nonenolizable β-keto esters (not shown) were unreactive. Of the enolizable β-keto esters, the cyclopentanone derivative was much faster than the cyclohexanone, which in turn was much faster than the α-substituted acyclic ketone. An α-unsubstituted acyclic ketone was intermediate in reactivity.

We speculate that formation of the pyridinum species **2** is the rate-determining step in this decarbalkoxylation. Formation of **2** could be faster with the enol form of the keto ester, since the enol could hydrogen bond to the ester carbonyl, activating it for 1,2-addition. It would follow that enol content of the keto ester would dictate reactivity in this process, a suggestion certainly in keeping with the data in Table I.

Other factors were briefly probed. The reaction is significantly accelerated at higher or lower pH. On the other hand, no difference in reactivity was seen between a methyl and an *n*-butyl ester. Neither DABCO,[2b] *N*,*N*-dimethylaniline, pyridine, nor tetrapentylammonium bromide was an effective mediator of decarbalkoxylation under these conditions.

It should be noted that neither isolated esters nor malonates are reactive under these conditions. Thus, in addition to being of interest mechanistically, this method for the decarbalkoxylation of enolizable β-keto esters could prove to be of preparative utility.

Experimental Section[6]

3-Benzylcyclopentanone (4). A 1-mL reaction vial charged with 133 mg (0.488 mmol) of **1**,[7] 24 mg (0.4 equiv) of 4-(dimethylamino)pyridine, 0.5 mL of 1.0 M phosphate buffer (pH 7), and 0.5 mL of toluene was maintained with stirring at 90 °C for 6 h. The reaction mixture was partitioned between aqueous NH_4Cl and ethyl acetate. The organic phase was dried ($MgSO_4$), concentrated in vacuo, and chromatographed[8] on 3 g of TLC mesh silica gel to give 61 mg (0.348 mmol, 71%) of **4** as a yellow oil. ^{1}H NMR: δ 7.3–7.1 (m, 5 H), 2.7 (d, $J = 7.8$, 2 H), 2.5–1.5 (m, 7 H). ^{13}C NMR: δ 219 (s), 140.0 (s), 128.8 (d, 2), 128.5 (d, 2), 126.2 (d), 44.9 (t), 41.5 (t), 38.8 (d), 38.3 (t), 29.1 (t). IR: 2920, 2875, 1760, 705 cm^{-1}. MS: *m/e* 91 (100), 115 (22), 117 (38), 174.104 (66) (M + H)$^+$.

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Registry No. **1**, 120853-06-7; **4**, 85163-16-2; **5**, 120853-07-8; **6**, 120853-08-9; **7**, 14171-89-2; **8**, 74851-58-4; **9**, 98-53-3; **10**, 120853-09-0; 4-DMAP, 1122-58-3.

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Quantitative Rearrangement of Monocyclic Endoperoxides to Furans Catalyzed by Co(II)

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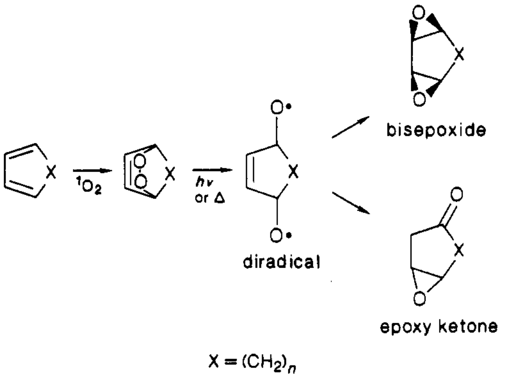
Cycloaddition of singlet oxygen to conjugated dienes provides a synthetically useful method of introducing oxygen at the 1,4-positions of 1,3-dienes.[1,2] The resulting unsaturated bicyclic endoperoxides can be converted both thermally and photolytically to a variety of stereospecifically oxygenated compounds[3] including bisepoxides. Rearrangement to the bisepoxide is usually favored over the competing retro-Diels–Alder reaction unless loss of oxygen leads to a particularly stable product (as with endoperoxides of polycyclic aromatic hydrocarbons).[4] Both thermal and photolytic paths appear to go via a biradical medium and give substantial amounts of side products such as epoxy ketone.[5]



