

Photochemical 2 + 2 Cycloaddition of Arenecarboxylic Acid Esters to Furans and 1,3-Dienes. 2 + 2 Cycloreversion of Oxetanes to Dienol Esters and Ketones

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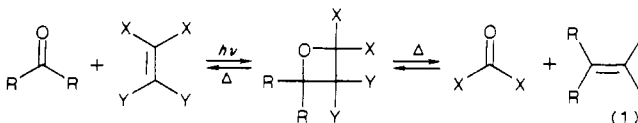
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Methyl benzoate and other simple arenecarboxylic acid esters have been found to undergo 2 + 2 photochemical cycloaddition at the carbonyl group to furans and certain 1,3-dienes. These additions afford mixtures of oxetanes and their 2 + 2 cycloreversion products: 4-aryl-4-alkoxy-1,3-butadienyl formates and acetates (from furan oxetanes) and dienyl aldehydes and ketones (from cyclic 1,3-dienes).

Introduction

The photochemical 2 + 2 cycloaddition of aldehydes and ketones to the carbon-carbon double bonds of certain alkenes is one of the oldest known organic photochemical reactions.^{1,2} Long neglected, adduct oxetanes did not initially appear to be of general interest. This process, termed the Paterno-Buchi reaction, has in recent years proven to be of considerable synthetic utility.^{2,3} The oxetanes that are the initial photoproducts are mixed cyclic acetals as well as, sometimes, cyclic enol ethers (with furans as substrates). These may subsequently undergo facile hydrolysis to dihydroxy carbonyl compounds possessing three or four contiguous asymmetric centers of known relative stereochemistry.³ Certain such oxetanes have proven to be extremely useful synthetic intermediates in the synthesis of polyoxygenated natural products.^{3b-d}

Furthermore, thermolysis of such oxetanes at relatively moderate temperatures (200–350 °C) results in a 2 + 2 cycloreversion in the alternate sense to the forward (photochemical) cycloaddition, affording carbonyl-alkene pairs different from the starting components^{2,3} (eq 1). In

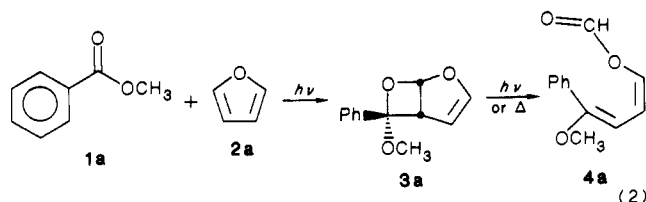


a number of cases where aldehydes or ketones were added to cyclic alkenes, the thermal 2 + 2 cleavage of the oxetanes afforded long-chain unsaturated carbonyl compounds of great use in the synthesis of insect pheromones, otherwise accessible only by far lengthier synthetic routes.²

We report here the results of an investigation of the photochemical 2 + 2 cycloadditions of arenecarboxylates with furan and substituted furans and other photoreactions. The facile photochemical and thermal transformations of these adducts are also discussed.

Results and Discussion

Irradiation of methyl benzoate (**1a**) through Vycor in the presence of excess furan, with repeated cleaning of dark polymer from the immersion well, gave mixtures of two products. The relative amounts depended on the ratio of the reactants, on the length of the irradiation period, and on the filter employed. These products were the alkoxy-oxetane **3** and its isomeric cycloreversion product **4**, an enol formate ester (eq 2). The reaction was capricious. Reactions conducted for shorter periods of irradiation and



with workup procedures involving short-path distillation at the lowest obtainable pressure often, but not always, gave mostly 6-methoxy-6-phenyl-2,7-dioxabicyclo[3.2.0]-hept-3-ene, a crystalline material stable at -20 °C. Prolonged reaction times or higher distillation temperatures during the workup resulted in increased consumption of ester **1a** and gave mixtures rich in **4a**, 1-(formyloxy)-4-methoxy-4-phenyl-1(*Z*),3-butadiene. This product is the result of 2 + 2 cycloreversion of **3** in the opposite sense to its formation. Indeed, the conversion of purified **3** to mixtures of **3** and **4** could be effected by (a) reirradiation at 254 nm; (b) contact with silica during flash chromatography; and (c) thermolysis at temperatures as low as 130 °C.⁴

The light-induced cycloreversion may well be the result of internal photosensitization by the toluene chromophore of oxetane **3a**, as previously reported.⁴ The thermal process has been very well discussed by Jones.²

The structure of **3a** was initially assigned on the basis of NMR data. Of particular note are the close similarities of the chemical shifts of the four furan-derived hydrogens of **3a** with those of the corresponding ¹H nuclei of **3b**, the oxetane photoproduct obtained from benzaldehyde and furan, shown in Table I.⁵ A full set of decoupling experiments yielded the coupling constants listed. Comparison of the ¹³C chemical shifts of **3a** with those of **3b** gave further support to structure **3a**.

The structure of **4a** was also deduced initially from its spectral parameters (see Experimental Section). We also

(1) (a) Paterno, L.; Chieffi, G. *Gazz. Chim. Ital.* **1909**, *39*, 341-344. (b) Buchi, G.; Inman, C. G.; Lipinsky, E. S. *J. Am. Chem. Soc.* **1954**, *76*, 4327-4332.

(2) Jones, G. In *Organic Photochemistry*; Padwa, A., Ed.; Wiley: New York, 1981; Vol. 5.

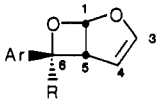
(3) (a) Schreiber, S. W. *Science (Washington, D.C.)* **1985**, *227*, 857-863 and references therein. See, inter alia: (b) Schreiber, S. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1984**, *106*, 7200-7202. (c) Schreiber, S. L.; Gatake, K. *J. Am. Chem. Soc.* **1983**, *105*, 6723-6725. (d) Schreiber, S. L.; Hoveyda, A. H.; Wu, H. J. *J. Am. Chem. Soc.* **1985**, *107*, 660-661.

(4) Cantrell, T. S.; Allen, A. C. *J. Org. Chem.*, preceding paper in this issue.

(5) Oxetane **3b** was prepared by irradiation of benzaldehyde and excess furan with Pyrex-filtered light: Toki, S.; Shima, K.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 760-762.

