distillation of the residue there was obtained 18 g of a colorless oil, bp 97–98 °C (0.1 mm).

Anal. Calcd for $C_{10}H_{16}O_3N_2S$: C, 49.18; H, 6.56; N, 11.47; S, 13.11. Found: C, 49.09, H, 6.62; N, 11.59; S, 13.15.

Valine (7). To approximately 35 mL of anhydrous ammonia cooled in a dry ice–acetone bath was added dropwise 18 g of **3**. A vigorous reaction occurs and when complete, the cooling bath was removed and the ammonia was allowed to evaporate. To the residue was added 75 mL of absolute ethyl alcohol and the mixture was heated to reflux. On cooling, 20 g of NaOH in 100 mL of water was added and the temperature increased to above 90 °C, allowing the alcohol to distill off. The mixture was refluxed for 24 h. After cooling, 100 mL of 6 N HCl was added and the mixture was taken to dryness under reduced pressure. A few milliliters of water was added to the residue and it was again taken to dryness. The residue was extracted several times with a total of 200 mL of hot absolute ethyl alcohol. The alcoholic solution was concentrated to approximately 50 mL, filtered, and treated with 15 mL of pyridine. After standing in the refrigerator overnight the crystals were collected, washed with alcohol, and air dried. The yield for several runs was from 8 to 9 g of very pure, almost colorless valine. Paper chromatography showed the sample to be homogeneous, having the same R_f value as a standard sample of valine (1-butanol/acetic acid/water/pyridine; 10:2:2:1).

Anal. Calcd for $C_5H_{11}O_2N$: C, 51.28; H, 9.4; N, 11.96. Found: C, 50.90: H, 8.96; N, 11.99.

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Registry No.—1, 78-84-2; **2**, 67226-50-0; **3**, 67226-51-1; **4**, 67226-52-2; **5**, 67226-53-3; **6**, 67226-54-4; **7**, 516-06-3.

References and Notes

(1) See J. R. Greenstein and M. Winitz, "Chemistry of the Amino Acids", Vol. 1, Wiley, New York, N.Y., 1961, p 698; *ibid.*, Vol. 3, pp 2371–2375.
(2) This amino nitrile has been prepared directly from **2** by the action of ammonia at high temperature and pressure. We carried out the reaction using liquid ammonia at atmospheric pressure, but no amino nitrile could be isolated. However, on a micro scale after hydrolysis some valine could be detected by paper chromatography: see W. T. Gresham and C. E. Schwertzer, U.S. Patent 2 520 312 (1950); *Chem. Abstr.*, **44**, 10732g (1950).
(3) The hydrolysis rate may be increased by increasing the temperature and pressure with no change in the purity of the final product: see ref 1, p 2372.

α-Diazo-β-oxycarboxylates

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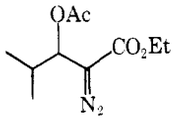
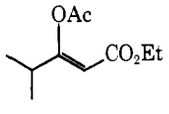
The aldol condensation of α-diazoacetic esters or α-diazomethyl ketones with aldehydes or ketones has been shown to be a facile method of synthesis of α-diazo-β-hydroxycarbonyl compounds,[1] whose pyrolysis has led to β-dicarbonyl substances. In order to study the effect of modification of the hydroxy group and introduction of a neighboring double bond, the following four α-diazo-β-oxy esters were prepared and their pyrolyses were investigated.



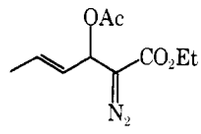
1



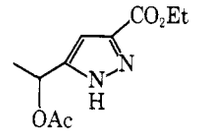
2

Treatment of a tetrahydrofuran solution of isobutyraldehyde and ethyl diazoacetate with *n*-butyllithium at −78 °C and interaction of the resultant lithio salt of the α-diazo-β-hydroxy ester with acetic anhydride yielded ester **1**, whose thermal decomposition gave the enol acetate of ethyl β-oxoisocaproate (**2**). This experience lays the groundwork for a simple, three-step method of preparation of unique enol esters of unsymmetrical β-diketones.