Boyd et al.[6] reported that cobalt(II) tetraphenylporphyrin (CoTPP) catalyzes the rearrangement of unsaturated bicyclic endoperoxides to bisepoxides in high yield. Balci[7] applied this reaction to unsaturated bicyclic endoperoxides from strained dienes and proposed a diradical mechanism. Noyori[8] used iridium and palladium to catalyze the rearrangement.

These reactions have previously been applied only to bicyclic endoperoxides. We now report that CoTPP-catalyzed rearrangement of monocyclic endoperoxides gives furans in quantitative yield.

cis-3,6-Dimethyl-1,2-dioxene was prepared from the reaction of (*E*,*E*)-2,4-hexadiene with singlet oxygen.[9] Treatment of the endoperoxide with 5–10 mol % CoTPP in chloroform at room temperature yielded a 1:1 mixture of hemiketals **1** and **2**. These compounds were characterized by a variety of NMR experiments, including 2D ^{1}H–^{1}H homonuclear correlation, 2D ^{1}H-^{13}C heteronuclear correlation, DEPT, and homonuclear decoupling experiments. The results are summarized in Table I (assignments of positions 2 and 3 are ambiguous). The hemiketals decompose on further standing at room temperature to give 2,5-dimethylfuran in quantitative yield (see paragraph at the end of the paper about supplementary material). Treatment of *cis*-3,6-diphenyl-1,2-dioxene with CoTPP gave 2,5-diphenylfuran,[10] also in nearly quantitative yield.

Several cobalt(II) complexes were investigated to help gain insight into the mechanism. Spin state, geometry, and

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Table I. Chemical Shifts and Coupling Information for Hemiketals I and II[a]

position	^{13}C, δ (ppm)	DEPT multiplicity	2D ^{13}C–^{1}H[b] connectivity	^{1}H, δ (ppm)	H–H[c] COSY
1	109.4	singlet			
	109.2	singlet			
2(3)	134.5	doublet	⇒	5.87 (2 H, m)[d]	
	134.3	doublet			
3(2)	129.9	doublet	⇒	5.72 (2 H, m)[d]	
	129.8	doublet			
4	80.3	doublet	→	4.87 (1 H, q)	
	80.9	doublet	→	4.73 (1 H, q)	
5	22.7	quartet	→	1.50 (3 H, s)	
	21.4	quartet	→	1.45 (3 H, s)	
6	31.3	quartet	→	1.25 (3 H, d)	
	27.5	quartet	→	1.17 (3 H, d)	
OH				2.88 (1 H, b s)	
				2.77 (1 H, b s)	

[a] Bruker AF-200, 200 MHz. [b] Arrow indicates C–H coupling observed. [c] Brace indicates H–H coupling observed. [d] Isomeric peaks not resolved.

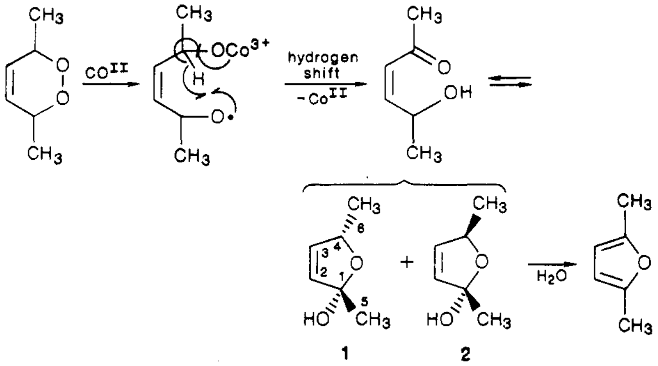
Table II. Catalytic Activity of Co(II) Complexes

