2,2′-Dibromo-6,6′-dichloro-4,4′-dinitrobiphenyl (4). Bromination of 12 by the method used by Harris and Mitchell[11] led to a quantitative yield of 4 as light orange plates, mp 157.8–160.0° (ethanol). Anal. Calcd for $C_{12}H_{14}Br_2Cl_2N_2O_4$: C, 30.61; H, 0.86; Br, 33.94. Found: C, 30.30; H, 0.91; Br, 34.70. Ir (KBr) 1360, 1530 cm^{-1} (NO_2).

Attempted Self-Coupling of 4-Benzyloxy-2,3,6-trimethyliodobenzene (8) via the Grignard Reagent. The reported procedure for preparation of bimesityl[13] was applied to **8**; the only product, formed in about 80% yield, was 3-benzyloxy-1,2,5-trimethylbenzene (see below).

3-Benzyloxy-1,2,5-trimethylbenzene. Benzylation of the phenol **6** by the procedure described above for the preparation of **8** led to a 75% yield of the ether as an oil. Elution through neutral alumina and distillation gave a colorless oil, bp 165° (2.7 mm), which crystallized (mp 34.5–37.5°). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.44; H, 7.97. NMR ($CDCl_3$) s, δ 2.13 (6 H, 1,2-CH_3); s, 2.20 (3 H, 5-CH_3); s, 5.14 (2 H, OCH_2); broad s, 6.50 (2 H, 4,6-H); m, 7.2 (5 H, C_6H_5); ir (neat) 1120, 1225, 1250, 1290 cm^{-1} ($ArOCH_2$–); no OH.

Registry No.—**1** (R = $CH_2C_6H_5$), 57362-66-0; **1** (R = H), 57362-67-1; **1** (R = n-C_8H_{17}), 57362-68-2; **2** (R = n-C_8H_{17}), 57362-69-3; **3** (R = C_2H_5; R′ = n-C_8H_{17}), 57362-70-6; **3** (R = H; R′ = n-C_8H_{17}), 57362-71-7; **4**, 57362-72-8; **6**, 697-82-5; **7**, 7282-02-2; **8**, 57362-73-9; **9**, 57362-74-0; **11**, 41252-96-4; **12**, 57362-75-1; **13**, 57362-76-2; **14** (R = C_2H_5), 57362-77-3; benzyl chloride, 100-44-7; n-octyl chloride, 629-27-6; p-cyanobenzaldehyde, 105-07-7; ethyl p-iodobenzoate, 51934-41-9; 3-benzyloxy-1,2,5-trimethylbenzene, 57362-78-4.

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A New γ-Keto Aldehyde Synthesis

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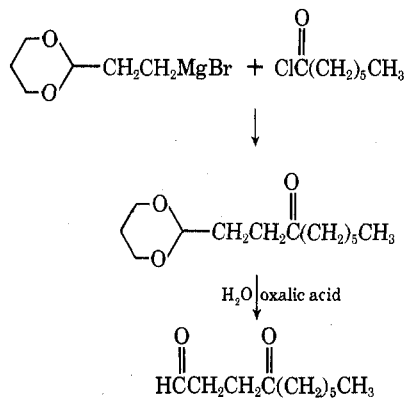
γ-Keto aldehydes are an important class of compounds especially as intermediates for the preparation of cyclopentenones.[1] 1,4-Diketones have found wide application in the Paal–Knorr synthesis of pyrroles, furans, and thiophenes,[2] as well as in pyridazine synthesis,[3] which suggests that γ-keto aldehydes may be useful in the synthesis of these heterocycles as well. The available routes to γ-keto aldehydes include ring opening of substituted furans,[4] radical addition of an aldehyde to acrolein diethyl acetal,[5] oxidative cleavage of olefins,[6] alkylation of 2,4,4,6-tetramethyldihydrooxazine with 2-iodomethyl-1,3-dioxolane,[7] and alkylation of 2-ethoxyallyl vinyl sulfide followed by thio-Claisen rearrangement.[8] Recently a route using condensation of the dianion of γ-oxosulfone acetals with esters followed by removal of activating and protecting groups,[9] and another based on ring opening of cyclopropyl ketones followed by oxidation, were reported.[10] Most of these routes are either lengthy, require multistep preparation of a special reagent, or give low overall yields.

