The second fraction was diethyl 3,3'-(1,2-phenylenedioxy)di-2-pentenoate (6d), a pale yellow viscous oil, yield 20%; ir (neat): 1740, 1720 cm^{-1} (C = O).

Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.14; H, 7.15.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted 1a.

Reaction of 1a with 2e.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed two spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using petroleum ether-ether (2:1) as eluent. Elution of the crude product gave two fractions. The first fraction was methyl 2-(carbomethoxymethyl)-1,3-benzodioxol-2-ylacetate (3e), a colourless oil, yield 58%; ir (neat): 1745 cm^{-1} (C = O).

Anal. Calcd. for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.51; H, 5.19.

The second fraction was tetramethyl 3,3'-(1,2-phenylenedioxy)-di-2-pentenedioate (6e), colourless crystals, yield 7%, mp 58-60°; ir (nujol): 1745, 1710 cm^{-1} (C = O).

Anal. Calcd. for $C_{20}H_{22}O_{10}$: C, 56.87; H, 5.25. Found: C, 56.74; H, 5.13.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted 1a.

Reaction of 1b with 2a.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a

residue, which was purified by column flash-chromatography. On elution with hexane-ethyl acetate (10:1) methyl 2-(2-methyl-1,3-benzoxathiol-2-yl)propanoate (**4a**) was obtained as a colourless oil, yield 25%; ir (neat): 1740 cm⁻¹ (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45. Found: C, 60.33; H, 5.81; S, 13.28.

The aqueous basic layer was acidified and extracted with ether. The ethereal extracts were washed with water and dried over anhydrous sodium sulfate. The tlc analysis showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction consisted of a small amount of unreacted **1b**.

The second fraction was methyl 3-[(2-hydroxyphenyl)thio]-2-methyl-2-butenoate (**10a**), colourless crystals, yield 50%, mp 79-81°; ir (nujol): 3380 (O–H), 1680 cm⁻¹ (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45. Found: C, 60.36; H, 5.79; S, 13.31.

Conversion of 10a to 4a.

A mixture of **10a** (10 mmoles), anhydrous potassium carbonate (20 mmoles) and dry acetone (15 ml) was stirred for almost 2 days and worked up in the same manner described above to furnish **4a** in almost quantitative yield. The ir and nmr spectra were identical with those of the product **4a** described above.

Reaction of 1b with 2b.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a residue, which was purified by column flash-chromatography. On elution with hexane-ethyl acetate (10:1) ethyl 2-(2-methyl-1,3-benzoxathiol-2-yl)propanoate (**4b**) was obtained as a colourless oil, yield 63%; ir (neat): 1740 cm⁻¹ (C=O).

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39; S, 12.71. Found: C, 61.70; H, 6.34; S, 12.59.

The aqueous basic layer was worked up in the same manner as described for the reaction with **2a**. The tlc analysis showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction was a small amount of unreacted **1b**.

The second fraction was an oil, which by hplc analysis turned out to be an admixture of several inseparable and unidentifiable products. One component of this mixture proved to be ethyl 3-[(2-hydroxyphenyl)thio]-2-methyl-2-butenoate (**10b**). In fact, by treatment of this oil with potassium carbonate in acetone, as described for the conversion of **10a** to **4a**, another products mixture was obtained, which was column flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. The first fraction gave **4b** in 14% yield; the ir and nmr spectra were identical with those of the product **4b** described above.

The second fraction gave an oil, which turned out to be an admixture of several inseparable and unidentifiable compounds.

Reaction of 1b with 2c.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed three significant spots. The solvent evaporation *in vacuo* gave a viscous oil, which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave three fractions. The first fraction was methyl 2-ethyl-1,3-benzoxathiol-2-ylacetate (**4c**), a colourless oil, yield 61%; ir (neat): 1740 cm⁻¹ (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45. Found: C, 60.30; H, 5.81; S, 13.28.

The second fraction was an oil (0.9 g), which by hplc analysis turned out to be an admixture of two compounds. By ¹H nmr spectra (see Discussion) these compounds were identified as **4c** (30%) and dimethyl 3,3'-(1,2-phenylenoxythio)di-2-pentenoate (**7c**) (70%), respectively.