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Table I^a


	Ar	R
3a	C ₆ H ₅	OCH ₃
b	C ₆ H ₅	H
c	2-C ₄ H ₃ O	OCH ₃
d	2-C ₄ H ₃ O	H

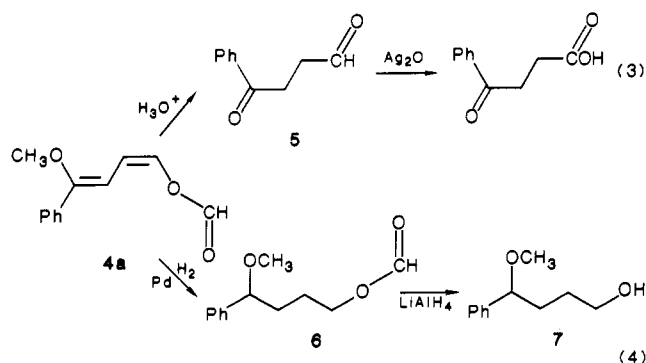
3a ¹ H shifts and couplings	3b ¹ H shifts ^b and couplings
C ₆ H ₅ , 7.3, s	C ₆ H ₅ , (7.25) 7.20
H ₁ , 6.43, d	H ₁ , (6.47) 6.53
H ₃ , 6.40, 2 d	H ₃ , (6.63) 6.73
H ₄ , 4.63, m	H ₄ , (5.38) 5.42
H ₅ , 4.01, m	H ₅ , (3.57) 3.63
CH ₃ O, 3.18, s	H ₆ , (5.50) 5.56
J _{1,5} = 3.8	J _{1,5} = 4.4
J _{1,3} = 0.8	J _{1,3} = 0.8
J _{1,4} = 0.0	
J _{3,4} = 2.9	J _{3,4} = 2.9
J _{3,5} = 1.2	J _{3,5} = 0.8
J _{4,5} = 2.9	J _{4,5} = 2.9

3a ¹³ C shifts	3b ¹³ C shifts
C ₆ H _{4-p} , 128.4	C ₆ H ₅ , 128.7
C ₆ H _{5-o} , 127.9	C ₆ H ₅ , 128.2
C ₆ H _{5-m} , 126.6	C ₆ H ₅ , 125.3
C ₁ , 105.0, d	C ₁ , 104.2, d
C ₃ , 148.5, d	C ₃ , 148.5, d
C ₄ , 101.5, d	C ₄ , 108.2, d
C ₅ , 56.5, d	C ₅ , 52.5, d
C ₆ , 114.4, d	C ₆ , 92.7, d
CH ₃ O, 50.2, q	

^a Shifts are in parts per million, and couplings are in hertz.

^b Values in parentheses are from ref 5.

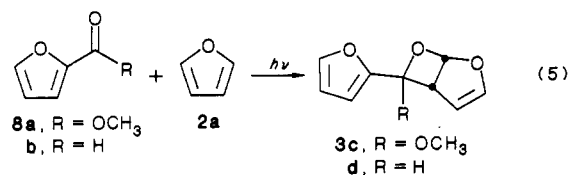
carried out chemical transformations in order to obtain additional evidence. Thus, hydrolysis of the enol ether and enol formate functions of **4a** in cold dilute aqueous HCl gave 3-benzoylpropanal, **5**. Its nature was apparent from ¹H NMR and mass spectral data and was confirmed by silver oxide oxidation to 3-benzoylpropanoic acid, identical with authentic material (eq 3). Further, catalytic hy-



drogenation of **4a** over 5% palladium-charcoal resulted in the uptake of 2.0 equiv of hydrogen gas and produced the saturated alkyl formate **6**. Reduction of **6** by lithium aluminum hydride gave primary alcohol **7** (eq 4). The NMR (¹H and ¹³C), IR, and mass spectral data of all of these compounds were in complete accord with the structures shown. The assignment of the *Z* geometry to the C₁-C₂ double bond of **4a** was based on the magnitude of the corresponding coupling constant *J*_{1,2} (5.6 Hz). These are in close agreement with the coupling in a dienyl formate recently reported as a retro 2 + 2 product of a photo oxetane derived from *N*-methyl-1,8-naphthalenedi-carboximide and furan.⁶ The geometry of the C₃-C₄

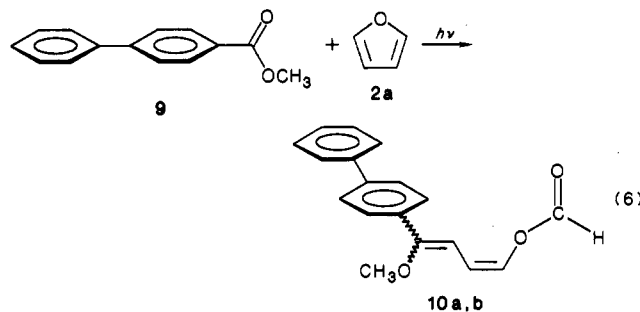
double bond is not known with certainty, but is shown as *E* in eq 2 for the major dienyl formate. This is assuming that a photochemically allowed concerted retro 2 + 2 cycloreversion of **3a** to **4a** has occurred with no inversion.

The reaction of methyl 2-furoate (**8**) with furan was also studied (eq 5). Oxetane **3c** was thereby obtained in very low yield and showed no tendency, thermally or photo-



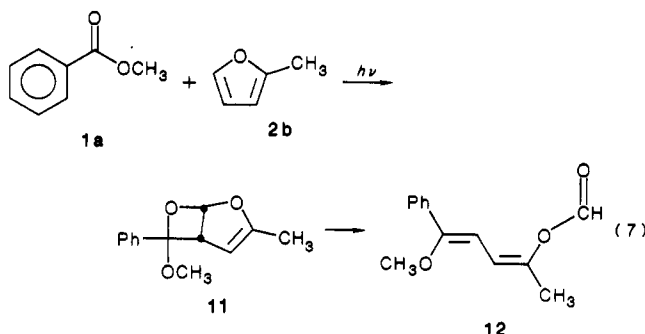
chemically, to undergo 2 + 2 cycloreversion to a dienol formate. Assignment of structure **3c** was accomplished on the basis of similarities between its ¹H NMR spectrum and that of **3d**. This demethoxy analogue (**3d**) was prepared by irradiation of furfural and excess furan with Pyrex-filtered light.⁵

Irradiation of methyl 4-biphenylcarboxylate (**9**) in the presence of excess furan with Vycor-filtered light gave a mixture of the *E* and *Z* geometric isomers (at the 3,4-double bond) of 1-(formyloxy)-4-(4-biphenyl)-4-methoxy-1(*Z*),3-butadiene, **10a,b** (36%, eq 6). The identities