We have found a short route which begins with readily available materials, and gives high yields of γ-keto aldehyde, as outlined in Scheme I. Grignard reagents have

Scheme I



found occasional use for preparation of ketones from acid chlorides but the yields are usually low owing to reaction with the ketone, leading to tertiary alcohols.[11–13] Even at dry ice temperature and using inverse addition, the yields are not improved.[14] We have found that the Grignard reagent derived from 2-(2-bromoethyl)-1,3-dioxane is exceptional; it affords ketone in high yield with no more than a trace of tertiary alcohol at dry ice temperature.

Grignard reagents derived from β-halo ketals and acetals are known to be unstable[15] owing to their tendency to undergo intramolecular attack leading initially to cyclopropyl ethers. Büchi[16] and others[17] have used the reagent derived from 2-(2-bromoethyl)-1,3-dioxolane by preparing it at 30–35°. This reagent is destroyed if the solvent tetrahydrofuran (THF) is allowed to reflux. We chose to use the six-membered ring acetal and found that its greater stability allowed quick, high-yield preparation of the Grignard reagent at reflux in THF. This then gave 2-(3-oxononyl)-1,3-dioxane in 92% yield based on the bromo compound or the acid chloride.

The six-membered-ring acetal apparently has greater equilibrium stability than the five-membered ring, since boiling the intermediate in aqueous acid gives only partial hydrolysis to the keto aldehyde. However, the equilibrium is easily displaced toward hydrolysis with removal of the product by continuous steam distillation as it is formed. This gave γ-ketodecanal in 89% yield. This particular product is an intermediate in a synthesis of dihydrojasmone.[8] The Grignard reagent derived from 2-(2-bromoethyl)-4,4,6-trimethyl-1,3-dioxane also gives ketones in better than 90% yields but the acetal is more stable and therefore less readily removed with aqueous acid.

The usual technique for preventing overreaction is to first convert the Grignard to the zinc or cadmium reagent, which then affords ketones in better yields.[13,18] In our earlier efforts, we prepared the zinc reagent directly from 2-(2-iodoethyl)dioxolane at 51° in dimethylformamide (DMF);[19] however, we were unable to isolate any ketone products from reaction with acid chlorides. The formation of the organozinc iodide compounds could be followed in the NMR,[20] e.g., that from the iodoacetal gave a high-field triplet at δ 0.13 ppm, comparable with a quartet at δ 0.01 obtained from ethyl iodide and Zn in DMF. The Grignard

reagents may also be observed by NMR; that derived from 2-(2-bromoethyl)-1,3-dioxane in THF exhibits a high-field triplet at δ-0.7 ppm.

Experimental Section

2-(2-Bromoethyl)-1,3-dioxane was prepared from 1,3-propanediol, acrolein, and hydrogen bromide:[21] bp 67–70° (2.8 mm); 60-MHz NMR (CCl_4) δ 1.3 (m, 1 H), 2.1 (m, 3 H), 3.36 (t, 2 H), 3.9 (m, 4 H), 4.57 ppm (t, 1 H).

2-(3-Oxononyl)-1,3-dioxane. A 50-ml flask was equipped with a reflux condenser, nitrogen atmosphere, and magnetic stirring. In it was placed 0.97 g (0.040 mol) of magnesium turnings, 25 ml of dry THF, and 5.85 g (0.0300 mol) of 2-(2-bromoethyl)-1,3-dioxane. This was heated to reflux and the heat immediately removed. The exothermal reaction was moderated at reflux by occasional application of an ice bath. After 10 min, heat was applied to maintain refluxing for an additional 10 min. After cooling to room temperature the solution was drawn up into a 50-ml syringe, leaving the excess magnesium behind.

A 100-ml flask was equipped with a nitrogen atmosphere and magnetic stirring. In it was placed 4.46 g (0.0300 mol) of heptanoyl chloride and 25 ml of dry THF. This was cooled in a dry ice–2-propanol bath, and the Grignard reagent solution was added dropwise from the syringe with stirring over a 20-min period. It was warmed to room temperature over 45 min and then rotary evaporated to remove the THF. The residual oil was poured into 75 ml of water, and 20 ml of cyclohexane was added to extract the product. The organic layer was separated and washed with two 60-ml portions of aqueous sodium carbonate, dried with potassium carbonate, and rotary evaporated. The residual oil was passed through a short column of silica gel eluting with 10% ethyl acetate in cyclohexane. All volatile materials were then removed by evaporation at 0.3 mm in a warm water bath. This gave 6.29 g (92%) of pale yellow oil: homogeneous by TLC and GC; ir (CCl_4) 1720 cm^{-1}, no absorption for OH; 60-MHz NMR (CCl_4) δ 0.7–2.0 (overlapping m's, 15 H), 2.3 (m, 4 H), 3.8 (m, 4 H), 4.43 ppm (t, 1 H).