Co(II) complex	% reaction[a]
cobalt(II) tetraphenylporphyrin	100
cobalt(II) salen	100
bis(salicylaldehyde)cobalt(II) dihydrate	no reaction
cobalt(II) acetylacetonate	no reaction

[a] 12 h, 25 °C.

the nature of the ligand affect the ability of Co(II) to catalyze the rearrangement. Four-coordinate low-spin planar complexes formed from tetradentate ligands (e.g. CoTPP and CoSalen) are active catalysts; however, the six-coordinate complexes investigated (bissalicylaldehyde dihydrate and AcAc) are not (Table II).

A probable mechanism for the rearrangement involves catalytic cleavage of the peroxide bond, presumably by electron transfer, followed by a hydrogen shift, loss of CoTPP, and closure to 2-hydroxy-2,5-dimethyl-2,5-dihydrofuran, as shown below. Loss of water yields 2,5-dimethylfuran. There is NMR evidence for intermediate formation of approximately 5% 5-hydroxy-3-hexen-2-one.[11]



Fujimori[12a] and Demole[12b] used the rearrangement of the addition product of singlet oxygen to neophytadiene to synthesize a terpenoid furan, but this route required harsh conditions (260 °C) and gave a poor yield (8%). The CoTPP-catalyzed rearrangement is a mild, high-yield, "one-pot" method of converting conjugated acyclic dienes to substituted furans. This route should be useful for synthesis of naturally occurring furanoterpenes and may mimic the path by which these substances are formed in nature.

Experimental Section

^{1}H and ^{13}C 2D NMR spectra were recorded on a Bruker AF-200 MHz instrument. Chemical shifts are given in ppm relative to TMS. Gas chromatograms were run on a Hewlett-Packard 5880A GC equipped with a 30-m DB-17 capillary column and a FID detector.

Materials. All the chemicals were purchased from Aldrich Chemical Co. and used within purification except for 1,4-diphenyl-(*E,E*)-1,3-butadiene, which was recrystallized from a solution of hexanes and ethanol. The solvents were used as received.

General Procedure for Photooxidation. Photooxidations were carried out at −78 °C with a vacuum-jacketed pipeline with temperature control with an accuracy of ±2.0 °C.[13] A 300-W Varian-Eimac xenon lamp without filter solution was used for irradiation. Oxygen, dried over KOH and Drierite, was continuously bubbled through the sample during photolysis.

***cis*-3,6-Dimethyl-1,2-dioxene.** A 200-μL aliquot of (*E,E*)-2,4-hexadiene and 5 mL of a Freon 11/mesoporphyrin IX dimethyl ester sensitizer solution were pipeted into a 13 × 100 mm Pyrex test tube. The solution was irradiated until no diene was detectable by gas chromatography. The solution was rotary evaporated to remove solvent and other volatile components such as acetaldehyde and butenal.[9] The remaining solution was placed under vacuum at 0.75 mmHg until most of the residue had been passed into a trap cooled by a dry ice/acetone bath. The trapped solution was >98% *cis*-3,6-dimethyl-1,2-dioxene by gas chromatography: ^{1}H NMR 1.35 (6 H, d), 4.66 (2 H, q), 5.96 (1 H, s) ppm; ^{13}C NMR 18.7, 74.7, 129.0 ppm; IR (film) 3010, 2900, 1450, 1380, 1100, 1040 cm^{-1}; MS m/z 114 (M^+), 99, 82 (base). ^{1}H NMR, IR, and MS data are virtually identical with those reported previously.[10]

***cis*-3,6-Diphenyl-1,2-dioxene.** 1,4-Diphenyl-(*E,E*)-1,3-butadiene (500 mg) and 2 mg of tetraphenylporphyrin were dissolved in 5 mL of chloroform. The solution was photooxidized until all the diene had reacted. Solvent evaporation yielded the *cis*-3,6-diphenyl-1,2-dioxene (98% pure): ^{1}H NMR 7.42 (10 H, m), 6.35 (2 H, s), 5.64 (2 H, s) ppm; ^{13}C NMR 138.3, 129.1, 128.9, 128.8, 127.8, 80.6 ppm; MS m/z 238 (M^+), 220, 105 (base), 77. ^{1}H NMR and MS data are virtually identical with those reported previously.[10]

