which is typical for an equilibration involving two rigid molecules. It does favor the cis isomer by +0.6 eu, while the calculation says it should favor the cis isomer by +1.32 eu.

We thus conclude that 2-decalone is quite unexceptional in its conformational behavior. The numbers reported by Augustine and Caputo are erroneous, because they measure steady-state concentrations rather than true equilibrium values, due to the unfortunate occurrence of side reactions at competing rates.[15]

Experimental Section

cis- and *trans*-2-Decalone. These compounds were prepared by the oxidation of *cis*- and *trans*-2-decalol using CrO_3 as reported.[11] The isomers were separated by gas chromatography using a Varian Aerograph Model 700 with a 3/8 in. × 20 ft 15% SE-30 on 30–60 Chromosorb W column at a temperature of 150° and a helium flow rate of 105 cc/min. The retention times of the cis and trans isomers were 104 and 78 min, respectively.

Equilibration. The equilibrations were carried out in 3-mm Pyrex ampoules. A sample of 2-decalone was mixed with an equal amount of acetic acid. The decalone–acetic acid solution (0.2 ml) was sealed in the ampoules with 25 mg of 5% Pd/C. The total volume of material in the ampoule was slightly over half of the volume of the ampoule. The ampoules were heated in metal tubes in an oven at constant temperature until equilibrium was reached (2–7 days). The metal tubes were then plunged into ice water, the ampoules were opened, and the samples were each taken up in 1 ml of hexane. The acetic acid was extracted with aqueous NaOH and the organic layer was washed with water. The hexane–decalone solution was allowed to stand for a few minutes, and then was decanted to separate any remaining catalyst.

Analysis. The analysis was carried out by gas chromatography using a Perkin-Elmer F-11 flame ionization instrument with a 50 ft × 0.02 in. Carbowax 20 M capillary column. The analyses were carried out at 150° using 4 lb of nitrogen carrier gas pressure. The retention times of *cis*- and *trans*-2-decalone were 12.7 and 9.9 min, respectively.

The relative areas under the peaks were determined by multiplying the peak height by its half-height width. It was found that the composition of a mixture of *cis*- and *trans*-2-decalone could be determined to a precision of 0.13%.

The equilibrium was approached from both sides. It was found that the mixtures which started on the trans side proceeded smoothly to equilibrium with very little formation of by-products, while most of the mixtures which started on the cis side formed a great deal of by-product and equilibrium was not attained. In the few cases where little by-product was formed, the same equilibrium mixtures was obtained as from the trans starting material. For this reason we have omitted from our study all samples which had a great deal of by-product. The remaining data are tabulated in Table I.

Table I

Temp, °K	1/T	ln K[a]
459	0.00218	2.38 ± 0.05
463	0.00216	2.36 ± 0.01
468	0.00214	2.41 ± 0.03
477	0.00210	2.30 ± 0.05
483	0.00207	2.38 ± 0.03
489	0.00204	2.29 ± 0.05
503	0.00119	2.17 ± 0.06
513	0.00195	2.18
516	0.00194	2.14 ± 0.08

[a] The values in the table are standard deviations.

In order to obtain ΔH° and ΔS° for the reaction of *trans*- ⇌ *cis*-2-decalone, the inverse of the temperature (°K) and natural logarithm of the equilibrium constant were calculated, and the best straight line through these points was calculated by the method of least squares. The slope is $-\Delta H^\circ/R$ and the intercept is $\Delta S^\circ/R$. The values obtained are $\Delta H^\circ_{488} = 2.51 \pm 0.31$ kcal/mol and $\Delta S^\circ_{488} = 0.6 \pm 0.6$ eu.

(15) After completion of this work, we were informed by Dr. Gerhard Mann in a private communication dated April 20, 1969, that he had independently come to conclusions rather similar to those which we reached and have reported herein. We are indebted to Dr. Mann for this information.

Condensations of Acyldiazomethanes with Aldehydes, Ketones, and Their Derivatives

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Contribution from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401. *Received April 27, 1972*

Abstract: Hydroxide-catalyzed condensations of ethyl diazoacetate and diazo ketones with aldehydes in alcohol solution yielding α-diazo-β-hydroxycarbonyl compounds are described. Similar condensations between the diazo esters and ketones of the small ring and α-dicarbonyl types are illustrated. Reactions of acyldiazomethanes with ketones under the influence of *n*-butyllithium and lithium diisopropylamide are depicted. Formation of α-diazo-β-amino esters by the condensation of aldehyde and ketone enamines with diazoacetic ester in alcohol solution as well as under metal ion catalysis in aprotic medium is portrayed. Hydrogenations, acid treatments, and pyrolyses of the condensation products are described.

While the thermal interaction of ethyl diazoacetate and aldehydes or ketones accompanied by nitrogen extrusion has been known for a long time,[2] three reports have indicated that reaction may occur even without nitrogen loss.[3,4] One observation, the base-catalyzed addition of the ester to isatins,[4] is especially interesting, since it suggests that condensations of the

(1) U. S. Public Health Service Postdoctoral Fellow, 1969–1971.

(2) For early references see Th. Curtius and E. Buchner, *Ber.*, 18, 2371 (1885); F. Schlotterbeck, *ibid.*, 40, 3000 (1907); 42, 2565 (1909); W. Dieckmann, *ibid.*, 43, 1024 (1910); M. Kharasch, T. Rudy, W. Nudenberg, and G. Büchi, *J. Org. Chem.*, 18, 1030 (1953); C. D. Gutsche and M. Hillman, *J. Amer. Chem. Soc.*, 76, 2236 (1954).

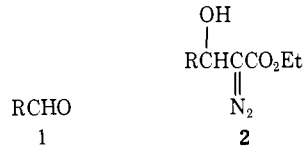
(3) (a) H. Biltz and E. Kramer, *Justus Liebigs Ann. Chem.*, 436, 154 (1924); (b) H. Plieninger and D. vor der Brück, *Tetrahedron Lett.*, 4371 (1968).

(4) B. Eistert and G. Borggrefe, *Justus Liebigs Ann. Chem.*, 718, 142 (1968).

aldol type between acyldiazomethanes (acting as nucleophiles $RCOC^-{=}N_2$ or $RCOCH{=}NN^-B$) and aldehydes and ketones may be a general process. In view of the potential importance of such reactions in organochemical synthesis its study was undertaken.[5]

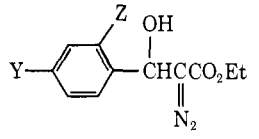
An initial qualitative investigation of the reaction between diazoacetone and benzaldehyde revealed that a base was needed as catalyst. While strong bases were avoided in view of the known tendency of α-diazo ketones to undergo self-condensation in their presence,[6] weak bases, *e.g.*, triethylamine, were found to be quite inefficient.[4,5a,7] Dilute solutions of potassium hydroxide in ethanol or methanol proved to be the most effective media for the condensation process. Proton magnetic resonance spectral analysis of the reaction showed it to be exceedingly fast[8] and reversible.[9] With these facts in hand the reactions of ethyl diazoacetate and some diazomethyl ketones with aliphatic and aromatic aldehydes were investigated.

Condensation of ethyl diazoacetate with aldehydes **1a–1g** in ethanolic potassium hydroxide solution

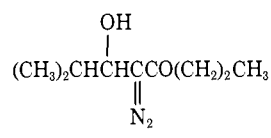


RCHO (1) — $RCH(OH)CCO_2Et$, N_2 (2)

a, R = Me
b, R = *n*-hexyl
c, R = 2,6-dimethyl-5-heptenyl
d, R = *i*-Pro
e, R = 3-heptyl
f, R = cyclohexyl
g, R = *t*-Bu



3a, Y = Z = H
b, Y = OMe; Z = H
c, Y = Z = Cl



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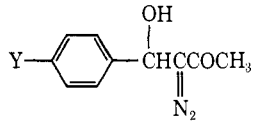
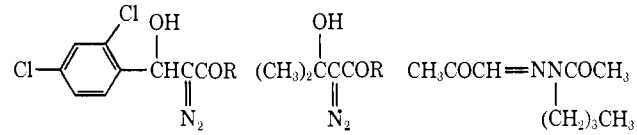


5a, Y = H
b, Y = NO_2

afforded α-diazo-β-hydroxy esters **2a–2g** in 70–90% yields. Similar condensation of diazoacetic ester with the aromatic compounds benzaldehyde, anisaldehyde, and 2,4-dichlorobenzaldehyde gave esters **3a**, **3b**, and **3c**, respectively. Comparison of the yields of these products indicates that electron-donating, aromatic substituents disfavor addition.