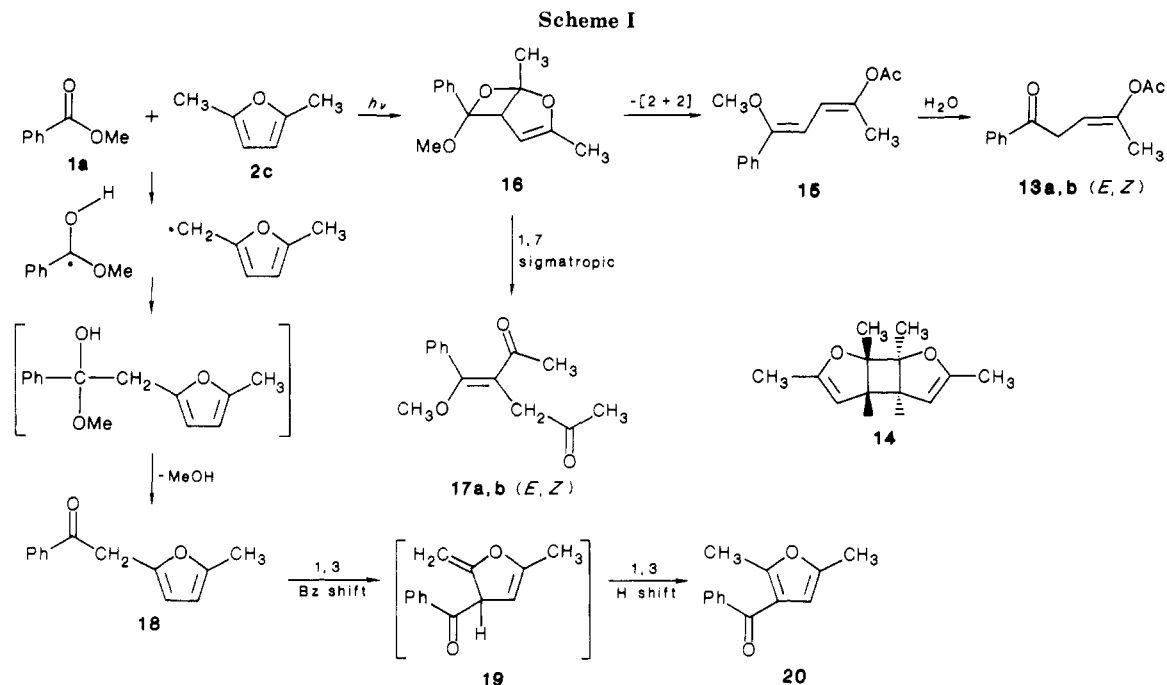


of **10a** and **10b** are not known with certainty, but are most likely as shown, on the grounds that the major product should be the less sterically hindered, **10a**. No oxetane could be found in the reaction mixture. This may be due to an efficient internal photosensitization of the retro 2 + 2 process by the strongly absorbing biphenyl chromophore.⁴

The effect of alkyl substitution on the substrate furan upon the reaction course was examined next. Irradiation of ester **1a** in excess 2-methylfuran, **2b**, gave a modest conversion to an inseparable mixture of oxetane **11** and dienyl formate **12** (eq 7), products analogous to **3a** and **4a**



from furan (eq 2). Structure assignments were made on the basis of ¹H and ¹³C NMR spectra, as well as IR and



mass spectral data. The initial 2 + 2 cycloaddition of the ester carbonyl of **1a** added entirely across the less substituted C_4 - C_5 bond of the 2-methylfuran. This contrasts with the behavior of benzaldehyde, which adds across both the C_2 - C_3 and the C_4 - C_5 bonds of this substrate.^{5,7} Neither reference cited reported a product ratio; however, in our hands this ratio was 64:36. The regioselectivity of the photoexcited ester **1a** addition to **2b** is noteworthy.

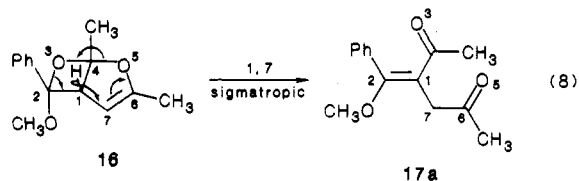
Photochemical reaction of excited methyl benzoate with 2,5-dimethylfuran produced a plethora of products. Separation, purification, and identification of these were accomplished by a combination of solvent partitioning, column chromatography (alumina), GC-MS, GC-FTIR, and HPLC. These were assigned the structures **13**-**20**, as shown in Scheme I, on the basis of their spectral parameters (see Experimental Section). In photolyses carried to ca. 50% consumption of starting ester **1a**, the total yield of products was 53%. A ratio of **13a**:**13b**:**14**:**15**:**16**:**17a**:**17b**:**18**:**19**:**20** was found by HPLC to be 7:4:6:11:8:26:18:3:3:14. This complex mixture was initially separated by extraction of the total short-path-distilled reaction mixture with hexane; products **13a,b**-**17a,b** were soluble, whereas ketones **18**-**20** were slightly soluble. This was followed by eluting the hexane solubles through neutral alumina; **14** eluted first, **16** and **15** eluted together with hexane, **18**-**20** (if any remained after initial hexane wash) eluted with diethyl ether, and **17a** and **17b** were removed by methylene chloride. Although **16** survived preparative GC or HPLC. Its identification was based on comparison of IR, MS, and ^1H NMR data with those of **3a**, **3c**, and **11**.

Dienyl acetate **15** is analogous to products **4**, **10**, and **12** previously discussed. β,γ -Enones **13a** and **13b** evidently arise from hydrolysis of the enol ether moiety of **15** by traces of moisture during workup, perhaps catalyzed by acidic sites on the GC and HPLC support.

The dimethylfuran 2 + 2 cyclodimer is assigned the head-to-head structure shown (**14**) by analogy with the photodimers formed from 1,3-cyclopentadiene and 1,3-

cyclohexadiene.⁹ It probably arises via photosensitization by excited state ester **1a**, either singlet or triplet.