Co(II)-Catalyzed Rearrangement. Treatment of the dioxenes with 5–10% CoTPP or CoSalen in chloroform at room temperature gave the corresponding furans quantitatively. While the *cis*-3,6-dimethyl-1,2-dioxene showed a mixture of hemiketals by NMR during the rearrangement (see Table I), no evidence for such intermediates was obtained during the *cis*-3,6-diphenyl-1,2-dioxene rearrangement. The GC and NMR spectra of authentic samples of 2,5-dimethylfuran and 2,5-diphenylfuran were identical with those obtained from the reaction products.

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[11] NMR experiments on the reaction mixture provide strong evidence for formation of 5% 5-hydroxy-3-hexen-2-one: ^{1}H NMR 6.20, 6.10, 4.80, 3.62, 1.37 ppm; ^{13}C NMR 200.7 (C), 152.3 (CH), 127.3 (CH), 64.8 (CH), 26.5 (CH_3), 22.5 (CH_3) ppm. Both ^{1}H–^{1}H and ^{1}H–^{13}C coupling patterns are consistent with the assigned structure.

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Supplementary Material Available: ^{1}H NMR spectra ($CDCl_3$, 200 MHz) of the CoTPP-catalyzed rearrangement of *cis*-3,6-dimethyl-1,2-dioxene after 45 min and 12 h at room temperature; the figure clearly displays the isomeric hemiketals and the clean quantitative formation of 2,5-dimethylfuran (1 page). Ordering information is given on any current masthead page.

A Facile Procedure for Synthesis of Capsaicin[1]

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Capsaicin (**1a**), a pungent principle of capsicums, has been known to exhibit a variety of biological activities,[2] including recent findings concerning its mutagenicity.[3-6] The family of natural capsaicinoids consists of more than 15 vanillylamides including nordihydrocapsaicins, capsaicin, dihydrocapsaicin, homocapsaicins, homodihydrocapsaicins, bishomocapsaicin, and trishomocapsaicin.[7] Recently Gannett et al. suggested adding two capsaicinoids (nornorcapsaicin and norcapsaicin) as new members to this group.[3] Several groups have reported interesting synthetic routes characterized by their own key reactions,[3,8-12] which were developed to introduce an *E* double bond at the C_6 position of the side chain of capsaicin.

It has been reported that *E*-olefins of fatty acids[13,14] or sex pheromones[15] are produced by the nitrous acid induced $Z \rightarrow E$ isomerization reaction of the carbon-carbon double bond.[14] We were interested in testing this technique of introducing the C_6-*E* double bond into the 8-methylnonenoic acid molecule. The results of our study show that by using this technique capsaicin is readily obtained in a concise route amenable to other capsaicinoids.

Phosphonium salt **2**, prepared from commercially available 6-bromohexanoic acid in 88% yield, was treated with ^{t}BuOK and isobutylaldehyde in DMF.[16-18] The product, (*Z*)-8-methyl-6-nonenoic acid (**3b**) (74%), was found to be contaminated with the *E* isomer in a 1:11 *E/Z* ratio by GLC analysis through esterification with diazomethane. Subsequent treatment of **3b** with HNO_2 in HNO_3 at 70 °C for 30 min[15] afforded the *E* isomer **3a** (77%, *E/Z* = 8:1). No other isomer due to double bond migration was detected.[14]