The condensations of 1-diazo-2-pentanone with isobutyraldehyde and of diazoacetone with benzaldehyde and *p*-nitrobenzaldehyde leading to α-diazo-β-hydroxy ketones **4**, **5a**, and **5b**, respectively, in high yields constituted representative examples of the feasibility of using diazo ketones in the base-catalyzed reaction. Condensation of 2,4-dichlorobenzaldehyde with isopropyl diazomethyl and *tert*-butyl diazomethyl ketones as well as with diazoacetophenone yielded ketones **6a**,



6a, R = *i*-Pro
b, R = *t*-Bu
c, R = C_6H_5

7a, R = OEt
b, R = Me

8

6b, and **6c**, respectively. The first product being the only one obtained in high yield in reactions in which the aldehyde component is an excellent electrophilic substrate shows that the addition process is affected seriously by both steric and electronic factors in the diazo ketone moiety.

The equilibrium nature of the reaction and its close analogy to the aldol condensation[10] precluded its use for the condensation of acyldiazomethanes with ketones in alcohol solution. A qualitative study of the hydroxide-induced interactions of diazoacetone with acetophenone as well as with cyclopentanone in methanol solution, monitored by spectral means, gave no evidence for the formation of addition products and showed starting materials to have remained unchanged. Furthermore, exposure of ethyl α-diazo-β-hydroxyisovalerate (**7a**) (*vide infra*), formally the addition product of ethyl diazoacetate and acetone, to methanolic hydroxide solution caused its fragmentation into the two components.

Since the hydroxylic solvent interfered in the acyldiazomethane–ketone reaction, an aprotic medium was sought for the condensation. In this connection the recent report[5c] of the successful addition of ethyl lithiodiazoacetate, formed at low temperature by the addition of *n*-butyllithium to ethyl diazoacetate and stable up to −50°, to benzoyl chloride, benzaldehyde, acetophenone, and cyclohexanone became of interest. The procedure was made more convenient by the *in situ* production of the organometallic derivative of the diazocarbonyl compound.[11] Thus, for example, ester **7a** was prepared in high yield by the addition of *n*-butyllithium to an equimolar mixture of diazoacetic ester and acetone in tetrahydrofuran solution at −78°. The organolithium reagent acted exclusively as a base in this

(5) Since its initiation there have appeared several reports related to this investigation: (a) an uncatalyzed addition of ethyl diazoacetate to an α-diketone [B. Eistert, R. Müller, I. Mussler, and H. Selzer, *Chem. Ber.*, 102, 2429 (1969)]; (b) some base-catalyzed, intramolecular condensations of diazomethyldicarbonyl compounds [T. L. Burkoth, *Tetrahedron Lett.*, 5049 (1969); G. Snatzke, B. Ehrig, and H. Klein, *Tetrahedron*, 25, 5601 (1969)]; (c) the addition of ethyl lithiodiazoacetate to four carbonyl compounds [U. Schöllkopf and H. Frasnelli, *Angew. Chem.*, 82, 291 (1970)].

(6) P. Yates and B. L. Shapiro, *J. Amer. Chem. Soc.*, 81, 212 (1959); P. Yates, R. G. F. Giles, and D. G. Farnum, *Can. J. Chem.*, 47, 3997 (1969).

(7) A reaction in ethanol solution at room temperature catalyzed by triethylamine produced less than a 30% yield of the adduct, 3-diazo-4-hydroxy-4-phenyl-2-butanone, in 1 week.

(8) A reaction of 1.2 mmol of reagents in 0.2 ml of 2% methanolic potassium hydroxide at room temperature was complete in less than 10 min, yielding 69% of adduct and the remaining starting materials.

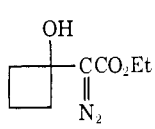
(9) Decomposition of 1.2 mmol of the adduct in 0.2 ml of 2% methanolic potassium hydroxide at room temperature was complete in less than 10 min, yielding 26% of a 1:1 mixture of diazoacetone and benzaldehyde and the remainder starting compound.

(10) A. T. Nielsen and W. J. Houlihan, *Org. React.*, 16, 1 (1968).

(11) Modification of the procedure was studied first on the reaction of diazoacetic ester and acetophenone. Exposure of a tetrahydrofuran solution of an equimolar mixture of the reagents at −78° to *n*-butyllithium led to a 51% yield of purified ethyl α-diazo-β-hydroxy-β-phenylbutyrate.

case and showed strong preference for the α-hydrogen of the diazo compound over that of the ketone. However, in a similar reaction between diazoacetone and acetone *n*-butyllithium participated both as base and nucleophile, thereby depleting the yield of desired ketone **7b** and creating a product of butylation of the terminal nitrogen of diazoacetone which was isolated as its *N*-acetyl derivative (**8**).[12] This difficulty was overcome by replacement of the organometallic reagent by lithium diisopropylamide.

Whereas α-diazocarbonyl compounds did not undergo condensation in alcohol medium with ordinary ketones, the reaction could be envisaged to have greater potential for highly electrophilic ketones, *e.g.*, small ring or α-keto ketones. In fact, some of the earliest reports of successful diazoacetic ester condensations involved α-dicarbonyl systems.[3a,4,5a] When ethyl diazoacetate was condensed with cyclobutanone and with ethyl phenylglyoxylate in alkaline ethanol, adducts



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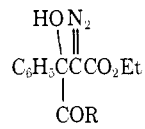
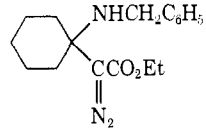


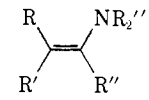
10a, R = OEt
b, R = C_6H_5



11

9 and **10a**, respectively, were obtained, albeit in low yield. A reaction between diazoacetic ester and benzil took a more unusual course and led to ethyl benzoate and **3a**, the adduct of benzaldehyde and diazoacetic ester. Apparently the condensation had taken place, but the intermediate **10b** had undergone ethanolysis. This reaction sequence is reminiscent of the cyanide-induced fragmentation of benzil into benzaldehyde and benzoic acid or its derivatives.[13]

The accumulated data showed the reaction between acyldiazomethanes and aldehydes or ketones to be general and suggested that it possibly might be extended to the field of aldimines and ketimines. When a preliminary experiment with a ketimine, diethyl ketone anil, showed it to be unreactive to diazoacetic ester, enhancement of the electrophilicity of the imino group was sought. On the assumption of silver ion coordination accomplishing this task, silver oxide was chosen as a catalyst, since it also was known to convert α-diazocarbonyl systems into more nucleophilic acyldiazomethylsilver species in aprotic medium.[14] Condensation of ethyl diazoacetate with the Schiff base of cyclohexanone and benzylamine in the presence of silver oxide in tetrahydrofuran produced the α-diazo-β-amino ester **11**, albeit in low yield. An alternative route to such diazoamines appeared to be the condensation of enamines with diazocarbonyl compounds in alcohol solution, since in this medium an enamine is converted in part into an immonium alkoxide whose cation could function as an excellent electrophilic reagent and anion as the basic catalyst in the addition process. Exposure of enamines **12a–12d** to ethyl diazo-