The semicarbazone was recrystallized from cyclohexane to mp 110–110.5°.

Anal. Calcd for $C_{14}H_{27}N_3O_3$: C, 58.92; H, 9.54; N, 14.72. Found: C, 59.14; H, 9.55; N. 14.68.

4-Oxodecanal. A Dean-Stark trap was modified to return the bottom layer and retain the upper layer, and fitted on a 50-ml flask. In the flask was placed 2.28 g (0.0100 mol) of the keto acetal, 1.00 g of oxalic acid, and 20 ml of water. The Dean-Stark trap was also filled with water. The mixture was heated at reflux with vigorous magnetic stirring for 3 hr, during which time the product continuously steam distilled into the trap. After cooling, the organic layer was taken up in ether, washed with aqueous sodium bicarbonate, dried ($MgSO_4$), and rotary evaporated, giving 1.52 g (89%). Vacuum distillation gave 1.28 g of colorless liquid: bp 70° (0.25 mm); ir (CCl_4) 2730, 1735 (shoulder), 1712 cm^{-1};[8,10] 60-MHz NMR (CCl_4) δ 0.70–2.0 (overlapping m's, 11 H), 2.40 (m, 2 H), 2.60 (s, 4 H), 9.58 ppm (s, 1 H).

Treatment with semicarbazide gave the bissemicarbazone, white crystals (ethanol), mp 180–181°.

Anal. Calcd for $C_{12}H_{24}N_6O_2$: C, 50.68; H, 8.51; N, 29.55. Found: C, 50.73; H, 8.66; N, 29.33.

Registry No.—2-(2-Bromoethyl)-1,3-dioxane, 33884-43-4; 2-(3-oxononyl)-1,3-dioxane, 57345-99-0; 2-(3-oxononyl)-1,3-dioxane semicarbazone, 57346-00-6; heptanoyl chloride, 2528-61-2; 4-oxodecanal, 43160-78-7; 4-oxodecanal bissemicarbazone, 57346-01-7.

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Synthesis of α-Carbalkoxy-γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolides

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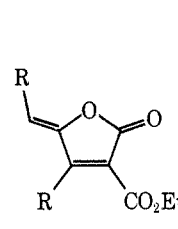
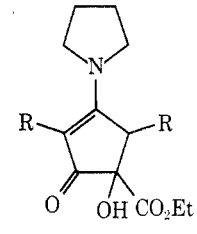
In connection with a projected synthesis of certain sesquiterpenes, several α-carbalkoxy-γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolides[1] were required, e.g., **1** and **10**. Although γ-arylidene analogues of **1** have been reported,[2] the methods employed did not seem compatible with an efficient synthesis of the desired butenolides.

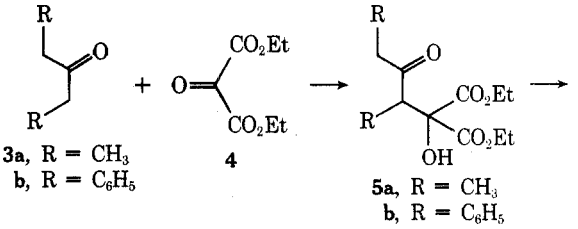


1a, R = CH_3
b, R = C_6H_5



2a, R = CH_3
b, R = C_6H_5

In principle, condensation of ketone **3** with diethyl ketomalonate (**4**) would give an α-hydroxy-γ-keto diester **5**, which might serve as a precursor to **1** via enol lactonization–dehydration. Direct condensation of diethyl ketomalonate (**4**) with tetrahydro-γ-pyrone in unspecified yield has been reported,[3] but we were unable to effectively react **3** with **4** under a variety of standard acid- or base-catalyzed conditions. Hence, we sought alternate methodology and now record a potentially general synthesis of α-carbalkoxy-γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolides from diethyl ketomalonate (**4**) and describe simple reaction modifications which allow preparation of 3-dialkylamino-2-cyclopenten-1-ones **2** as well.



3a, R = CH_3
b, R = C_6H_5

4

5a, R = CH_3
b, R = C_6H_5

Reaction of the morpholine enamine **6a**[4] of 3-pentanone with 1 equiv of diethyl ketomalonate (**4**) in benzene solution at 25°, followed by treatment with sodium acetate–aqueous acetic acid solution, gave α-hydroxy-γ-keto diester **5a** in excellent yield (80% isolated; analytically pure). In-