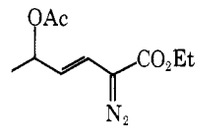
The presence of a double bond vicinal to the acyloxylated carbon causes the pyrolysis to take a different path. Thus, whereas the condensation of crotonaldehyde with diazoacetic ester and subsequent acetylation led to the expected diester **3**, its thermolysis afforded pyrazole **4**. Presumably, ester **3** had



3



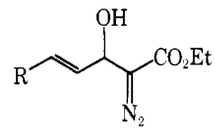
4



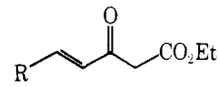
5

experienced an allyl acetate rearrangement and the resultant isomer (**5**) had undergone the known transformation of vinyl diazo compounds into pyrazoles.[2]

Interaction of ethyl lithiodiazoacetate with acrolein and with crotonaldehyde yielded esters **6a** and **6b**, respectively, whose pyrolysis resulted in the formation of β-keto esters **7a**[3] and **7b**,[3c] respectively. This two-step reaction scheme con-



6



7

a, R = H
b, R = Me

stitutes the shortest, presently known method of preparation of vinyl keto ester annelating agents, such as the Nazarov reagent **7a**. Their use in natural products synthesis is already on record.[3e,4,5]

Experimental Section

Infrared spectra of neat liquids were measured on a Perkin-Elmer 137 spectrophotometer and ^1H NMR spectra of deuteriochloroform solutions on a Varian EM-390 spectrometer.

General Procedure for the Preparation of Diazoesters 1, 3, and 6. The aldehyde and ethyl diazoacetate (in 87% methylene chloride solution), 20 mmol each, were added separately to 50 mL of anhydrous tetrahydrofuran, kept constantly at −78 °C. A 2.4 M hexane solution of *n*-butyllithium, 20 mmol, was added dropwise over a period of 45 min to the stirring, yellow solution under nitrogen at −78 °C and the mixture was stirred for 30 min more at the same temperature. Thereafter 2 mL of acetic anhydride in 50 mL of dry ether (for the preparation of **1** or **3**) or 2 mL of glacial acetic acid in 50 mL of anhydrous ether (for the preparation of **6**) was added at one time to the stirring solution and the resultant yellow suspension was stirred at room temperature for 1 h. The mixture was washed four times with 20 mL each of saturated sodium bicarbonate solution, dried ($MgSO_4$), and evaporated under vacuum at room temperature. (Increase of the temperature of the reaction and workup decreased the product yields and led to oils with colors deeper than the yellow color characteristic of α-diazocarbonyl compounds!)

The above procedure used on isobutyraldehyde and ethyl diazoacetate, followed by acetylation, gave 3.9 g of crude diester **1**, which was used in the next reaction without purification. Chromatography of the substance on 200 g of neutral alumina (activity III) and elution with hexane yielded 1.3 g of **1**: IR 4.76 (s, N_2), 5.76, 5.89 (s, C=O) μm; ^1H NMR δ 0.96 (d, 3, J = 6 Hz, Me), 0.99 (d, 3, J = 6 Hz, Me), 1.23 (t, 3, J = 7 Hz, Me of Et), 1.7–2.5 (m, 1, CH), 2.03 (s, 3, Me of Ac), 4.20 (q, 2, J = 7 Hz, CH_2), 5.23 (d, 1, J = 9 Hz, OCH). Anal. Calcd for

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$C_{10}H_{16}O_4N_2$: C, 52.62; H, 7.07; N, 12.27. Found: C, 52.89; H, 7.16; N, 12.25.

The procedure applied to crotonaldehyde and ethyl diazoacetate, followed by acetylation, produced 4.1 g of oil, the rapid filtration of whose 9:1 hexane–ethyl acetate solution through 200 g of neutral alumina (activity III) yielded 2.1 g of yellow, liquid ester **3:** IR 4.75 (s, N_2), 5.75, 5.88 (s, C=O) μm; ^{1}H NMR δ 1.26 (t, 3, J = 7 Hz, Me of Et), 1.30 (d, 3, J = 7 Hz, Me), 2.06 (s, 3, Me of Ac), 4.20 (q, 2, J = 7 Hz, CH_2), 5.33 (dd, 1, J = 14, 7 Hz, δ-H), 5.43 (s, 1, OCH), 6.00 (d, 1, J = 14 Hz, γ-H).

Use of the procedure on acrolein and ethyl diazoacetate afforded 4.5 g of oil whose alumina filtration as in the case of ester **3** above led to 1.2 g of yellow, liquid hydroxy ester **6a:** IR 3.00 (m, OH), 4.80 (s, N_2), 5.94 (s, C=O) μm; ^{1}H NMR δ 1.23 (t, 3, J = 7 Hz, Me), 4.20 (q, 2, J = 7 Hz, OCH_2), 5.20 (s, 1, OCH), 5.3–6.1 (m, 3, CH, CH_2).