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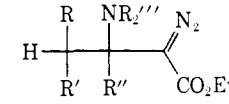
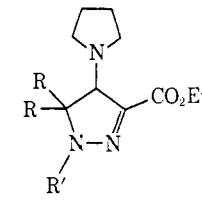
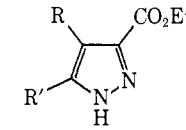


13

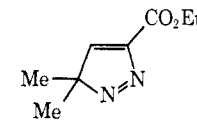
a, R = R′ = Me; R″ = H; $R_2''' = (CH_2)_4$
b, R + R′ = $(CH_2)_5$; R″ = H; $R_2''' = (CH_2)_4$
c, R = H; R′ + R″ = $(CH_2)_4$; $R_2''' = (CH_2)_4$
d, R = H; R′ = Me; R″ = Et; $R_2''' = O(CH_2CH_2)_2$



14a, R = Me; R′ = H
b, $R_2 = (CH_2)_5$; R′ = H
c, R = R′ = Me



15a, R + R′ = $(CH_2)_4$
b, R = Et; R′ = Me



16

acetate in methanol or ethanol solution resulted in the formation of adducts **13a–13d**, respectively. Unfortunately the reactions were inefficient presumably because of the low concentrations of immonium alkoxides. This concentration effect was reflected by exceedingly low reaction rates (lowest for the least basic morpholino enamine **12d**) and by competitively favorable side reactions, 1,3-dipolar additions of diazoacetic ester to the enamines,[15] leading to dihydropyrazoles **14a** and **14b** in the case of the aldehyde enamines (**12a** and **12b**, respectively) and pyrazoles **15a** and **15b** emanating from ketone enamines (**12c** and **12d**, respectively).[16] The dihydropyrazoles proved to be quite unstable compounds, *e.g.*, **14a** yielding isopyrazole **16** on distillation, alumina chromatography, or attempted acetylation. But the *N*-methyl derivative **14c**, prepared by alkylation of **14a** with methyl iodide and sodium hydride, could be isolated. The complications accompanying the desired reaction between enamines and α-diazocarbonyl compounds could be avoided by the application of another condensation method (*vide infra*).[17]

The recent observation of an attempted cyclopropanation of **12b** with ethyl diazoacetate under cuprous

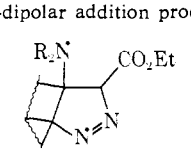
(12) *Cf.* M. O. Forster and D. Cardwell, *J. Chem. Soc.*, 103, 861 (1913); E. Zerner, *Monatsh.*, 34, 1609 (1913); L. Canonica and C. Tadeschi, *Gazz. Chim. Ital.*, 84, 175 (1954).

(13) F. Jourdan, *Ber.*, 16, 659 (1883); D. H. Dakin and C. R. Harrington, *J. Biol. Chem.*, **55**, 487 (1923); W. Dilthey and P. Scheidt, *J. Prakt. Chem.*, **142**, 125 (1935); M. Weiss and M. Appel, *J. Amer. Chem. Soc.*, 70, 3666 (1948); H. Kwart and M. M. Baevsky, *ibid.*, 80, 580 (1958); J. P. Kuebrich and R. L. Schowen, *ibid.*, **93**, 1220 (1971).

(14) U. Schöllkopf and N. Rieber, *Angew. Chem.*, **79**, 238 (1967); *Chem. Ber.*, 102, 488 (1969).

(15) F. Piozzi, A. Umani-Ronchi, and L. Merlini, *Gazz. Chim. Ital.*, 48, 814 (1965).

(16) The primary 1,3-dipolar addition products i tautomerized into

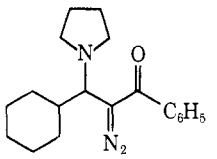


i

compounds of structure type 14 prior to work-up and in the case of the products from the ketone enamines underwent spontaneous elimination of the tertiary amine.

(17) A condensation of ethyl diazoacetate and enamine **12a** could be carried out also in acetonitrile solution in the apparent absence of a proton source (see Experimental Section). The reaction was slow and yielded 14a and a trace of 13a.

chloride catalysis leading to the addition product **13b**[18] indicated that metal salt catalysis might make the enamine condensation synthetically useful. An exhaustive study of the cuprous chloride induced reaction of **12a** and diazoacetic ester revealed that the presence of the salt prevents formation of a dihydropyrazole. When the reaction was executed in acetonitrile solution, it gave **13a**, albeit in only 31% yield. Further study of reaction conditions led to the discovery of silver oxide or carbonate as catalyst and hexane, ether, or tetrahydrofuran as solvent producing optimum yields of α-diazo-β-aminoacyl compounds, 75% or higher for adducts **13a–13c**. Only the adducts **13d** and **17**, from a less basic enamine (**12d**) and from a diazo



17

18a, R = Me
b, R = C_6H_5

19a, R = C_6H_5; R′ = H; R″ = OEt
b, R = C_6H_5; R′ = H; R″ = Me
c, R = CO_2Et; R′ = C_6H_5; R″ = OEt

ketone (diazoacetophenone) instead of diazo ester, respectively, were obtained in lower proportion.

The trifunctional products of condensations of acyldiazomethanes with aldehydes, ketones, and their derivatives can be expected to be endowed with rich chemistry. The following discussion illustrates their behavior in three deamination reactions—hydrogenative, acid-catalyzed, and thermal nitrogen extrusion processes. Palladium-catalyzed hydrogenation of esters **2a** and **3a** yielded ethyl β-hydroxybutyrate (**18a**) and β-hydroxy-β-phenylpropionate (**18b**), respectively, aldol products of aldehydes and ethyl acetate which, however, cannot be obtained by aldol condensation of these carbonyl compounds by classical means.[10,19] Both acid treatment and refluxing in benzene solution converted diazo ester **2a** into ethyl acetoacetate,[2,4,5a] while pyrolyses of diazo compounds **3a**, **5a**, and **10a** transformed them in high yield into **19a**, **19b**, and **19c**, respectively.[2] Thus a two-step scheme for the formation of unsymmetrical β-dicarbonyl systems is on hand.[20] Finally, ring expansions can be executed on adducts of α-diazocarbonyl compounds to cyclic ketones or their derivatives. For example, pyrolysis of **9** gave ethyl cyclopentanone-α-carboxylate and acid hydrolysis of **13c** yielded ethyl cycloheptanone-α-carboxylate.[21]

Experimental Section

Boiling points and melting points, determined on a Reichert micro hot stage, are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Model 137 spectrophotometer. Proton magnetic resonance spectra of carbon tetrachloride solutions (unless otherwise noted) containing tetramethylsilane (δ 0 ppm) as internal standard were taken on a Varian Associates Model A-60 spectrometer. Mass spectra were recorded at 70 eV on an AEI MS-9 spectrometer.

Ethyl 2-Diazo-3-hydroxyalkanoates (2 and 3). A 10% methanolic potassium hydroxide solution, 0.5 ml, was added dropwise to a stirring solution of 4.0 g of acetaldehyde (**1a**) and 8.0 g of ethyl diazoacetate in 20 ml of methanol and the mixture stirred at room temperature for 30 min. Water was added and the mixture extracted with chloroform. The extract was evaporated under vacuum and 4.0 g of the residual yellow oil (9.4 g) chromatographed on alumina (activity IV). Elution with 9:1 hexane–ether yielded 3.2 g of **2a**. Alternatively, 3.0 g of acetaldehyde was added dropwise to an ice-cold, stirring solution of 5.4 g of ethyl diazoacetate and 1 ml of 3% ethanolic potassium hydroxide in 10 ml of ethanol. After 15 min 2 ml more of 3% ethanolic potassium hydroxide and subsequently 3.0 g of acetaldehyde were added dropwise and the solution stirred for another 30 min. Water was added and the mixture extracted with methylene chloride. Evaporation of the extract under vacuum gave 6.7 g (90%) of ethyl α-diazo-β-hydroxybutyrate (**2a**): ir (neat) 2.89 (m, OH), 4.74 (s, C=N_2), 5.94 μ (br s, C=O); pmr δ 1.29 (t, 3, J = 7.0 Hz, ethyl Me), 1.35 (d, 3, J = 6.5 Hz, Me), 4.21 (q, 2, J = 7.0 Hz, CH_2), 4.80 (q, 1, J = 6.5 Hz, CH).