Diketones **17a** and **17b**, and *E,Z* mixture formed in a 58:42 ratio, amounted to 44% of the photoproduct mixture. A likely pathway for the formation of these rearrangement products is shown in eq 8, involving what could be regarded



as either a 1,2- or a 1,7-sigmatropic rearrangement. Since the Woodward-Hoffmann orbital symmetry conservation rules predict that a suprafacial 1,7-sigmatropic rearrangement is photochemically allowed to proceed in a concerted manner,¹⁰ we feel that it is correctly regarded as 1,7. The hydrogen migrating is, in a sense, undergoing a 1,2-shift; however, these are almost unknown events in photochemistry.¹¹

Reduction of the acetyl groups of the **17a,b** mixture by means of lithium aluminum hydride in ether afforded diols whose spectral properties were in full accord with **21a** and **21b**.

The furans **18** and **20** were obtained in pure form and identified; however, the 5-methylene-4,5-dihydrofuran (**19**) could not be isolated. Since capillary GC-FTIR-MS reveals three isomeric substituted furan derivatives (m/z 200), we inferred the following from mechanistic considerations. Abstraction of a hydrogen atom from the allylic methyl of **2c** by the carbonyl oxygen of photoexcited ester **1a**, as shown in Scheme I, produces an α -hydroxyalkyl radical and the 5-methyl-2-furanylmethyl radicals. These

(8) Evanega, G.; Whipple, E. *Tetrahedron Lett.* 1967, 2163-2168.

(9) (a) Valentine, D.; Turro, N. J.; Hammond, G. S. *J. Am. Chem. Soc.* 1964, 86, 5202-5208. (b) Cantrell, T. S. *J. Org. Chem.* 1974, 39, 3063-3070.

(10) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Springer: Berlin, 1971.

(11) Schuster, D. I. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Wiley-Interscience: New York, 1981; Vol. 3, Chapter 17, pp 167-281.

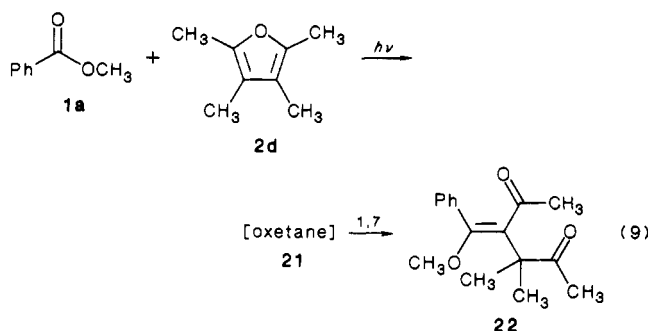
(7) Ogata, M.; Watanabe, H.; Kano, H. Y. *Tetrahedron Lett.* 1967, 533-536.

Table II. Flash Vacuum Pyrolysis of Oxetanes

oxetane	1:3:4		
	250 °C	300 °C	350 °C
3a	41:55:6	66:21:13	70:5:25
3b	25:63:2	70:19:11	-

combine (likely in a solvent cage)⁴ to produce a hemiketal. This unstable species quickly loses methanol to afford α -benzoyl-2,5-dimethylfuran (18). Ketone 18, upon absorption of a photon of 220–290-nm light, undergoes a photochemically allowed 1,3-acyl shift of the benzoyl group (C₅ to C₄), giving methylenedihydrofuran 19. This rather unstable compound undergoes a second 1,3-sigmatropic rearrangement, this time a hydrogen, to give 3-benzoyl-2,5-dimethylfuran, 20. Regeneration of the intact furan ring, with its moderate degree of aromatic character, enhances stability.¹²

Since the observed formation of rearrangement product 17a and 17b constitutes an unusual process in photochemistry, we felt it advisable to find another example of a 1,7-sigmatropic (or 1,2) rearrangement within the structural limitation of oxetane 16. In ground-state rearrangements of carbocations and of radical intermediates, migrations of alkyl groups are always much faster than the corresponding shifts of hydrogen atoms. Thus 2,3,4,5-tetramethylfuran (2d) was photochemically reacted with methyl benzoate (1a) to afford oxetane 21. This alkyl-substituted oxetane readily underwent alkyl migration/ring opening to give 95% pure diketone 22 (eq 9).



The structure of dimethyl diacetyl product 22 followed from its ¹H and ¹³C NMR data and from the properties of diol 23, obtained by reduction of 22 via LiAlH₄.

Photochemical cycloaddition of ester 1a to 1,3-dienes, carbocyclic analogues of furans, proceeded very slowly and very inefficiently. Irradiation of ester 1a in the presence of 1,3-cyclopentadiene or 1,3-cyclohexadiene (24a or 24b) gave large amounts of diene 2 + 2 cyclodimers, probably by direct photochemical excitation of the dienes by the Vycor-filtered light and photosensitization of the diene by ester excited states.^{9a} By careful fractional distillation followed by GC, there was obtained a very small amount of liquid whose spectra indicated it to be ca. 90% pure 25b. Due to the light-absorbing properties of cyclic 1,3-dienes, photochemical addition of aromatic ester carbonyl groups is far less efficient than the reaction with furans.

Finally, the thermolysis of oxetanes 3a and 3b was conducted in the gas phase via a flow apparatus (FVP) at 200–350 °C. The results are summarized in Table II.

At 350 °C there was significant loss of material in the form of nonvolatile polymer on the walls of the quartz tube and on the helices used for packing (ca. 30% of starting oxetane).

The rather small amount of dienyl esters such as 4a formed in these purely thermal processes argues against the major portion of the 1,3-dienyl esters arising from thermally forbidden 2 + 2 cycloreversion. These data would reinforce the conclusion that the dienyl formates and acetates obtained in the reactions studied arise via internal photosensitization through the phenyl moiety of oxetane leading to 2 + 2 cycloreversion.⁴

Experimental Section

All high-performance liquid chromatography (HPLC) was done on a Waters Model 6000A, utilizing a Sorbax ODA analytical column measuring 16 cm × 4.6 mm ID and interfaced with a 254-nm UV detector. Preparative HPLC was done on a Sorbax column measuring 25 cm × 21.2 mm ID and interfaced with a refractive index detector. The solvent system used was acetonitrile/water (40:60) at a flow rate of about 10 mL/min. Liquid-solid chromatography was performed with MCB 80–325-mesh neutral activated alumina or E. Merck 200–400-mesh silica gel in 25 cm × 22 mm glass columns. Preparative chromatography (GC) was performed on a 10 ft × 1/4 in. column coated with SE-30 in a Varian A-90-P instrument. Infrared (IR) spectra were recorded, on solids or liquids, in or on KBr using a Beckman IR-4 instrument. Gas-phase IR spectra were obtained via a Hewlett-Packard 5965 gas-phase IR detector interfaced with a HP 5890 GC instrument using a 25 m × 0.31 mm HP-5 cross-linked methyl silicone column. The low-resolution mass spectrometers used were a Finnigan 4600 quadrupole mass analyzer, a Hewlett-Packard 5987A quadrupole mass analyzer, and a Hewlett-Packard 5970 series selective detector. All spectrometers were operated in the EI mode at 70 eV with a source temperature of 200 °C and interfaced with GC capillary introduction via a 25 m × 0.31 mm fused-silica column with either cross-linked 5% phenyl-methyl silicone or HP-5 methyl silicone. Nuclear magnetic resonance (¹H and ¹³C NMR) spectra were obtained on a Nicolet NT-200WB-FT, a Varian XL-300, a Varian XL-200, a Varian HR-220, or a Varian Gemini-300 spectrometer. Spectra were recorded in CDCl₃ with Me₄Si as internal standard.