The third fraction (1.2 g) was a mixture of several compounds (hplc). The major components were identified by ¹H nmr spectra (see Discussion) as **7c** (50%) and methyl 3-[2-[(1-ethyl-2-carbomethoxyethenyl)thio]phenoxy]-3-pentenoate (**11c**) (40%).

The aqueous basic layer was acidified and extracted with ether. The ethereal extracts were washed with water and dried over anhydrous sodium sulfate. The tlc analysis showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction was a small amount of unreacted **1b**.

The second fraction was methyl 3-[(2-hydroxyphenyl)thio]-2-pentenoate (**10c**), white crystals, yield 16%, mp 74-75°; ir (neat): 3400 (O–H), 1710 cm⁻¹ (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.45. Found: C, 60.28; H, 5.86; S, 13.33.

Conversion of 10c to 4c.

The reaction was performed in the same manner described for the conversion of **10a** to **4a**. Only **4c** was obtained in almost quantitative yield. The ir and nmr spectra were identical with those of the product **4c** described above.

Reaction of 10c with 2c.

A mixture of **10c** (6 mmoles), **2c** (6 mmoles), anhydrous potassium carbonate (6 mmoles) and dry acetone (15 ml) was stirred for almost 2 days and worked up in the same manner as described above. The tlc analysis of the ethereal solution showed three significant spots. The solvent evaporation *in vacuo* gave a viscous oil, which was flash-chromatographed using hexane-ethyl acetate (5:1) as eluent. Elution of the crude product gave three fractions. The first fraction was **4c**, yield 40%. The ir and nmr spectra were identical with those of the product **4c** described above.

The second fraction was an oil (0.15 g), which by hplc analysis turned out to be an admixture of two compounds. By ¹H nmr spectra (see Discussion) these compounds were identified as **4c** (30%) and **7c** (70%), respectively.

The third fraction was a mixture (0.2 g) of several components. By ¹H nmr spectra (see Discussion) two of these compounds were identified as **7c** (50%) and **11c** (35%), respectively.

Reaction of 1b with 2d.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a residue which was purified by column flash-chromatography. On elution with petroleum ether-ether (20:1) ethyl 2-ethyl-1,3-benzoxathiol-2-ylacetate (**4d**) was obtained as a colourless oil, yield 68%; ir (neat): 1735 cm⁻¹ (C=O).

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39; S, 12.71. Found: C, 61.70; H, 6.30; S, 12.55.

The aqueous basic layer was acidified and extracted with ether. The ethereal extracts were washed with water and dried over anhydrous sodium sulfate. The tlc analysis showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction was a small amount of unreacted **1b**.

The second fraction was ethyl 3-[(2-hydroxyphenyl)thio]-2-pentenoate (**10d**), white crystals, yield 3%, mp 83-85°; ir (carbon tetrachloride): 3460 (O–H), 1710 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39; S, 12.71. Found: C, 61.73; H, 6.28; S, 12.59.

Conversion of 10d to 4d.

The reaction was performed in the same manner as described for the conversion of **10a** to **4a**. Only **4d** was obtained in almost quantitative yield. The ir and nmr spectra were identical with those of the product **4d** described above.

Reaction of 1b with 2e.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was separated by preparative hplc using ethanol-water (4:1) as eluent. Elution of the crude product gave two fractions. The first fraction was methyl 2-(carbomethoxymethyl)-1,3-benzoxathiol-2-ylacetate (**4e**), a pale yellow oil, yield 30%; ir (neat): 1745 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{14}O_4S$: C, 55.30; H, 5.00; S, 11.36. Found: C, 55.22; H, 4.93; S, 11.20.

The second fraction gave tetramethyl 3,3'-(1,2-phenylenoxythio)di-2-pentenedioate (**7e**), yellow crystals, yield 8%, mp 83-84°; ir (nujol): 1755, 1725 cm^{-1} (C=O).

Anal. Calcd. for $C_{20}H_{22}O_9S$: C, 54.78; H, 5.06; S, 7.31. Found: C, 54.62; H, 5.01; S, 7.15.