Anal. Calcd for $C_6H_{10}O_3N_2$: C, 45.57; H, 6.37; N, 17.71. Found: C, 45.80; H, 6.55; N, 17.62.

A 10% ethanolic potassium hydroxide solution, 1 ml, was added dropwise to a stirring solution of 3.1 g (27 mmol) of enanthaldehyde (**1b**) and 3.1 g (27 mmol) of ethyl diazoacetate in 5 ml of ethanol and the solution kept stirring at room temperature for 1 hr. Water was added and the mixture extracted with methylene chloride The extract was dried over sodium sulfate and evaporated under vacuum and the residue, 5.3 g, was chromatographed on Florisil. Elution with 2:1 hexane–ether yielded 4.2 g (68%) of yellow, liquid ethyl α-diazo-β-hydroxypelargonate (**2b**): ir (neat) 2.89 (m, OH), 4.76 (s, C=N_2), 5.92 μ (br s, C=O); pmr δ 0.8–1.8 (m, 13, Me and $(CH_2)_5$), 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 4.19 (q, 2, J = 7.0 Hz, ethyl CH_2), 4.50 (t, 1, J = 6.0 Hz, CH).

Anal. Calcd for $C_{11}H_{20}O_3N_2$: C, 57.87; H, 8.83. Found: C, 58.07; H, 8.74.

Treatment of 4.9 g of citronellal (**1c**) as **1b** above, chromatography of the crude product on alumina (activity II), and elution with 9:1 petroleum ether–ether gave 7.4 g (87%) of yellow, liquid ethyl 2-diazo-3-hydroxy-5,9-dimethyl-8-decenoate (**2c**): ir (neat) 2.93 (m, OH), 4.77 (s, C=N_2), 5.91 (s, C=O), 5.99 μ (s, C=O); pmr ($CDCl_3$) δ 0.95 (d, 3, J = 5.0 Hz, C-5 Me), 1.1–1.7 (m, 4, $(CH_2)_2$), 1 27 (t, 3, J = 7.0 Hz, ethyl Me), 1.60, 1.68 (br s, three each, olefinic Me_2), 1.7–2.3 (m, 3, CH and allyl CH_2), 4.20 (q, 2, J = 7.0 Hz, ethyl CH_2), 4.70 (t, 1, J = 4.0 Hz, OCH), 5.08 (t, 1, J = 6.0 Hz, olefinic H).

Anal. Calcd for $C_{14}H_{24}O_3N_2$: C, 62.66; H, 9.01; N, 10.44. Found: C, 62.87; H, 8.92; N, 10.25.

Treatment of 6.2 g of isobutyraldehyde (**1d**) as **1b** above, chromatography of 4.1 g of crude product (13.7 g) on alumina (activity IV), and elution with 9:1 hexane–ether gave a 3.9 g (80%) of yellow, liquid ethyl α-diazo-β-hydroxyisocaproate (**2d**): ir (neat) 2.94 (m, OH), 4.79 (s, C=N_2), 5.95 μ (br s, C=O); pmr δ 0.91, 1.02 (d, three each, J = 6.5 Hz, Me_2), 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 1.5–2.1 (m, 1, CH), 4.19 (d, 1, J = 7.0 Hz, OCH), 4.19 (q, 2, J = 7.0 Hz, CH_2).

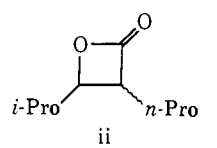
Anal. Calcd for $C_8H_{14}O_3N_2$: N, 15.04. Found: N, 15.28.

Treatment for 3.0 g of α-ethylcaproaldehyde (**1e**) as **1b** above, chromatography of 2.4 g of crude product (5.0 g) on alumina (activ-

(18) E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sathe, D. J. Scharf, and G. Tosi, *J. Amer. Chem. Soc.*, **92**, 7428 (1970).

(19) *Cf.* H. Weinhaus and H. Ziehl, *Ber.*, **65**, 1464 (1932); L. Birkhofer, *Chem. Ber.*, **80**, 83 (1947); W. Gruber and H. Renner, *Monatsh.*, **81**, 751 (1950).

(20) Refluxing a benzene solution of 4 produced a 40% yield of 2-methyloctane-3,5-dione [ir (neat) C=O 5.77 (s), C=C 6.24 (s) μ] and a 30% yield of a stereoisomer mixture of β-lactones ii [ir (neat) C=O



ii

5.46 (s) μ; pmr δ 1.02 (d, 6, J = 6.5 Hz, i-ProMe), 0.8–2.1 (m, 8, Me, methylenes and methine), 3.0–3.7 (m, 1, ketomethine), 3.72 (d of d, 1, J = 4.0, 8.0 Hz, oxymethine of one isomer), 4.06 (d of d, 1, J = 6.0, 10.0 Hz, oxymethine of other isomer); *m/e* 156 (M), 113(M − *i*-Pr), 112 (M − CO_2), 84 (M − *i*-PrCHO); gpc (10 ft × 1/8 in. 10% Carbowax 20M column, 150°, 30 ml/min nitrogen flow) retention time 3.5 and 4.7 min]. The surprising latter products were the consequence of migration of the *n*-propyl group during the nitrogen extrusion followed by cyclization of the resultant hydroxyketene.

(21) *Cf.* W. L. Mock and M. E. Hartman, *J. Amer. Chem. Soc.*, **92**, 5767 (1970).

ity IV), and elution with 9:1 ether–hexane yielded 1.9 g (68%) of yellow, liquid ethyl α-diazo-β-hydroxy-γ-ethylcaprylate (**2e**): ir (neat) 2.88 (m, OH), 4.75 (s, C=N$_2$), 5.91 (s, C=O), 5.99 μ (s, C=O); pmr δ 0.7–1.7 (m, 15, Me$_2$, (CH$_2$)$_4$, CH), 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 4.20 (q, 2, J = 7.0 Hz, ethyl CH$_2$), 4.3–4.6 (m, 1, OCH).

Anal. Calcd for $C_{12}H_{22}O_3N_2$: C, 59.48; H, 9.15; N, 11.56. Found: C, 59.22; H, 8.99; N, 11.46.

Treatment of 2.0 g of cyclohexanecarboxaldehyde (**1f**) as **1b** above, chromatography of 1.3 g of crude product (4.0 g) on alumina (activity IV), and elution with 9:1 hexane–ether gave 1.2 g (90%) of yellow, liquid ethyl α-diazo-β-hydroxy-β-cyclohexylpropionate (**2f**): ir (neat) 2.90 (m, OH), 4.76 (s, C=N$_2$), 5.96 μ (br s, C=O); pmr δ 0.9–2.1 (m, 11, (CH$_2$)$_5$ and CH), 1.28 (t, 3, J = 7.0 Hz, Me), 4.19 (q, 2, J = 7.0 Hz, ethyl CH$_2$), 4.1–4.4 (m, 1, OCH).

Anal. Calcd for $C_{11}H_{18}O_3N_2$: C, 58.39; H, 8.02; N, 12.38. Found: C, 58.47; H, 8.12; N, 12.22.

Treatment of 0.6 g of pivaldehyde (**1g**) as **1b** above, chromatography of the crude product on alumina (activity IV), and elution with 9:1 hexane–ether afforded 1.0 g (70%) of yellow, liquid ethyl α-diazo-β-hydroxy-γ,γ-dimethylvalerate (**2g**): ir (neat) 2.87 (m, OH), 4.75 (s, C=N$_2$), 5.91 (s, C=O), 5.98 μ (s, C=O); pmr δ 0.95 (s, 9, Me$_3$), 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 4.10 (s, 1, CH), 4.18 (q, 2, J = 7.0 Hz, CH$_2$).