Photochemical Reaction of Methyl Benzoate with Furan.

A solution of redistilled methyl benzoate (1a), (5.0 g, 0.037 mol) and furan (2a) (20 g, 0.30 mol) and spectrograde pentane (90 mL) was irradiated with a Hanovia 450-W medium-pressure mercury arc lamp through a Vycor filter sleeve for 44 h. The immersion well was scoured free of dark polymer after 20 and 32 h. Solvent and excess furan were removed by evaporation; vacuum distillation of the reaction mixture gave recovered 1a (bp 35–38 °C (0.1 mm), 2.8 g). Short-path distillation of the residue gave a faintly yellow oil, bp 60–65 °C (bath) (0.07 mm) (1.1 g, 37%). Trituration of this material with pentane and cooling overnight at –20 °C gave oxetane 3a as colorless prisms: mp 71–74 °C dec (0.86 g, 31%); NMR (CDCl₃) see Table I; IR 1130, 1065, 1010 cm⁻¹; MS (CI, isobutane) 204 (P, 100), 136 (53). Anal. Calcd for C₁₂H₁₂O₃: C, 70.54; H, 5.98. Found: C, 70.2; H, 6.1.

The above filtrate from 3a was combined with the filtrate of two other such runs and redistilled to give dienyl formate 4a as a pale yellow oil (0.35 g per run, 13%): bp 95–98 °C (0.1 mm); ¹H NMR (CDCl₃) δ 8.07 (1 H, s, HCOO), 7.36–7.20 (6 H, s, br, 5 aryl H + H₁), 6.95 (1 H, d, J = 5.6, H₃), 5.72 (1 H, 2 d J = 5.6, J = 8, H₂), and 3.78 (3 H, s, OCH₃); ¹³C NMR (CDCl₃) δ 159.1 (d, HCOO), 157.1 (s, C=CHO, C₄), 135.0, 129.3, 127.8 (aryl), 126.8 (d, C₁), 111.2 (d, C₂), 93.3 (d, C₃), and 55.2 (OCH₃); IR 1728, 1220, 1080, 1050 cm⁻¹; UV (EtOH) 287 (ε = 32 000), 241 nm (46 000); MS (EI), m/z 204 (P, 88), 176 (37), 147 (55), 115 (100), 105 (60), and 81 (44). Anal. Found: C, 70.13; H, 5.75 (compound was sensitive to oxygen).

In other runs of methyl benzoate with furan, in which longer reaction times were used (72–100 h), with repeated cleaning of the immersion well, and especially with standard vacuum fractional distillation of the reaction mixture (photoproduct distills at 100–110 °C, pot temperature probably ~120–130 °C) at 0.1 mm, the distillate was 90% dienyl formate 4a. Yield under such conditions: 31% 4a and ca. 5–6% 3a.

Hydrolysis of 4a. To a solution of dienyl formate 4a (0.50 g, 2.3 mmol) in 10 mL of 90% aqueous THF was added 2 drops of concentrated HCl. The solution was allowed to stand for 4

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h at 25 °C, was then poured onto 40 g of ice-H₂O, and was extracted with 3 × 10 mL of dichloromethane. Washing of the combined extracts with water, drying (MgSO₄), and evaporation of the solvent gave an oil, which was distilled to afford 3-benzoylpropanal (**5**) (0.21 g, 50%): bp (short-path) 105–110 °C (0.08 mm); ¹H NMR (CDCl₃) δ 9.27 (1 H, s), 8.0 (2 H, m), 7.6, 7.4 (3 H, m), 3.15 (2 H, t, *J* = 7 Hz), 2.98 (2 H, t, *J* = 7 Hz); IR 2820, 2720 (w), 1715 (s) cm⁻¹; MS (EI), *m/z* 162 (P, 8), 161 (29), 105 (100).

Oxidation of **5** with Ag₂O in aqueous ethanol gave 3-benzoylpropanoic acid, mp 148 °C, identical with authentic material (IR, NMR, mixed melting point).

Hydrogenation of Dienyl Formate 4a. A solution of enol formate **4a** (1.02 g, 5.0 mmol) in 95% ethanol (50 mL) was shaken with 50 mg of 5% Pd-C under 1.0–1.5 atm pressure of hydrogen until absorption ceased (35 min). At the end of this time, when 1.96 equiv of hydrogen gas had been absorbed, the reaction mixture was filtered and the solvent evaporated. Distillation gave saturated alkyl formate **6**, bp 90–93 °C (0.08 mm) (0.96 g, 95%), a colorless oil: ¹H NMR (CDCl₃) δ 8.19 (1 H, s, HCOO), 7.3–7.2 (5 H, s), 4.3 (3 H, m, C₁CH₂ + C₄CH), 3.38 (3 H, s, CH₃O), and 2.0–1.75 (4 H, CCH₂C, H₂, H₃); ¹³C NMR (CDCl₃) δ 160.7 (1 H, d, HCOO), 147.7, 128.5, 127.7, 126.7 (aryl, ipso, meta, para, ortho), 83.6 (d, C₄), 53.8 (d, C₁), 56.6 (q, CH₃O), 34.4 (t, C₂ or C₃), and 25.2 (t, C₂ or C₃); IR 1725 cm⁻¹ (C=O); MS, *m/z* 208 (P, 6), 121 (100), and 77 (28). Anal. Calcd for C₁₂H₁₆O₃: C, 66.34; H, 7.74. Found: C, 66.61; H, 7.89.

