The Reactions of α-Alkoxy-Substituted Styrenes with Dimethyl Acetylenedicarboxylate and Dimethyl Fumarate Novel Adducts in the Reaction with Dimethyl Fumarate

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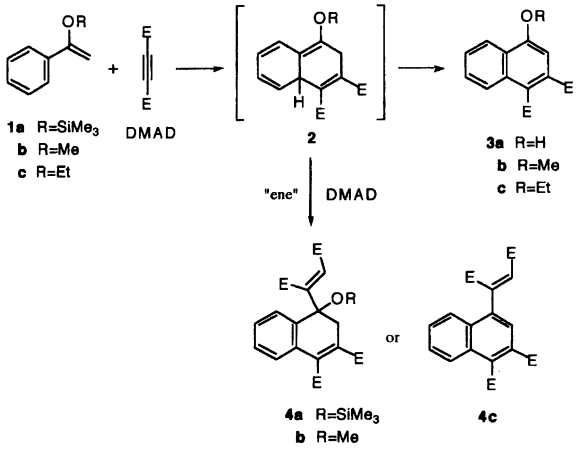
Synopsis. The reactions of α-trimethylsiloxy-, α-methoxy-, and α-ethoxystyrene with dimethyl acetylenedicarboxylate (DMAD) and dimethyl fumarate (DMFM) have been investigated. With DMAD the 1 : 1 Diels–Alder and the 1 : 2 Diels–Alder ene adducts were obtained, while the reaction with DMFM gave novel open-chain adducts through alkyl group migration and incorporation of the solvent.

The Diels–Alder reaction of styrenes is frequently used in a short-cut process for the construction of fused aromatic systems.[1] In spite of its potential importance, the application to organic synthesis is rather limited probably due to the sluggish nature of reactivity as a diene component and, hence, the drastic conditions necessary to promote the desired reactions. In some cases, it has been recognized that the reactivity of styrenes can be increased by introduction of an electron-donating group on the side chain or on the aryl ring.[2] Herein, we wish to describe the reaction of α-alkoxy-substituted styrenes **1**[3] with dimethyl acetylenedicarboxylate (DMAD) and dimethyl fumarate (DMFM) at elevated temperatures.

From the reaction of **1a—c** with DMAD the 1 : 1 adducts **3** and the 1 : 2 adducts **4** were isolated (Scheme 1, Table 1). The former 1-naphthol derivatives should be derived from the intermediate Diels–Alder adducts **2** via aromatization and the latter dihydronaphthalene ones by "ene" addition of a second molecule of DMAD to **2**. The ^{1}H NMR evidence supports the structures of **4a**[4] and **4b** as a characteristic signal of methylene protons at $\delta=3.00$ and 3.29 ($J_{AB}=17$ Hz) and $\delta=3.11$ and 3.33 ($J_{AB}=18$ Hz), respectively, as a typical AB-quartet pattern. The *Z*-configuration of the bis(methoxycarbonyl)vinyl side chain in **4** was identified from the proton coupled ^{13}C NMR spectra: The ester CO of **4b** at $\delta=167.0$ is coupled to the olefinic proton with $J=12$ Hz.[5] Apparently, lowering the reaction temperature and increasing the molar ratio of DMAD gave better results for obtaining the "ene" adducts **4**, implying that the "ene" process is much faster than aromatization. Under the conditions the adduct from **1c** was found to be the aromatized **4c** as a result of further elimination of ethanol.

Under appropriate conditions, it has been reported that styrenes give the "Wagner-Jauregg type" 1 : 2 adducts (two consecutive Diels–Alder reactions),[1b] but no such adducts could be detected.

On the other hand, the reaction with DMFM gave a completely different result (Scheme 2, Table 2). In this case, α-trimethylsiloxystyrene **1a** showed no reactivity. However, the reaction of **1b** with DMFM in toluene in a sealed tube at 200 °C gave **6a** and **7a** in 39 and 19% yields, respectively (Run 3).[6] The IR spectra of **6a** and **7a** resembled each other, suggesting the presence of diester and conjugated carbonyl functions (1730 and 1690 cm^{-1}). The ^{1}H NMR, MS, and elemental analyses results agreed with the proposed structures for **6a** and **7a** as depicted in Scheme 2. To clarify the ^{1}H NMR splittings, **6a** was converted into the corresponding ethylene acetal derivative **8**, which provided an unambiguous assignment of each proton–proton coupling constant as measured by NMDR experiments (Fig. 1). Similarly, **1c** yielded **6b** along with a trace of **7a** (Run 10). There is no doubt that dimethyl maleate gave a comparable