Anal. Calcd for $C_9H_{16}O_3N_2$: C, 53.99; H, 8.05; N, 13.99. Found: C, 53.96; H, 8.16; N, 14.12.

Treatment of 4.1 g of benzaldehyde as **1b** above except for removal of starting materials from crude product (6.0 g) by distillation at 0.3 Torr (bath temperature less than 80°) after the reaction, chromatography of 3.4 g of product on alumina (activity IV), and elution with 9:1 hexane–ether produced 2.9 g (60%) of ethyl α-diazo-β-hydroxy-β-phenylpropionate (**3a**): ir (neat) 2.90 (m, OH), 4.76 (s, C=N$_2$), 5.93 μ (br s, C=O); pmr δ 1.19 (t, 3, J = 7.0 Hz, Me), 4.15 (q, 2, J = 7.0 Hz, CH$_2$), 5.85 (d, 1, J = 3.0 Hz, CH), 7.1–7.5 (m, 5, aromatic H's).

Anal. Calcd for $C_{11}H_{12}O_3N_2$: C, 59.99; H, 5.49. Found: C, 59.74; H, 5.54.

Treatment of 5.4 g of anisaldehyde as **1b** above except for rapid extraction of excess aldehyde by an aqueous sodium bisulfite solution at the end of the reaction, chromatography of the crude product (4.5 g) on alumina (activity IV), and elution with 9:1 hexane–ether yielded 2.2 g (25%) of ethyl α-diazo-β-hydroxy-β-(*p*-methoxyphenyl)propionate (**3b**): ir (neat) 2.83 (m, OH), 4.70 (s, C=N$_2$), 5.94 (br s, C=O), 6.20 μ (m, C=C); pmr δ 1.22 (t, 3, J = 7.0 Hz, Me), 3.70 (s, 3, OMe), 4.15 (q, 2, J = 7.0 Hz, CH$_2$), 5.78 (d, 1, J = 3.0 Hz, CH), 6.80 (d, 2, J = 9.0 Hz, ortho H$_2$), 7.27 (d, 2, J = 9.0 Hz, meta H$_2$).

Anal. Calcd for $C_{12}H_{14}O_4N_2$: C, 57.59; H, 5.64. Found: 57.49; H, 5.38.

Treatment of 10.9 g of 2,4-dichlorobenzaldehyde as **1b** above and crystallization of the crude product from hexane gave 14.2 g (79%) of yellow ethyl α-diazo-β-hydroxy-β-(2,4-dichlorophenyl)propionate (**3c**): mp 70–71°; ir (CHCl$_3$) 2.91 (br w, OH), 4.76 (s, C=N$_2$), 5.98 (s, C=O), 6.28 (m, C=C), 6.41 μ (w, C=C); pmr δ 1.28 (t, 3, J = 7.0 Hz, Me), 4.23 (q, 2, J = 7.0 Hz, CH$_2$), 6.01 (s, 1, CH), 7.26 (d of d, 1, J = 8.0, 2.5 Hz, C-5 H), 7.37 (d, 1, J = 2.5 Hz, C-3 H), 7.68 (d, 1, J = 8.0 Hz, C-6 H).

Anal. Calcd for $C_{11}H_{10}O_3N_2Cl_2$: C, 45.67; H, 3.48; N, 9.73. Found: 45.76; H, 3.71; N, 9.67.

α-Diazo-β-hydroxy Ketones (4, 5 and 6). A solution of 10% methanolic potassium hydroxide, 1 ml, was added dropwise to a solution of 1.43 g of 1-diazo-2-pentanone and 0.92 g of isobutyraldehyde in 5 ml of methanol and the mixture stirred at room temperature for 30 min. Water was added and the mixture extracted with methylene chloride. The extract was dried over magnesium sulfate and evaporated under vacuum. Chromatography of the residue, 2.09 g, on alumina (activity IV) and elution with 9:1 hexane–ether yielded 1.68 g (72%) of yellow, liquid 5-diazo-7-methyl-6-octanol-4-one (**4**): ir (neat) 2.88 (s, OH), 4.78 (s, C=N$_2$), 6.16 μ (br s, C=O); pmr δ 0.90, 1.01 (d, three each, J = 6.5 Hz, i-Pr Me$_2$), 0.8–2.0 (m, 6, *n*-Pr Et and *i*-Pr CH), 2.42 (t, 2, J = 7.0 Hz, α-keto CH$_2$), 4.34 (d, 1, J = 7.5 Hz, OCH).

Anal. Calcd for $C_9H_{16}O_2N_2$: N, 15.20. Found: N, 15.28.

Treatment of 3.5 g of diazoacetone and 4.1 g of benzaldehyde as in the above preparation of **4** gave 7.4 g of crude product. Rapid extraction of a portion thereof, 3.5 g, with sodium bisulfite and crystallization of the residue (2.6 g), mp 70–75°, yielded 2.4 g (68%) of yellow 3-diazo-4-phenyl-4-butanol-2-one (**5a**): mp 75–77°; ir (CHCl$_3$) 2.94 (w, OH), 4.76 (s, C=N$_2$), 6.13 μ (s, C=O); pmr δ 2.17 (s, 3, Me), 5.90 (br s, 1, CH), 7.30 (br s, 5, aromatic H's).

Anal. Calcd for $C_{10}H_{10}O_2N_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.03; H, 5.50; N, 14.79.

Treatment of 1.2 g of diazoacetone and 1.9 g of *p*-nitrobenzaldehyde as in the above preparation of **4** and crystallization of the product from methanol gave 2.7 g (86%) of yellow 3-diazo-4-(*p*-nitrophenyl)-4-butanol-2-one (**5b**): mp 122–123°; ir (Nujol) 2.94 (s, OH), 4.79 (s, C=N$_2$), 6.20 μ (br s, C=O); pmr (CDCl$_3$) δ 2.30 (s, 3, Me), 6.10 (br s, 1, CH), 7.59 (br d, 2, J = 8.5 Hz, ortho H$_2$), 8.23 (d, 2, J = 8.5 Hz, meta H$_2$).

Anal. Calcd for $C_{10}H_9O_4N_3$: C, 51.07; H, 3.86; N, 17.87. Found: C, 51.06; H, 4.08; N, 17.85.

Treatment of 4.4 g of isopropyl diazomethyl ketone and 6.9 g of 2,4-dichlorobenzaldehyde as in the above preparation of **4** and crystallization of the product from methanol led to 0.45 g of starting aldehyde and 8.8 g (78%) of yellow prisms of 2-diazo-1-(2,4-dichlorophenyl)-4-methyl-1-pentanol-3-one (**6a**): mp 111–113°; ir (CHCl$_3$) 2.92 (w, OH), 4.79 (s, C=N$_2$), 6.14 (s, C=O), 6.29 (w, C=C), 6.41 μ (w, C=C); pmr (CDCl$_3$) δ 1.14 (d, 6, J = 7.0 Hz, Me$_2$), 2.84 (sept, 1, J = 7.0 Hz, CH), 6.13 (br s, 1, OCH), 7.27 (d of d, 1, J = 8.0, 2.5 Hz, C-5 H), 7.32 (d, 1, J = 2.5 Hz, C-3 H), 7.65 (br d, 1, J = 8.0 Hz, C-6 H).

Anal. Calcd for $C_{12}H_{12}O_2N_2Cl_2$: C, 50.19; H, 4.21; N, 9.76. Found: C, 50.01; H, 4.64; N, 10.00.