$(CH_3)_2CHCH{=}CH(CH_2)_4COR$
a = *E*, *b* = *Z* double bond

$Br^-Ph_3P^+(CH_2)_5COOH$
2

1: $R = NHCH_2C_6H_3\text{-}3\text{-}OCH_3, 4\text{-}OH$
3: $R = OH$
4: $R = Cl$

The other end of the capsaicin molecule is a vanillylamine moiety, which had been prepared by reduction of vanillin oxime.[3,10,19] The Leuckart reaction of vanillin using ammonium formate[20] could also produce pure vanillylamine hydrochloride (47.5%). The (*E*)-acid chloride **4a** was treated with free vanillylamine to yield the crude amide (91%, *E/Z* = 8:1), whose fractional crystallizations from hexane-ether furnished capsaicin (**1a**) (53%) in a pure state. Similar treatment of the (*Z*)-acid chloride **4b** led to *cis*-capsaicin (**1b**) (66%), which does not occur naturally.[2a,21,22]

Experimental Section

Melting points were determined on a MEL-TEMP apparatus (Laboratory Devices) and are uncorrected. Boiling points are uncorrected. Infrared spectra were recorded on a FTS-65 (BIO-RAD) spectrophotometer. ^{1}H NMR spectra were run in $CDCl_3$ solution with Me_4Si as an internal standard (δ = 0 ppm) and resistered on a JEOL GX-270 (270 MHz) or JEOL PS-100 (100 MHz) spectrometer. Mass spectra were obtained on a INCOS 50 (Finnigan MAT Instruments, Inc.) at 70 eV under electron impact conditions, or a JEOL JMS-D300 instrument under field ionization condition. Gas chromatography was carried out on a YANACO G180 instrument [Yanagimoto, a 30-m glass capillary column (0.28 mm in diameter) coated with Silicone OV-101; column temperature 140 °C; injector temperature 200 °C; detector temperature 200 °C; carrier gas N_2; flow rate 0.51 mL/min].

(6-Carboxyhexyl)triphenylphosphonium Bromide (2). A mixture of 6-bromohexanoic acid (25.8 g, 0.13 mol) and triphenylphosphine (34.7 g, 0.13 mol) was heated to 145 °C for 4 h. The cooled glassy reaction mixture was triturated with dry $CHCl_3$ and diluted with ether. The precipitate (58.3 g, 96%), mp 200-203 °C, was recrystallized from $CHCl_3$ to give an analytically pure white powder **2** (53.4 g, 88%): mp 202-203 °C; IR (KBr) 3200-2600 (COOH), 1705 (C=O) cm^{-1}; ^{1}H NMR (270 MHz) δ 1.62-1.72 (6 H, m, $C_{3,4,5}$-H), 2.39 (2 H, t, *J* = 7.0 Hz, C_2-H), 3.58-3.70 (2 H, m, C_6-H), 7.70-7.84 (15 H, m, Ar-H); (100 MHz) δ 10.75 (1 H, br s, COOH). Anal. Calcd for $C_{24}H_{26}O_2PBr$: C, 63.03; H, 5.73; Br, 17.47. Found: C, 62.90; H, 5.75; Br, 17.32.

(*Z*)-8-Methyl-6-nonenoic Acid (3b). A mixture of the salt **2** (22.8 g, 50 mmol) and isobutylaldehyde (3.6 g, 59 mmol) in dry DMF (100 mL) was added to a suspension of KO^{t}Bu (11.55 g, 102.5 mmol) in dry DMF (125 mL) under an atmosphere of N_2 at 0 °C during the course of 15 min. After vigorous stirring for 15 h at room temperature, the resulting slurry was poured into ice-water (150 mL). Precipitated triphenylphosphine oxide was removed by suction filtration. The filtrate was washed with benzene (30 mL × 2) and acidified with 2 M HCl. The product was extracted with ether (20 mL × 4), washed with saturated brine (15 mL × 4), dried over anhydrous Na_2SO_4, and subjected to short pass distillation to give the acid **3b** (6.25 g, 74%): bp 109-110 °C (3 Torr) [lit.[23] bp 150-150 °C (13 Torr)]; IR (neat) 3000-2500

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