Reduction of Formate Ester 6 to Primary Alcohol 7, 4-Phenyl-4-methoxy-1-butanol. To a suspension of lithium aluminum hydride (0.8 g, 20 mmol) in ether (30 mL) was added dropwise a solution of formate ester **6** (1.04 g, 5 mmol) in 10 mL of ether. The reaction mixture was stirred and refluxed for 40 min. The solution was then decomposed by the dropwise addition, with cooling, of 0.8 g of water (in 10 mL of THF), 1 mL of 10% aqueous NaOH, and finally 3 mL of water. After being stirred at 20 °C for an additional 2 h, the cream suspension was filtered and the solid washed with THF (3 × 20 mL). The ether and THF solutions were combined and the solvents evaporated to a residue, which was distilled under reduced pressure to afford primary alcohol **7**, bp 115–119 °C (0.08 mm) (0.63 g, 77%), as a colorless oil: ¹H NMR (CDCl₃) δ 7.2 (5 H, m, br, C₆H₅), 4.34 (1 H, d, *J* = 7.3, *J* = 5.0, H₄), 3.78 (2 H, t, *J* = 6.9, H₁), 3.29 (3 H, s, OCH₃), 1.97 (2 H, m, CH₂), 1.80 (2 H, m, C₃CH₂), and ca. 4.0 (1 H, s, br, OH; but 4.48, 1 H, t, *J* = 6.8 in DMSO-*d*₆); IR 3440–3380 (s, v br), 1085 and 1040 (s) cm⁻¹; MS, *m/z* 180 (P, 1.3), 121 (100), 91 (14), and 7 (29). Anal. Calcd for C₁₁H₁₆O₂: C, 73.32; H, 8.94. Found: C, 73.55; H, 9.05.

Photochemical Reaction of 2-Furaldehyde with Furan. A solution of freshly distilled 2-furaldehyde (4.0 g, 0.020 mol) and furan (20 g) in spectrograde pentane (100 mL) was irradiated at 350 nm in the Rayonet chamber reactor under an atmosphere of purified nitrogen for 30 h. After evaporation of solvent and excess furan, vacuum distilled of the residue gave, first, recovered furfural (1.2 g), followed by oxetane **3d**: bp 60–65 °C (bath) (0.1 mm) (2.8 g, 61%); ¹H NMR (CDCl₃) δ 7.46 (1 H, s, H₅ of furyl), 6.67 (1 H, d, *J* = 2.8, CH=CHO), 6.46 (1 H, d, *J* = 3.2, OCHO), 6.32 (2 H, s, H₃, H₄ of furyl), 5.30 (2 H, d, *J* = 3.2, CHCH=CHO), and 3.93 (1 H, d, br); MS (CI), *m/e* 164 (P, 40) and 96 (100).

Further irradiation of oxetane **3d** (>220 nm) or passage of a solution in methylene chloride over a short silica gel column (1.0 cm × 10 cm, 10-min contact time) led to 2 + 2 cycloversion to afford furyl dienyl formate **4d** (4-furyl-1-(formylxy)butadiene): IR 1738, 1232, 1160, and 1084 cm⁻¹; ¹H NMR (CDCl₃) δ 8.05 (1 H, s, OOH), 7.35 (1 H, s, br, H₅ of furyl), 7.16 (1 H, d, *J* = 6.0, H₁), 6.97 (1 H, dd, *J* = 15.5, *J*' = 11.5, H₃), 6.31 (3 H, m, H₄ of diene and H₃, H₄ of furyl), and 5.64 (1 H, dd, *J* = 11.5, *J*' = 6.0, H₂); MS (CI), *m/z* 164 (P, 26), 135 (100), and 79 (25). Anal. Calcd for C₉H₈O₃: C, 65.87; H, 4.97. Found: C, 65.53; H, 4.87.

Photochemical 2 + 2 Cycloaddition of Benzaldehyde to Furan. A solution of freshly distilled benzaldehyde (2.1 g, 20 mmol) and furan (20 g) in spectro pentane (90 mL) was irradiated through Pyrex (450-W source) for 3 h. Evaporation of solvent and excess furan gave an oily residue, which was distilled to afford known oxetane **3b**, a colorless liquid, bp 85–88 °C (0.1 mm) (1.7 g, 56%): NMR data given in Table I; MS, *m/z* 174 (P, 13), 143 (30), and 105 (100).

Irradiation of Methyl 4-Biphenylcarboxylate (9) with Furan. Formation of Dienyl Formates 10a,b. A solution of ester (2.1 g, 10 mmol) and freshly distilled furan (40 mL) in spectro pentane (80 mL) was irradiated with the 450-W source through a Vycor filter sleeve (30 h), with cleaning of dark material from the immersion well after 10 and 22 h. Evaporation of solvent and furan gave a yellow residue, which was triturated with chloroform-hexane and allowed to stand at -20 °C overnight. Recrystallization from ethyl acetate-hexane at -5 °C gave the isomer mixture (80:20) as dull creamy prisms, mp 78–81 °C (0.94 g, 36%). Major isomer (**10a**): ¹H NMR (CDCl₃) δ 8.08 (1 H, HCOO), 7.6–7.3 (10 H, m) 6.95 (1 H, d, *J* = 5.8, H₃), 5.84 (1 H, 2 d, *J* = 10.0, *J* = 5.8, H₂), and 3.82 (3 H, s, OCH₃); IR (KBr) 1730 cm⁻¹; MS, *m/z* 280 (100), 252 (30), 248 (28), and 180 (22). Minor isomer (**10b**): ¹H NMR δ (CDCl₃) δ 8.04 (1 H, s), 7.6–7.3 (10 H, m, aryl and H₁), 7.22 (1 H, d, *J* = 5.6, H₃), 5.75 (1 H, 2 d, *J* = 10.2, *J* = 5.6, H₂), and 3.95 (3 H, s, OCH₃). Anal. Calcd for C₁₈H₁₆O₃: C, 77.18; H, 5.40. Found: C, 77.0; H, 5.21.