Treatment of 2.1 g of pivalyldiazomethane and 3.0 g of 2,4-dichlorobenzaldehyde as in the above preparation of **4**, chromatography of the crude product (4.7 g) on alumina (activity IV), and elution with petroleum ether gave 1.7 g of starting aldehyde and 1.4 g of starting diazo compound. Elution with 2:1 petroleum ether–ether yielded 1.5 g (28%) of yellow 2-diazo-1-(2,4-dichlorophenyl)-4,4-dimethyl-1-pentanol-3-one (**6b**): mp 113–115°; ir (CHCl$_3$) 2.92 (br w, OH), 4.79 (s, C=N$_2$), 6.18 (s, C=O), 6.27 (w, C=C), 6.45 μ (w, C=C); pmr (CDCl$_3$) δ 1.22 (s, 9, Me$_3$), 6.18 (br s, 1, CH), 7.29 (d of d, 1, J = 8.0, 2.5 Hz, C-5 H), 7.35 (d, 1, J = 2.5 Hz, C-3 H), 7.67 (br d, 1, J = 8.0 Hz, C-6 H).

Anal. Calcd for $C_{13}H_{14}O_2N_2Cl_2$: C, 51.84; H, 4.68; N, 9.30. Found: C, 51.68; H, 4.74; N, 9.40.

Treatment of 3.2 g of diazoacetophenone and 3.8 g of 2,4-dichlorobenzaldehyde as in the above preparation of **4**, chromatography of the crude product (6.6 g) on alumina (activity IV), and elution with petroleum ether led to 1.9 g of starting aldehyde. Elution with 20:1 petroleum ether–ether yielded 1.8 g of starting diazo compound and elution with 1:1 petroleum ether–ether gave 2.8 g (40%) of yellow 2-diazo-3-(2,4-dichlorophenyl)-1-phenyl-3-propanol-1-one (**6c**): mp 108.5–110°; ir (Nujol) 2.93 (m, OH), 4.78 (s, C=N$_2$), 6.14 (s, C=O), 6.24 (s, C=C), 6.35 μ (s, C=C); pmr (CDCl$_3$) δ 6.29 (s, 1, CH), 7.1–7.8 (m, 8, aromatic H's).

Anal. Calcd for $C_{15}H_{10}O_2N_2Cl_2$: C, 56.10; H, 3.14; N, 8.72. Found: C, 56.00; H, 3.35; N, 8.70.

Ethyl α-Diazo-β-hydroxyisovalerate (7a). A hexane solution of *n*-butyllithium, 15 ml of 1.6 *M*, was added dropwise over a 0.5-hr period to a stirring solution of 2.57 g of ethyl diazoacetate and 1.30 g of acetone in 50 ml of tetrahydrofuran being cooled in a Dry Ice–acetone bath and the mixture was stirred for 30 min. It then was poured into a solution of 1.3 g of acetic acid in 50 ml of ether at −78°. The bright yellow solution was washed with water, dried over sodium sulfate, and evaporated under vacuum. Chromatography of 1.26 g of the residual oil, 3.86 g, on alumina (activity IV) and elution with 9:1 hexane–ether gave 961 mg (76%) of yellow liquid **7a**: ir (neat) 2.87 (m, OH), 4.74 (s, C=N$_2$), 5.94 μ (br, s, C=O); pmr (CDCl$_3$) δ 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 1.53 (s, 6, Me$_2$), 4.24 (q, 2, J = 7.0 Hz, CH$_2$).

Anal. Calcd for $C_7H_{12}O_3N_2$: C, 48.83; H, 7.02; N, 16.27. Found: C, 49.12; H, 7.21; N, 16.07.

One drop of 3% methanolic potassium hydroxide was added to a solution of 67 mg of **7a** in 0.2 ml of deuteriochloroform in an nmr tube. The pmr spectrum of the solution 4 min after mixing showed complete disappearance of the dimethylcarbinol methyl singlet at 1.53 ppm and the appearance of a methyl singlet for acetone at 2.12 ppm.

3-Diazo-4-methyl-4-pentanol-2-one (7b). A hexane solution of *n*-butyllithium, 10 ml of 1.6 *M*, was added dropwise over a 20-min period to a stirring solution of 1.34 g of diazoacetone and 0.93 g of acetone in 25 ml of tetrahydrofuran being cooled in a Dry Ice–acetone bath and the dark red mixture was stirred for 30 min. Acetic anhydride, 1.62 g, was added and the mixture stirred for another 30 min. It then was poured into a mixture of 25 ml of ether and 25 ml of water and the solutions separated. The organic solution was extracted with brine and the combined aqueous solutions extracted with ether. The combined organic solutions were dried and evaporated under vacuum. Chromatography of the residue

(2.66 g) on alumina (activity IV) and elution with hexane yielded 817 mg (28%) of liquid methylglyoxal *N*-(*n*-butyl)-*N*-acetylhydrazone (**8**): ir (neat) 5.89 (s, C=O), 6.36 μ (s); pmr δ 0.8–1.7 (m, 7, *n*-Pr H's), 2.31, 2.37 (s, three each, Me_2), 3.89 (t, 2, J = 7.0 Hz, NCH_2), 7.09 (s, 1, imino H).

Anal. Calcd for $C_9H_{16}O_2N_2$: C, 58.67; H, 8.75; N, 15.20. Found: C, 58.77; H, 8.99; N, 15.15.

Further elution with 9:1 hexane–ether gave 722 mg (32%) of yellow, liquid **7b**: ir (neat) 2.89 (m, OH), 4.79 (s, C=N_2), 6.14 μ (br s, C=O); pmr δ 1.45 (s, 6, Me_2), 2.20 (s, 3, α-keto Me).[22]

A hexane solution of *n*-butyllithium, 10 ml of 1.6 *M*, was added to a solution of 1.7 ml of diisopropylamine in 10 ml of tetrahydrofuran at −78° and the resultant solution of lithium diisopropylamide was added dropwise over 15 min into a stirring solution of 1.34 g of diazoacetone and 0.93 g of acetone in 10 ml of tetrahydrofuran cooled in a Dry Ice–acetone bath. The mixture was stirred at −78° for another 30 min and then poured into a solution of 1 ml of acetic acid in 25 ml of ether. The mixture was washed with brine and with water and the washings extracted with ether. The combined organic solutions were dried and evaporated under vacuum. Chromatography as above gave 1.58 g (70%) of **7b**.

1-Carboethoxydiazomethylcyclobutanol (9). An ethanolic potassium hydroxide solution, 1 ml of 10%, was added dropwise to a stirring solution of 3.70 g of ethyl diazoacetate and 1.13 g of cyclobutanone in 4 ml of ethanol at room temperature and the stirring continued for 30 min. Work-up as for the above preparation of **2b** and chromatography of the crude product on alumina led to recovery of 1.42 g of diazoacetic ester on elution with hexane. Elution with 1:1 hexane–ether yielded 499 mg (16%) of yellow liquid **9**: ir (neat) 2.89 (m, OH), 4.74 (s, C=N_2), 5.94 μ (br s, C=O); pmr ($CDCl_3$) δ 1.25 (t, 3, J = 7.0 Hz, Me), 1.6–2.0 (m, 2, C-3 H_2), 2.30 (t, 4, J = 7.5 Hz, C-2 H_2 and C-4 H_2), 4.20 (q, 2, J = 7.0 Hz, CH_2).

Anal. Calcd for $C_8H_{12}O_3N_2$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.22; H, 6.74; N, 15.15.

Further elution with ether and with 50:1 ether–methanol yielded 407 mg of a 3:1 mixture of ethyl cyclopentanone-α-carboxylate and **9**. Refluxing of a solution of the mixture in 10 ml of benzene for 12 hr gave 296 mg of ethyl cyclopentanone-α-carboxylate, identical in all properties with an authentic sample.

Ethyl α-Diazo-β-carbethoxy-β-hydroxy-β-phenylpropionate (10a). An ethanolic sodium ethoxide solution, 2 ml of 10%, was added dropwise to a stirring solution of 1.00 g of ethyl diazoacetate and 1.56 g of ethyl phenylglyoxylate[23] in 2 ml of ethanol and the mixture stirred at room temperature for 2 hr. Work-up as above, chromatography of the crude product (2.50 g) on Florisil, and elution with 9:1 hexane–ether yielded 1.32 g (52%) of yellow, liquid diester **10a**: ir (neat) 2.84 (m, OH), 4.73 (s, C=N_2), 5.72 (s, C=O), 5.89 μ (s, C=O); pmr ($CDCl_3$) δ 1.22 (t, 6, J = 7.0 Hz, Me_2), 4.24 (q, 4, J = 7.0 Hz, $(CH_2)_2$), 7.2–7.9 (m, 5, aromatic H's).