When the procedure was applied to crotonaldehyde and ethyl diazoacetate, it yielded 3.7 g of an oil whose alumina chromatography, following the above route for ester **3**, gave 2.4 g of yellow, liquid hydroxy ester **6b:** IR 2.98 (m, OH), 4.80 (s, N_2), 5.93 (s, C=O) μm; ^{1}H NMR δ 1.26 (t, 3, J = 7 Hz, Me of Et), 1.73 (d, 3, J = 6 Hz, Me), 4.20 (q, 2, J = 7 Hz, CH_2), 5.23 (s, 1, OCH), 5.4–6.1 (m, 2, $(CH)_2$).

General Procedure for Pyrolysis. All pyrolyses were carried out by passage of neat diazo esters down a vertical, 25-cm long 2-cm i.d. glass tube, filled with glass helices and kept at 280 °C under 0.25 Torr pressure, and the products were trapped in a receiver cooled by dry ice. (Pyrolyses of cyclohexane solutions or pyrolyses of the neat diazo esters at atmospheric pressure yielded substances of different structures than those below.)

The thermolysis of crude diester **1** yielded an oil whose distillation [at 70–75 °C (0.25 Torr)] produced 1.06 g of liquid, air-sensitive ester **2** (27% overall yield for the two reactions): IR 5.68, 5.86 (s, C=O), 6.10 (s, C=C) μm; ^{1}H NMR δ 1.06 (d, 6, J = 7 Hz, Me_2), 1.23 (t, 3, J = 7 Hz, Me of Et), 2.20 (s, 3, Me of Ac), 2.43 (pentet, 1, J = 7 Hz, CH), 4.06 (q, 2, J = 7 Hz, CH_2), 5.53 (s, 1, olefinic H). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.05; H, 8.14.

After pyrolysis of pure diester **3** the heating chamber was washed with ethyl acetate and the washings were evaporated. Chromatography of the residue, 1.68 g, on 100 g of neutral alumina (activity III) and elution with 9:1 hexane–ethyl acetate yielded 0.31 g of unidentified material and then 1.05 g of viscous liquid pyrazole **4** (23% overall yield): IR 2.89 (w, NH), 5.82, 5.89 (s, C=O), 6.31 (m, C=C) μm; ^{1}H NMR δ 1.33 (t, 3, J = 7 Hz, Me of Et), 1.60 (d, 3, J = 6 Hz, Me), 2.06 (s, 3, Me of Ac), 4.33 (q, 2, J = 7 Hz, CH_2), 5.96 (q, 1, J = 6 Hz, OCH), 6.76 (s, 1, CH).

Pyrolysis of pure hydroxy ester **6a** yielded 0.55 g of keto ester **7a** (20% overall yield); IR and ^{1}H NMR spectra were identical with those reported earlier.[3c]

Pyrolysis of pure hydroxy ester **6b** and subsequent heating of the pyrolysate at 60 °C (30 Torr) for the removal of volatile, unidentified material gave 1.6 g of liquid keto ester **7b** (53% overall yield); IR and ^{1}H NMR spectra were identical with those quoted earlier.[3c]

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Registry No.—**1,** 67272-01-9; **2,** 67272-02-0; **3,** 67272-03-1; **4,** 67272-04-2; **6a,** 67272-05-3; **6b,** 67272-06-4; **7a,** 22418-80-0; **7b,** 17544-47-7; isobutyraldehyde, 78-84-2; ethyl diazoacetate, 623-73-4; crotonaldehyde, 4170-30-3; acrolein, 107-02-8.

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(4) S. W. Pelletier, R. L. Chappell, and S. Prabhakar, *J. Am. Chem. Soc.*, **90,** 2889 (1968); G. Stork and R. N. Guthikonda, *ibid.*, **94,** 5109 (1972).
(5) **Note Added in Proof:** An alternate short synthesis of esters of type **7** is described by P. Pollet and S. Gelin, *Synthesis*, 142 (1978).