Photochemical Reaction of Methyl Benzoate with 2-Methylfuran. A solution of methyl benzoate (6.0 g, 0.41 mol) and 2-methylfuran (20 g, 0.25 mol), in spectrograde pentane was flushed with argon for 45 min and then was irradiated thru a Vycor filter for a total of 30 h. The irradiation was stopped after intervals of 10 and 20 h to scrub tan polymer off the quartz immersion well. After removal of solvent and excess 2-methylfuran by rotary evaporation, the residues from two such runs were combined and distilled under reduced pressure to afford (a) recovered ester **1a**, bp 35–40 °C (0.3 mm) (4.5 g), and (b) a mixture of products **11** and **12** (ratio 3:7, 1.9 g), bp 90–95 °C (0.1 mm): IR (neat) 1730 cm⁻¹ (s), 1220 (s, br), 1180 (s), and 1050 (s); partial separation by flash chromatography on silica was achieved, although with concomitant loss of material, resulting in obtaining fractions enriched in enol formate **12**. Oxetane **11**: ¹H NMR (CDCl₃) δ 7.3 (5 H, br, s), 6.28 (1 H, 2 d, *J* = 4.6, *J* = 2.1, H₁), 4.52 (1 H, t, br, s), 3.82 (3 H, s, OCH₃), and 1.77 (3 H, s, br, CCH₃); ¹³C NMR δ 146.9, 130.3, 128.8, 127.1, 106.2, 104.8, 101.4, 52.9, and 23.6; MS (CI), *m/z* 218 (P). Enol formate **12**, 1-methoxy-1-phenyl-4-(formylxy)-1,3-butadiene: ¹H NMR δ 7.3 (5 H, s, br, aryl), 7.2 (1 H, d, br, *J* = 6, H₂), 5.9 (1 H, d, *J* = 6, H₃), 3.35 (3 H, s, OCH₃), and 1.90 (3 H, s, CCH₃).

Photochemical Reaction of Methyl Benzoate (1a) with 2,5-Dimethylfuran (2c). A solution of ester **1a** (6 g, 0.04 mol) and 2,5-dimethylfuran (**2c**) (20 g, 0.22 mol) in spectro hexane (100 mL) was irradiated through Vycor for 12 h. The reaction was then stopped, and the dark polymer was scoured from the quartz immersion well. The reaction mixture was irradiated for two more 12-h periods with one additional scraping, following which the solvent and unchanged furan were removed by evaporation. Short-path distillation of the reaction mixtures from two such runs gave 2.4 g of distillate: bp 65–70 °C (bath) (0.06 mm); IR 1710–1700 (s, br); analytical HPLC (20–100% acetonitrile-H₂O gradient) shows the components in the ratio 7:4:6:11:8:26:18:3:14. The five most abundant were collected on a preparative column (25 cm × 2.1 cm) with the same solvent gradient. The first peak to be eluted proved to be the *E,Z* mixture of β,γ-enones **13**, 4-acetoxy-1-phenyl-3-penten-1-one: ¹H NMR (CDCl₃) δ 8.04 (2 H, d, ortho aryl), 7.7–7.5 (3 H, meta and para aryl), 5.09 (1 H, t, *J* = 7, H₃), 3.19 and 3.07 (2 H each, d, *J* = 7, CH₂ of *E* and *Z* isomers), 2.23 and 2.18 (3 H each, OOCCH₃ of *E* and *Z* mixture), and 1.80 and 1.83 (3 H each, C=CCH₃ of *E* and *Z* mixture); MS (CI via NH₃) 219 (P + 1), 105 (100); IR 1680 (s), 1220 (s, br), and 1060 cm⁻¹ (s). Anal. Calcd for C₁₃H₁₄O₃: C, 71.08; H, 6.42. Found: C, 70.75; H, 6.25.

The second preparative HPLC peak (44% of total) was the rearranged diacetyl compounds, **17a,b** (*E,Z* mixture), 1-phenyl-1-methoxy-2-acetyl-1-penten-4-one: ¹H NMR (isomer A, 54%) δ 7.6–7.2 (5 H, m, br), 3.43 (3 H, s, OCH₃), 3.06 (2 H, s, CH₂), 2.51 (3 H, s, CH₃COC=C), and 2.03 (3 H, s, COCH₃), (isomer B, 46%) 7.6–7.2 (5 H, m, br), 3.60 (2 H, s, CH₂), 3.34 (3 H, s, OCH₃), 2.18 (3 H, s, CH₃COC=C), and 1.56 (3 H, s, CH₃COCH₂); MS (EI, isomer A or B) 232 (P, 4), 217 (2), 189 (90), and 115 (100); IR (via GC-FTIR, isomer A or B) 1731 (s), 1680 (s), 1630 (m) cm⁻¹; ¹³C NMR (major isomer, A) δ 208.0 (C=O), 199.8 (C=O), 133.8, 130.9, 129.5, and 129.1 (aryl), 167.1 (C₁), 57.8 (OCH₃), 44.1 (CH₂), 32.2 (C=COCH₃), and 30.0 (CH₂COCH₃), (minor isomer, B) 207.4 (C=CCOCH₃), 201.1 (CH₂COCH₃), 167.1

(C₁), 134.1, 130.4, 130.3, and 129.3 (aryl), 119.7 (C₂), 57.5 (oCH₃), 42.2 (CH₂), 30.3 (C=CCOCH₃), and 29.6 (CH₂COCH₃). Anal. Calcd for C₁₄H₁₆O₃: C, 72.39; H, 6.81. Found: C, 72.16; H, 6.62.

Also isolated by extraction (i.e., removal) of the other seven components of the 1a-2c photochemical reaction mixture with pentane or petroleum ether were the three ketones 18, 19, and 20. These three ketones could be further isolated from components 13a,b, 14, 15, 16, 17a, and 17b by column chromatography on neutral alumina as described above.

Ketone 18, 2-phenacyl-5-methylfuran: IR (GC-FTIR) 1705 (s), 1605 (w), and 1267 (br) cm⁻¹; ¹H NMR (CDCl₃) δ 7.9 (2 H, m, ortho aryl), 7.3-7.2 (3 H, m, meta and para aryl), 6.3 (2 H, m, furyl), 3.1 (2 H, CH₂) and 2.21 (3 H, CH₃); MS (EI), *m/z* 200 (P, 15), 105 (100), and 77 (42). **Methylenedihydrofuran 19** was unstable to heat and air and was not obtained pure: IR (GC-FTIR) 1669 (s), 1570 (s), 1203 (m), and 903 cm⁻¹; ¹H NMR δ 7.9-7.8 (2 H, m), 7.8-7.7 (3 H, m, meta and para aryl), 3.39 (1 H, s, br, H₄), 4.90 (2 H, m, C=CH₂), and 2.38 (3 H, s, CH₃); MS (EI), *m/z* 200 (P, 100), 123 (78), and 77 (85). **Ketone 20, 3-benzoyl-2,5-dimethylfuran,** was obtained pure by HPLC: IR (GC-FTIR) 1694 (s) cm⁻¹; ¹H NMR (CDCl₃) δ 7.83 (2 H, m, ortho aryl), 7.38 (3 H, m, meta and para aryl), 6.35 (1 H, s, H₄), 2.38 (3 H, s, C₂ CH₃), and 2.32 (3 H, s, C₅ CH₃); MS (EI), *m/z* 206 (P, 14), 129 (100), and 77 (40); ¹³C NMR δ 196.9 (C=O) 133.6, 128.9, 128.7 (aryl), 155.8 (C₃), 151.9 (C₆), 123.8 (C₂), 108.7 (C₄), 29.8 (C₂ CH₃), and 13.3 (C₅ CH₃); MS (EI), *m/z* 200 (P, 60), 185 (100), 105 (40), and 77 (30). Anal. Calcd for C₁₃H₁₈O₂: C, 75.73; H, 8.87. Found: C, 75.71; H, 8.68.