The aqueous basic layer was acidified and extracted with ether. The ethereal extracts were washed with water and dried over anhydrous sodium sulfate. The tlc analysis showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (10:1) as eluent. Elution of the crude product gave two fractions. The first fraction was a small amount of unreacted **1b**.

The second fraction was dimethyl 3-[(2-hydroxyphenyl)thio]-2-pentenedioate (**10e**), white crystals, yield 28%, mp 177-178°; ir (nujol): 3440 (O–H), 1710 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{14}O_5S$: C, 55.30; H, 5.00; S, 11.36. Found: C, 55.17; H, 4.89; S, 11.15.

Conversion of 10e to 4e.

The reaction was performed in the same manner as described for the conversion of **10a** to **4a**. Only **4e** was obtained in almost quantitative yield. The ir and nmr spectra were identical with those of the product **4e** described above.

Reaction of 1c with 2a.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed one significant spot. The solvent evaporation *in vacuo* gave a residue, which was purified by column flash-chromatography. On elution with hexane-ethyl acetate (20:1) methyl 2-(2,5-dimethyl-1,3-benzodithiol-2-yl)propanoate (**5a**) was obtained as a pale yellow viscous oil, yield 51%; ir (neat): 1740 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.01; S, 23.89. Found: C, 58.05; H, 5.94; S, 23.70.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted **1c**.

Reaction of 1c with 2c.

The reaction was performed according to the procedure described above. The tlc analysis of the ethereal solution showed two significant spots. The solvent evaporation *in vacuo* gave a viscous oil which was flash-chromatographed using hexane-ethyl acetate (30:1) as eluent. Elution of the crude product gave two fractions. The first fraction was methyl 2-ethyl-5-methyl-1,3-benzodithiol-2-ylacetate (**5c**), a pale yellow viscous oil, yield 55%; ir (neat): 1745 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.01; S, 23.89. Found: C, 58.01; H, 5.96; S, 23.75.

The second fraction was dimethyl 3,3'-(4-methyl-1,2-phenylenedithio)di-3-pentenoate (**9c**), a pale yellow viscous oil, yield 15%; ir (neat): 1745 cm^{-1} (C=O).

Anal. Calcd. for $C_{19}H_{24}O_4S_2$: C, 59.97; H, 6.36; S, 16.85. Found: C, 59.79; H, 6.27; S, 16.68.

The aqueous basic layer was acidified and extracted with ether to give a small amount of unreacted **1c**.

Reaction of Phenol with 2c.

A mixture of phenol (44 mmoles), **2c** (44 mmoles), anhydrous potassium carbonate (50 mmoles) and anhydrous acetone (50 ml) was worked up following the general procedure described above. The tlc of the ethereal solution showed three spots. The solvent evaporation *in vacuo* gave an oil which was separated by preparative hplc using ethanol-water (4:1) as eluent. Elution of the crude product gave three fractions. The first fraction was methyl *Z*-3-phenoxy-2-pentenoate (*Z*-**12c**), a pale yellow oil, yield 51%; ir (neat): 1720 cm^{-1} (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.97; H, 6.81.

The second fraction was methyl 3-phenoxy-3-pentenoate (**13c**), a pale yellow oil, yield 20%; ir (neat): 1745 cm^{-1} (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.79; H, 6.80.

The third fraction was *E*-**12c**, a pale yellow oil, yield 13%; ir (neat): 1725 cm^{-1} (C=O).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.78.

Reaction of 12c and 13c with Phenol.

A mixture of **12c** (8 mmoles), phenol (8 mmoles), anhydrous potassium carbonate (10 mmoles) and anhydrous acetone was stirred for 2 days and worked up in the same manner as described above. The solvent evaporation *in vacuo* gave only unreacted **12c**.

On the contrary, **13c** was converted into **12c** (*Z* + *E*) in almost quantitative yield.

The isomer **13c** gave **12c** (*Z* + *E*) also from the reaction without phenol.

Acknowledgement.

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[19] The minimun yield necessary to obtain a pure product varies from 3% to 10-15% according to the product separation which could be obtained by the described column chromatography procedure (see Experimental).

[20] The monoaddition intermediates did not react with a second molecule of phenol even when the reaction was repeated with the pure isolated intermediates.

[21] Possible retro-Michael reaction might also be included in Scheme 2.

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