Anal. Calcd for $C_{14}H_{16}O_5N_2$: C, 57.53; H, 5.52; N, 9.58. Found: C, 57.39; H, 5.56; N, 9.35.

Condensation of Benzil with Diazoacetic Ester. An ethanolic potassium hydroxide solution, 0.5 ml of 10%, was added to a solution of 1.10 g of ethyl diazoacetate and 2.04 g of benzil in 3 ml of ethanol and the mixture stirred at room temperature for 30 min. Work-up as above, chromatography of the crude product (3.5 g) on alumina (activity II), and elution with hexane gave 1.29 g (88%) of ethyl benzoate, identical with authentic compound. Elution with 50:1 hexane–ether led to a mixture of benzaldehyde, ethyl benzoate, and ethyl diazoacetate, while elution with 5:1 hexane–ether yielded 1.19 g (56%) of diazo ester **3a**, spectrally identical with an authentic specimen (*vide supra*).

1-Benzylamino-1-carboethoxydiazomethylcyclohexane (11). A solution of 6.02 g of cyclohexanone benzylimine in 5 ml of tetrahydrofuran was added slowly to a mixture of 3.67 g of ethyl diazoacetate and 2.4 g of silver oxide in 5 ml of tetrahydrofuran at 0° and the mixture stirred at 0° for 1 hr and then at room temperature for 2 hr. It was filtered and the filtrate evaporated under vacuum. Chromatography of 3.0 g of the residue (7.13 g) on alumina (activity IV) gave 972 mg of ester **11**: ir (neat) 2.97 (w, NH), 4.79 (s, C=N_2), 5.92 (s, C=O), 6.24 μ (w, C=C); pmr ($CDCl_3$) δ 1.19 (t, 3, J = 7.0 Hz, Me), 1.2–2.1 (m, 10, $(CH_2)_5$), 3.50 (s, 2, NCH_2), 4.12 (q, 2, J = 7.0 Hz, OCH_2), 7.16 (br s, 5, aromatic H's).

Anal. Calcd for $C_{17}H_{23}O_2N_3$: N, 13.94. Found: N, 13.80.

Ethyl α-Diazo-β-(*N*-pyrrolidinyl)isovalerate (13a). A solution of 3.76 g of ethyl diazoacetate and 4.15 g of 2-methyl-1-(*N*-pyrrolidinyl)-propene (**12a**)[24] in 17 ml of ethanol was left at room temperature for 3 days. Water was added and the mixture extracted with chloroform. The extract was dried and evaporated under vacuum. Chromatography of 1.33 g of the residue (7.11 g) on alumina (activity IV) and elution with hexane yielded 480 mg (33%) of liquid, orange ester **13a**: ir (neat) 4.77 (s, C=N_2), 5.83 μ (s, C=O); pmr δ 0.90, 1.00 (d, three each, J = 6.5 Hz, *i*-Pr Me_2), 1.28 (t, 3, J = 7.0 Hz, ethyl Me), 1.6–1.9 (m, 4, $(CH_2)_2$), 1.8–2.2 (m, 1, CH), 2.4–2.7 (m, 4, $(NCH_2)_2$), 3.14 (d, 1, J = 7.5 Hz, NCH), 4.18 (q, 2, J = 7.0 Hz, OCH_2).

Anal. Calcd for $C_{12}H_{21}O_2N_3$: C, 60.23; H, 8.84; N, 17.56. Found: C, 60.22; H, 8.94; N, 17.75.

Elution with ether yielded 780 mg of a mixture of **14a** and **16** (*vide infra*).

A solution of 4.00 g of ethyl diazoacetate and 4.40 g of **12a**[24] in 17 ml of acetonitrile (distilled from calcium hydride) was left at room temperature for 3 days. Ether and water were added and the organic solution was washed with brine and with water, dried, and evaporated under vacuum. The viscous oily residue (7.63 g) was partitioned into several fractions for further experimentation. Chromatography of 1.08 g on alumina (activity IV) and elution with hexane gave 55 mg (4%) of ester **13a**, while elution with ether yielded 746 mg of a 1:1 mixture of **14a** and **16** (*vide infra*). Crystallization of a portion of crude reaction product at −78° from hexane led to dihydropyrazole **14a** as a viscous, orange oil: ir (neat) 2.97 (s, NH), 5.87 (s, C=O), 6.46 μ (s); pmr ($CDCl_3$) δ 1.15, 1.30 (s, three each, Me_2), 1.38 (t, 3, J = 7.0 Hz, ethyl Me), 1.5–1.9 (m, 4, $(CH_2)_2$), 2.5–3.1 (m, 4, $(NCH_2)_2$), 3.85 (s, 1, NCH), 4.37 (q, 2, J = 7.0 Hz, OCH_2), 6.92 (s, 1, NH). Attempted purification of **14a** by distillation failed and gave a mixture of **14a** and **16a**. The latter was not present in the original crude reaction product (exhaustive pmr analysis).

A 2.39-g fraction of the crude reaction product was added to a mixture of 0.25 g of sodium hydride in 30 ml of ether. After the cessation of gas evolution 3 ml of methyl iodide was added and the mixture refluxed for 12 hr. Filtration of the mixture and evaporation of the filtrate under vacuum yielded 2.16 g of yellow oil whose chromatography on alumina and elution with hexane produced 118 mg of **13a**. Elution with 5:1 hexane–ether afforded 1.40 g of liquid ethyl 4-(*N*-pyrrolidinyl)-1,5,5-trimethyl-4,5-dihydropyrazole-3-carboxylate (**14c**): ir (neat) C=O 5.84 (s), 5.91 (s), 6.56 μ (s); pmr δ 1.03, 1.25, (s, three each, Me_2), 1.32 (t, 3, J = 7.0 Hz, ethyl Me), 1.5–1.8 (m, 4, $(CH_2)_2$), 2.4–3.0 (m, 4, $(NCH_2)_2$), 3.00 (s, 3, NMe), 3.78 (s, 1, NCH), 4.17 (q, 2, J = 7.0 Hz, OCH_2); molecular ion *m/e* 253.1812 (calcd for $C_{13}H_{23}O_2N_3$, 253.1790).

Anal. Calcd for $C_{13}H_{23}O_2N_3$: C, 61.63; H, 9.15. Found: C, 61.58; H, 9.45.

A solution of a 0.85-g portion of the crude reaction product and 1 ml of acetic anhydride in 10 ml of acetonitrile was heated at 100° for 2 hr. Water was added and the mixture extracted with ether. The extract was dried and evaporated under vacuum. Chromatography of the residue and elution with 5:1 hexane–ether yielded 0.36 g (60%) of colorless, crystalline ethyl 3,3-dimethyl-3*H*-pyrazole-5-carboxylate (**16**): mp 59–60°; ir (CCl_4) 5.79 (s, C=O), 6.17 μ (m, C=C); pmr δ 1.44 (t, 3, J = 7.0 Hz, ethyl Me), 1.52 (s, 6, Me_2), 4.51 (q, 2, J = 7.0 Hz, CH_2), 7.80 (s, 1, olefinic H); molecular ion *m/e* 168.0917 (calcd for $C_8H_{12}O_2N_2$, 168.0900).

Anal. Calcd for $C_8H_{12}O_2N_2$: C, 57.13; H, 7.19; 16.66. Found: C, 57.27; H, 7.29; N, 16.77.