From the hexane-soluble extracts of the total reaction mixture after short-path distillation was also obtained via column chromatography on neutral alumina, eluting with hexane, the 2 + 2 furan cyclodimer 16: IR (GC-FTIR) 1221, 1019, and 778 cm⁻¹; ¹H NMR (CDCl₃) δ 2.17 (C=CCH₃) and 1.45 (CCH₃); MS (EI), *m/z* 190 (P, 19), 95 (100), 43 (18). Later fractions from the alumina chromatography (with hexane) contained a mixture of *exo*-phenyl- and *endo*-phenyloxetanes 16, 1,3-dimethyl-6-methoxy-6-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-enes: ¹H NMR (CDCl₃) δ 7.3 (5 H, m), 5.82 and 5.78 (1 H, m, OC=CH), 4.16 and 3.41 (1 H, br s, H₅ of *endo*-phenyl and *exo*-phenyl isomers), 3.08 (3 H, s, OCH₃ of both isomers), 1.80 and 1.71 (3 H, s, C=CCH₃ and CCH₃); MS (EI), *m/z* 232 (P, 20), 217 (63), and 136 (100).

Finally, there was obtained the *E,Z* isomeric mixture of dienyl acetates 15: IR (GC-FTIR) 1772, 1692, 1617, 1202 (vs) cm⁻¹; ¹H NMR (CDCl₃) δ 7.3 (5 H, m, aryl), 5.92 (1 H, m), 5.83 (1 H, m), 3.15 (3 H, s, OCH₃), 2.22 (3 H, s, C=CCH₃), and 2.17 (3 H, s, OOCCH₃); MS (EI), *m/z* 232 (P, 20), 190 (100), 175 (35), and 43 (90).

Hydrolysis of *E* and *Z* Mixture 17a,b. To a solution of 17a,b (0.1 g) in 90% aqueous THF was added 2 drops of concentrated HCl. The solution was allowed to stand for 4 h at 25 °C and was then poured onto 40 g of ice-water and extracted with 3 × 10 mL of dichloromethane. Washing of the combined extracts with water,

drying (Na₂SO₄), and evaporation of the solvent gave an oil, **3-benzoylhexane-2,5-dione:** ¹H NMR (CDCl₃) δ 7.98 (2 H, d, ortho aryl), 7.59 (1 H, t, para aryl), 7.48 (2 H, t, meta aryl), 5.04 (1 H, t, *J*_{3,4} = 7.1, H₃), 2.97 and 3.17 (1 H each, dd, *J*_{4,3} = 7.1, *J*_{4,4} = 8.2, H₄), 2.14 and 2.19 (3 H each, s, CH₃); IR (GC-FTIR) 1731 (vs), 1693 cm⁻¹; MS (EI), *m/z* 175 (3), 158 (20), 133 (30), 105 (100), 96 (20), 77 (50), 43 (65%); ¹³C NMR (CDCl₃) δ 206.2 (C₅), 203.1 (C₂), 196.9 (PhC=O), 136.6 (1-aryl), 134.5 (para aryl), 129.6 (meta aryl), 129.4 (ortho aryl), 57.2 (C₃), 42.35 (C₄), 30.0 and 29.6 (CH₃).

Photochemical Reaction of Methyl Benzoate with 2,3,4,5-Tetramethylfuran (2d). A solution of ester 1a (6 g, 0.04 mol) and 2,3,4,5-tetramethylfuran (2d)¹³ (12 g, 0.10 mol) in spectrograde pentane (120 mL) was irradiated with a Rayonet chamber reactor using 254-nm lamps for 60 h. Evaporation of solvent and distillation of unreacted ester and furan left a yellow residue, which was short-path distilled to afford dione 22, bp 70-80 °C (0.8 mm) (1.4 g, 41% based on unrecovered ester 1a): ¹H NMR (CDCl₃) δ 8.00 (2 H, d, ortho aryl), 7.6-7.3 (3 H, m, aryl), 3.88 (3 H, s, OCH₃), 2.07 (6 H, s, CH₃CO), and 1.80 (6 H, s, CCH₃); ¹³C NMR (CDCl₃) δ 216.0 (C=O), 199.3 (C=O), 143.9 (C=CO-CH₃), 132.7, 129.5, 128.2 (aryl), 114.8 (C=COCH₃), 51.9 (OCH₃), 14.9 (COCH₃), 17.2 (C=OOCH₃), 13.9, 13.8, 11.2, and 9.98 (CH₃C and CH₃C); MS (CI), *m/z* 260 (14), 245 (6), 217 (30), and 43 (100).

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Synthesis of Racemic (*E*)- and (*Z*)-2,3-Methanotyrosine: New Cyclopropane Analogues of Tyrosine

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Both (*E*)- and (*Z*)-2,3-methanotyrosine [(*E*)-2,3-MeTyr and (*Z*)-2,3-MeTyr] have been synthesized from the monoester 5, which was prepared by cyclopropanation of the benzalmalonate 3, followed by regioselective saponification and Curtius rearrangements to introduce the amino group stereoselectively. The *E* and *Z* configurations resulting unambiguously from these synthetic transformations were corroborated by the vicinal coupling constants of the cyclopropane ring protons. Ultraviolet spectroscopy confirmed the conjugative ability of the cyclopropane ring.

For some years now we have been engaged in the synthesis of 2,3-methano amino acids¹ both for incorporation

into peptide hormones² in order to selectively restrict the peptide conformation³ and stabilize amide bonds and as