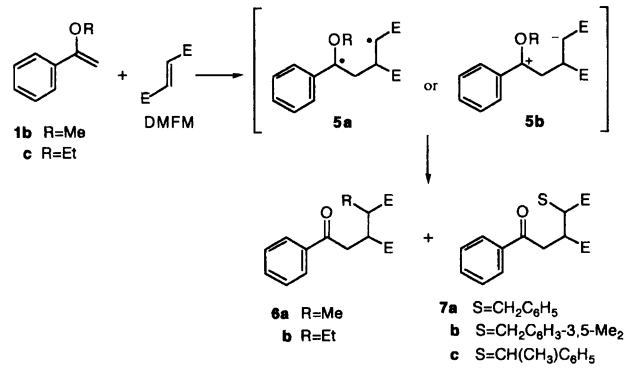


Scheme 1. (E=COOMe).

Table 1. Diels–Alder Reaction of Styrenes (**1a—c**) with DMAD[a]

1	Ratio 1 : DMAD	Reaction temp/°C	Reaction time/h	Solvent	Products (Yield/%)[b]
1a	1 : 1	200	20	Toluene	**3a** (34)[c] **4a** (26)
	1 : 2	200	24	Toluene	**3a** (21)[c] **4a** (35)
	1 : 5	100	20	Benzene	**3a** (15)[c] **4a** (39)
1b	1 : 1	200	20	Toluene	**3b** (23) **4b** (29)
	1 : 2	150	24	Toluene	**3b** (21) **4b** (28)
	1 : 5	100	20	Benzene	**3b** (20) **4b** (68)
1c	1 : 1	200	20	Toluene	**3c** (11) **4c** (19)

a) All reactions were performed in a sealed tube. b) Isolated yields. c) Trimethylsilyl group was hydrolyzed during isolation.



Scheme 2. (E=COOMe).

Table 2. Diels–Alder Reaction of Styrenes (**1b** and **1c**) with DMFM[a)]

Run	1	Solvent	Products (Yield/%)[b)]	
1	**1b**	—[c)]	**6a** (35)	
2		Benzene	**6a** (18)	
3		Toluene	**6a** (39)	**7a** (19)
4		Toluene[d)]	**6a** (53)	**7a** (15)
5		Toluene[e)]	**6a** (13)	**7a** (5)
6		1,3,5-Trimethylbenzene	**6a** (15)	**7b** (16)
7		Ethylbenzene	**6a** (39)	**7c** (11)
8		Chlorobenzene	**6a** (32)	
9		Toluene[f)]	**6a** (30)	**7a** (15)
10	**1c**	Toluene	**6b** (38)	**7a** (trace)

a) All reactions were performed in a sealed tube at 200 °C for 20 h unless otherwise noted. The ratio of **1** to DMFM was constantly 1:1. b) Isolated yields. c) No solvent and reaction time was 8 h. d) A catalytic amount of AIBN was added. e) A catalytic amount of TBMP was added. f) Dimethyl maleate was used in place of DMFM.

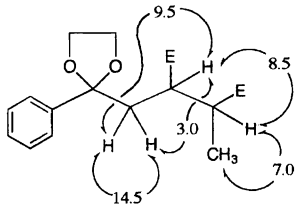
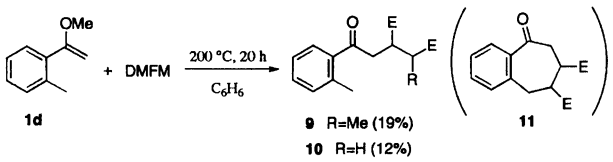


Fig. 1. Proton–proton coupling constants of the acetal **8** (*J*, Hz).

result with DMFM (Run 9), since thermal isomerization of dimethyl maleate to DMFM is well-established.[7)]

From these results we concluded that the compound **6** should be formed by migration of the alkyl portion of an alkoxyl group in styrenes through the intermediates **5** and **7a** by incorporation of toluene at the benzylic position. In accordance with this expectation, the reaction of **1b** with DMFM in the solvent having no benzylic hydrogens or without use of the solvent caused only methyl-group migration giving **6a** (Runs 1, 2, and 8). When the solvent was replaced by 1,3,5-trimethylbenzene and ethylbenzene, each solvent was incorporated to afford **7b** and **7c** accompanying the formation of **6a** (Runs 6 and 7).