Oxidation of Substituted Hydroquinone Monoalkyl Ethers to *p*-Benzoquinone Monoketals

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Blocked benzoquinones are potentially attractive intermediates in synthesis, but until recently no widely applicable methods were known for their preparation. Cyanotrimethylsilyloxycyclohexadienones[2,3,4] and *p*-benzoquinone ketals have received most of the attention. Olefination of the latter class of compounds produced protected quinone methides,[5] and other transformations led to polycyclic biaryls.[6] Carbonium ions derived from *p*-quinone monoketals by carbon–oxygen heterolysis were found to undergo [2 + 4] cycloadditions with olefins.[7] The resulting adducts were easily transformed to neolignans[8] of the bicyclo[3.2.1]octane, hydrobenzofuran, and spiro[5.5]undecane types.

In the past, quinone ketals were prepared sporadically, usually in low yields, by the oxidation of 4-alkoxy- or 4-aryloxyphenols in alcohol with copper(II) species, ceric salts, silver oxide, manganese dioxide, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).[9] Consequently, these reagents were used only rarely until McKillop and Taylor described their preparation using thallium(III) nitrate as the oxidant.[10]

We have prepared a number of *p*-quinone ketals by this procedure (see Table I) and noticed that the yield of the acid-sensitive products could be increased by performing the oxidations in the presence of suspended potassium bicarbonate (see Experimental Section). To replace the toxic thallium salt and also because ketals **9** and **15** were not available by this method, other oxidants were examined. Of those tried, DDQ and ferric chloride proved to be most satisfactory. To suppress acid-catalyzed transformations of the resulting ketals, it is advisable to perform the oxidations with ferric chloride in the presence of potassium carbonate. Some of the more highly oxygenated ketals display significant water solubility, and the yields given in Table I could undoubtedly be improved if continuous extraction was used in the workup procedure.

Experimental Section

Melting points were determined on a Reichert hot-stage microscope and are corrected. Proton magnetic resonance (^{1}H NMR) spectra (90 MHz) were recorded on a Perkin-Elmer R-22 spectrometer and are reported in parts per million (δ) downfield from tetramethylsilane as an internal standard. Mass spectra were determined on a Varian MAT 44 instrument. Ultraviolet (UV) spectra were obtained on a Perkin-Elmer 202 spectrometer. Infrared (IR) spectra were taken with a Perkin-Elmer 247 or 237B grating spectrometer. Elemental analyses were performed by Robertson Laboratory, Florham Park, N.J.

Physical Properties of the New *p*-Quinone Ketals. 2-Allyl-4-methoxy-4,5-methylenedioxycyclohexa-2,5-dienone (4): mp 49–50 °C (ether–pentane); IR ($CHCl_3$) 1690, 1655, 1630 cm^{-1}; NMR (CCl_4) δ 3.09 (br d, 2, J = 7 Hz, C=CCH$_2$), 3.26 (s, 3, –OCH$_3$), 4.98–5.26 (m, 2, CH$_2$=C), 5.49 (s, 1, –OCH$_2$O–), 5.55 (s, 1, –OCH$_2$O–), 5.60 (s, 1, CO—CH=C), 5.70–6.10 (m, 1, C=CH), 6.53 (t, 1, J = 1 Hz, C=CH); UV (95% EtOH) 237 nm (ε 9350), 295 (3200); mass spectrum (70 eV), *m/e* (relative intensity) 208 (M$^+$, 13), 69 (100); ^{13}C NMR ($CDCl_3$) δ 32.6 (t of m), 51.2 (q), 97.6 (br), 98.9 (d), 98.9 (t), 117.9 (t of m), 127.8 (d of t), 134.4 (d of m), 142.8 (br), 168.3 (s), 186.8 (s). Exact mass calcd for $C_{11}H_{12}O_4$: 208.07356. Found: 208.07275.

2-Allyl-4-(2-chloroethoxy)-4,5-methylenedioxycyclohexa-2,5-dienone (5): mp 105–106 °C (ether–pentane); IR ($CHCl_3$) 1690, 1655, 1630 cm^{-1}; NMR ($CDCl_3$) δ 3.15 (br d, 2, J = 7 Hz, C=CCH$_2$), 3.53–3.92 (m, 4, –OCH$_2$CH$_2$Cl), 5.04–5.32 (m, 2, CH$_2$=C), 5.66 (s, 1, –OCH$_2$O–), 5.68 (s, 1, –OCH$_2$O–), 5.82 (s, 1, CO—CH=), 5.73–6.13

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