Scheme 3. (E=COOMe).

Although there is no precedent for this type of reaction, it has a close analogy to the thermal alkylation of **1b** with toluene.[8)] Thus, in analogy with the reported mechanism,[9)] the formation of **6** and **7** might be explained by the biradical or zwitterionic intermediate (**5a** or **5b**) (Scheme 2). Unfortunately, trapping experiments of the zwitterionic intermediate like **5b** in methanol resulted in a complete decomposition of the styrenes themselves. On the contrary, the use of a radical initiator such as α,α'-azobisisobutyronitrile (AIBN) enhanced the formation of **6a** (Run 4) and the use of 4,4′-thiobis(2-*t*-butyl-5-methylphenol) (TBMP), a radical inhibitor, prevented a process to afford both **6a** and **7a** (Run 5). Accordingly, in these reactions the biradical intermediate **5a** might be more plausible than the zwitterionic **5b**, although we could not completely preclude the latter process.

Further application of this strategy toward 2-methyl-α-methoxystyrene (**1d**) was also examined (Scheme 3). However, the reaction of **1d** with DMFM under a variety of conditions produced only **9** and **10**, and no traces of the expected cyclic ketone **11** were detected. Although the reason for this disappointing result is unclear, it might be that the biradical intermediate could not survive long enough to permit intramolecular cyclization.

The reactions of styrenes **1** with DMFM described above hardly proceeded at the temperatures below 200 °C and other vinyl ethers such as 1-methoxy-3,4-dihydronaphthalene and 1-methoxycyclohexene gave no adducts.

Experimental

General Procedure. A mixture of styrene **1**[3)] and a dienophile (DMAD or DMFM) was dissolved in a dried solvent and heated in a sealed tube under the conditions indicated in Tables 1 and 2. After evaporation of the solvent, the crude product was purified by preparative TLC for the adducts with DMAD or by silica gel column chromatography followed by LOBAR column chromatography (Merck LiChroprep Si 60) for the adducts with DMFM.

Dimethyl 4-Hydroxy-1,2-naphthalenedicarboxylate (3a). Mp 173—175 °C (from hexane–Et_2O); IR ($CHCl_3$) 3200, 1720, and 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 3.89, 4.03 (each 3H, s), 6.40 (1H, s), 7.26 (1H, s), 7.44—7.66 (2H, m), 7.86, 8.20 (each 1H, m). Found: C, 64.62; H, 4.65%. Calcd for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65%.

Dimethyl 4-Methoxy-1,2-naphthalenedicarboxylate (3b). Mp 112—114 °C (from hexane–Et_2O); IR ($CHCl_3$) 1720, 1580, and 1510 cm^{-1}; ^1H NMR (CCl_4) δ=

3.89, 3.91, 4.04 (each 3H, s), 7.17 (1H, s), 7.43—7.60 (2H, m), 7.83, 8.22 (each 1H, m). Found: C, 65.70; H, 5.14%. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15%.

Dimethyl 4-Ethoxy-1,2-naphthalenedicarboxylate (3c). Mp 106—107 °C (from hexane–Et_2O); IR ($CHCl_3$) 1720, 1590, and 1510 cm^{-1}; ^1H NMR (CCl_4) δ=1.59 (3H, t, J=7 Hz), 3.89, 3.91 (each 3H, s), 4.27 (2H, q, J=7 Hz), 7.16 (1H, s), 7.43—7.60 (2H, m), 7.83, 8.24 (each 1H, m). Found: C, 66.77; H, 5.67%. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59%.

Dimethyl 4-[(*Z*)-1,2-Bis(methoxycarbonyl)vinyl]-4-trimethylsiloxy-3,4-dihydro-1,2-naphthalenedicarboxylate (4a). Oil; IR (neat) 1730, 1630, 1575, and 1435 cm^{-1}; ^1H NMR (CCl_4) δ=−0.11 (9H, s), 3.00, 3.29 (each 1H, d, J_{AB}=17 Hz), 3.64, 3.67, 3.78, 3.86 (each 3H, s), 6.05 (1H, s), 7.1—7.6 (4H, m); MS (rel intensity) m/z 476 (M^+, 1), 461 (2), 444 (8), 429 (5), 412 (15), 401, (6), 386 (14), 369 (12), 355 (25), 326 (44), 301 (100), 295 (29), 253 (19), 89 (15), 73 (44). Found: C, 58.31; H,5.83%. Calcd for $C_{23}H_{28}O_9Si$: C, 57.97; H,5.92%.

Dimethyl 4-[(*Z*)-1,2-Bis(methoxycarbonyl)vinyl]-4-methoxy-3,4-dihydro-1,2-naphthalenedicarboxylate (4b). Bp 173 °C/0.15 mmHg (1 mmHg=133.322 Pa); IR ($CHCl_3$) 1730 and 1635 cm^{-1}; UV (EtOH) λ_{max} 228 (17000), 295 (12000) nm; ^1H NMR ($CDCl_3$) δ=3.11 (3H, s), 3.11, 3.33 (each 1H, d, J_{AB}=18 Hz), 3.72 (6H, s), 3.82, 3.94 (each 3H, s), 6.07 (1H, s), 7.1—7.5 (4H, m); ^{13}C NMR ($CDCl_3$) δ=168.2, 167.0, 165.5, 165.0, 151.5, 139.2, 133.4, 130.5, 130.2, 129.3, 127.8, 126.7, 124.0, 121.0, 78.9, 52.5, 52.4 (×2), 52.0, 51.8, 32.4; MS (rel intensity) m/z 418 (M^+, 1), 386 (19), 355 (43), 326 (65), 295 (55), 243 (100). Found: C, 60.23; H, 5.36%. Calcd for $C_{21}H_{22}O_9$: C, 60.28; H, 5.30%.

Dimethyl 4-[(*Z*)-1,2-Bis(methoxycarbonyl)vinyl]-1,2-naphthalenedicarboxylate (4c). Mp 133.0—134.5 °C (from hexane–Et_2O); IR ($CHCl_3$) 1730, 1440, and 1270 cm^{-1}; ^1H NMR (CCl_4) δ=3.77, 3.80, 3.93, 3.97 (each 3H, s), 6.13 (1H, s), 7.58 (2H, m), 7.90 (1H, m), 7.97 (1H, s), 8.16 (1H, m). Found: C, 62.25; H, 4.73%. Calcd for $C_{20}H_{18}O_8$: C, 62.17; H, 4.70%.

Dimethyl 5-Phenylpentan-5-one-2,3-dicarboxylate (6a). Bp 153 °C/0.35 mmHg; IR (neat) 1730, 1690, 1595, and 1585 cm^{-1}; ^1H NMR (CCl_4) δ=1.16 (3H, d, J=7 Hz), 2.8—3.6 (4H, m), 3.64 (6H, s), 7.41 (3H, m), 7.92 (2H, m); MS (rel intensity) m/z 278 (M^+, 2), 247 (8), 218 (6), 186 (4), 159 (16), 111 (16), 105 (100), 77 (22), 51 (4). Found: C, 64.66; H, 6.52%. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52%.

Dimethyl 1-Phenylhexan-1-one-3,4-dicarboxylate (6b). Bp 174 °C/1.4 mmHg; IR (neat) 1735, 1690, 1600, and 1585 cm^{-1}; ^1H NMR (CCl_4) δ=0.93 (3H, t, J=7 Hz), 1.3—1.8 (2H, m), 2.6—3.4 (4H, m), 3.63 (6H, s), 7.40 (3H, m), 7.91 (2H, m). Found: C, 65.95; H, 6.92%. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90%.

Dimethyl 1,5-Diphenylpentan-5-one-2,3-dicarboxylate (7a). Mp 91.0—92.0 °C (from hexane–Et_2O); IR ($CHCl_3$) 1735, 1690, 1600, and 1585 cm^{-1}; ^1H NMR (CCl_4) δ=2.6—3.4 (6H, m), 3.53, 3.66 (each 3H, s), 7.14 (5H, m), 7.42 (3H, m), 7.92 (2H, m); MS (rel intensity) m/z 354 (M^+, 1), 323 (5), 291 (1), 262 (7), 192 (78), 160 (21), 131 (20), 105 (100), 91 (35), 87 (62), 77 (45), 51 (6), 77 (45), 51 (6). Found: C, 71.08; H, 6.26%. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26%.

Dimethyl 1-(3,5-Dimethylphenyl)-5-phenylpentan-5-one-2,3-dicarboxylate (7b). Mp 94.5—96.0 °C (from hexane–Et_2O); IR ($CHCl_3$) 1730, 1680, 1600, and 1590 cm^{-1}; ^1H NMR (CCl_4) δ=2.23 (6H, s), 2.4—3.4 (6H, m), 3.51, 3.63 (each 3H, s), 6.68 (3H, m), 7.41 (3H, m), 7.87 (2H, m); MS (rel intensity) m/z 382 (M^+, 2), 351 (3), 319 (4), 291 (8), 230 (10), 192 (100), 159 (67), 119 (33), 105 (87), 87 (81), 77 (45), 55 (6). Found: C, 72.24; H, 6.85%. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85%.

Dimethyl 1,5-Diphenylhexan-1-one-3,4-dicarboxylate (7c). Mp 116.0—119.0 °C (from hexane–Et_2O); IR ($CHCl_3$) 1735, 1685, 1600, and 1585 cm^{-1}; ^1H NMR (CCl_4) δ=1.26 (3H, d, J=6 Hz), 2.7—3.4 (5H, m), 3.58, 3.65 (each 3H, s), 7.14 (5H, m), 7.37 (3H, m), 7.85 (2H, m). Found: C, 71.77; H, 6.56%. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57%.

Dimethyl 5,5-Ethylenedioxy-5-phenyl-2,3-pentanedicarboxylate (8). This compound was prepared by conventional treatment of **6a** with ethylene glycol and $(MeO)_3CH$ in the presence of catalytic amounts of *p*-TsOH.

8: Oil; IR (neat) 1735, 765, and 705 cm^{-1}; ^1H NMR (CCl_4) δ=1.06 (3H, d, J=7 Hz), 1.79 (1H, dd, J=14.5, 3.0 Hz), 2.32 (1H, dd, J=14.5, 9.5 Hz), 2.56 (1H, dq, J=8.5, 7.0 Hz), 2.86 (1H, ddd, J=9.5, 8.5, 3.0 Hz), 3.59 (6H, s), 3.6—4.1 (4H, m), 7.1—7.4 (5H, m).

Dimethyl 5-(2-Methylphenyl)-pentan-5-one-2,3-dicarboxylate (9). Oil; IR (neat) 1735, 1685, 1600, and 1565 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.21 (3H, d, J=7.0 Hz), 2.46 (3H, s), 2.7—3.5 (4H, m), 3.69 (6H, s), 7.26 (3H, m), 7.66 (2H, m); ^{13}C NMR ($CDCl_3$) δ=21.07, 21.11, 39.48, 40.21, 42.61, 51.88, 52.04, 125.56, 128.27, 128.34, 131.23, 138.01, 173.50, 175.54, 201.31; MS (rel intensity) m/z 292 (M^+, 4), 260 (26), 232 (10), 200 (21), 173 (19), 159 (3), 145 (7), 141 (7), 134 (4), 119 (100), 91 (11). Found: m/z 292.1306. Calcd for $C_{16}H_{20}O_5$: M, 292.1311.

Dimethyl 4-(2-Methylphenyl)-butan-4-one-1,2-dicarboxylate (10). Oil; IR (neat) 1740, 1690, 1600, and 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.48 (3H, s), 2.68 (1H, dd, J=16.6, 6.6 Hz), 2.81 (1H, dd, J=16.6, 6.1 Hz), 3.16 (1H, dd, J=16.7, 5.0 Hz), 3.42 (2H, m), 3.69, 3.71 (each 3H, s), 7.26 (2H, m), 7.39 (1H, m), 7.65 (1H, d, J=7.8 Hz); ^{13}C NMR ($CDCl_3$) δ=21.16, 35.33, 36.94, 42.25, 51.80, 52.16, 125.75, 128.52, 131.51, 132.03, 137.50, 138.32, 172.02, 174.18, 201.22, MS (rel intensity) m/z 278 (M^+, 3), 246 (25), 218 (7), 186 (16), 173 (6), 159 (12), 145 (7), 127 (6), 119 (100), 91 (15). Found: m/z 278.1138. Calcd for $C_{15}H_{18}O_5$: M, 278.1154.

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