A solution of 1.46 g of ethyl diazoacetate in 10 ml of acetonitrile was added slowly over a 1-hr period to a stirring mixture of 1.61 g of enamine **12a**[24] and 0.2 g of cuprous chloride in 20 ml of acetonitrile and the mixture stirred at room temperature for 1 hr. Water was added and the mixture extracted with chloroform. The extract was dried and evaporated under vacuum. Chromatography of the residue (1.90 g) on alumina (activity IV) and elution with hexane gave 950 mg (31%) of ester **13a**.

A mixture of 1.74 g of ethyl diazoacetate, 1.91 g of enamine **12a**[24], and 0.23 g of silver oxide in 5 ml of tetrahydrofuran was prepared at 0° and then left at 0° for 1 hr and room temperature for 8 hr. It was filtered and the filtrate dried and evaporated under vacuum. Chromatography of the residue (3.69 g) on alumina (activity IV) and elution with hexane yielded 2.96 g (81%) of **13a**.

(22) Despite repeated attempts this most unstable α-diazo-β-hydroxycarbonyl compound refused to yield a satisfactory elemental analysis. Its extrusion of nitrogen with appreciable rate was reflected in high C and H and low N values. The complete absence or low appearance of molecular ion peaks in the mass spectra of the diazo substances precluded an exact mass measurement of **7b**.

(23) J. P. Schaefer and E. J. Corey, *J. Org. Chem.*, 24, 1827 (1959).

(24) C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936).

Ethyl α-Diazo-β-cyclohexyl-β-(*N*-pyrrolidinyl)propionate (13b). A solution of .00 g of ethyl diazoacetate and 1.44 g of *N*-pyrrolidinomethylenecyclohexane (**12b**)[18] in 2 ml of methanol was left at room temperature for 2 days. Evaporation of the solvent under reduced pressure left 2.08 g of residue whose chromatography on alumina (activity I) and elution with hexane gave 1.30 g (56%) of yellow, liquid ester **13b**: ir (neat) 4.79 (s, C=N$_2$), 5.89 μ (s, C=O); pmr δ 0.8–2.1 (m, 15, (CH$_2$)$_7$ and CH), 1.28 (t, 3, *J* = 7.0 Hz, Me), 2.4–2.7 (m, 4, (NCH$_2$)$_2$), 3.30 (d, 1, *J* = 7.5 Hz, NCH), 4.20 (q, 2, *J* = 7.0 Hz, ethyl CH$_2$).

Anal. Calcd for $C_{15}H_{25}O_2N_3$: C, 64.49; H, 9.02; N, 15.04. Found: C, 64.30; H, 8.94; N, 15.26.

The more polar chromatographic fractions were not investigated.

A mixture of 1.78 g of ethyl diazoacetate, 2.56 g of enamine **12b**,[18] and 0.5 g of silver carbonate in 20 ml of hexane was stirred at room temperature for 1 hr and then filtered. Evaporation of the fitrate under vacuum and chromatography of the oily residue (4.30 g) on alumina (activity II) gave 3.49 g (81%) of **13b**.

1-(*N*-Pyrrolidinyl)-1-carboethoxydiazomethylcyclohexane (13c). A solution of 0.79 g of ethyl diazoacetate and 1-(*N*-pyrrolidinyl)-cyclohexene (**12c**)[25] in 10 ml of ethanol was left at room temperature for 42 hr. Water and ether were added and the organic solution washed with brine, dried and evaporated under reduced pressure. Chromatography of the residual oil (1.72 g) on alumina (activity IV) and elution with hexane produced 315 mg (17%) of liquid, yellow ester **13c**: ir (neat) 4.79 (s, C=N$_2$), 5.89 μ (s, C=O); pmr δ 1.26 (t, 3, *J* = 7.0 Hz, Me), 1.4–2.1 (m, 14, (CH$_2$)$_7$), 2.4–2.7 (m, 4, (NCH$_2$)$_2$), 4.12 (q, 2, *J* = 7.0 Hz, OCH$_2$).

Anal. Calcd for $C_{14}H_{23}O_2N_3$: C, 63.37; H, 8.74. Found: C, 63.57; H, 8.98.

Elution with ether afforded 1.01 g of ethyl 4,5,6,7-tetrahydro-1*H*-indazole-3-carboxylate (**15a**): mp 88.5–90° (lit.[16] mp 89°).

A mixture of 1.63 g of ethyl diazoacetate, 2.16 g of enamine **12c**,[25] and 0.23 g of silver oxide in 25 ml of ether was stirred at room temperature for 24 hr and then filtered. Evaporation of the fitrate under vacuum, chromatography of the residue (3.63 g) on alumina (activity IV), and elution with hexane gave 2.81 g (75%) of ester **13c**.

Ethyl α-Diazo-β-ethyl-β-(*N*-morpholino)valerate (13d). A solution of 7.98 g of ethyl diazoacetate and 10.8 g of 3-(*N*-morpholino)-2-pentene (**12d**)[25] in 20 ml of methanol was left at room temperature for 13 days. Distillation of the low-boiling components under reduced pressure, chromatography of 10.0 g of the residual oil (15.2 g) on alumina (activity III), and elution with hexane produced 3.10 g (25%) of liquid, yellow ester **13d**: ir (neat) 4.78 (s, C=N$_2$), 5.90 μ (s, C=O); pmr δ 0.85 (t, 6, *J* = 7.5 Hz, Me$_2$), 1.28 (t, 3, *J* = 7.0 Hz, ester Me), 1.78, 1.88 (q, two each, *J* = 7.5 Hz, (CH$_2$)$_2$), 2.4–2.7 (m, 4, (NCH$_2$)$_2$), 3.4–3.7 (m, 4, (OCH$_2$)$_2$), 4.15 (q, 2, *J* = 7.0 Hz, ester CH$_2$).

Anal. Calcd for $C_{13}H_{23}O_3N_3$: C, 57.97; H, 8.61; N, 15.60. Found: C, 57.70; H, 8.87; N, 15.59.

Elution with ether gave a solid whose crystallization from hexane yielded 3.79 g (45%) of crystalline ethyl 4-ethyl-5-methylpyrazole-3-carboxylate (**15b**): mp 79–80°; ir (CHCl$_3$) 2.90 (w, NH), 5.85 μ (s, C=O); pmr δ 1.09 (t, 3, *J* = 7.5 Hz, ethyl Me), 1.25 (t, 3, *J* = 7.0 Hz, ester Me), 2.20 (s, 3, aromatic Me), 2.61 (q, 2, *J* = 7.5 Hz, CH$_2$), 4.26 (q, 2, *J* = 7.0 Hz, OCH$_2$); molecular ion *m/e* 182.1037 (calcd for $C_9H_{14}O_2N_2$, 182.1055).

A mixture of 1.48 g of ethyl diazoacetate, 2.01 g of enamine **12d**,[25] and 1.6 g of silver oxide in 20 ml of tetrahydrofuran was stirred at room temperature for 24 hr and then filtered. Evaporation of the filtrate under vacuum, chromatography of the residue on alumina (activity IV), and elution with hexane gave 783 mg of ester **13d**.

(25) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

1-Diazo-1-benzoyl-2-cyclohexyl-2-(*N*-pyrrolidinyl)ethane (17). Silver oxide, 1.2 g, was added in small portions over a 1-hr period to a stirring solution of 1.5 g of diazoacetophenone in 2 ml of tetrahydrofuran at 0°. Thereafter a solution of 1.7 g of enamine **12b**[18] in 2 ml of tetrahydrofuran was added and the mixture stirred at 0° for 2 hr. Aqueous sodium bicarbonate was added and the mixture extracted with hexane. Evaporation of the extract under vacuum, chromatography of the residual oil (2.90 g) on alumina (activity IV), and elution with hexane gave 1.44 g (36%) of liquid ketone **17**: ir (neat) 4.84 (s, C=N$_2$), 6.17 (s, C=O), 6.36 μ (m, C=C); pmr δ 1.0–2.0 (m, 15, (CH$_2$)$_7$ and CH), 2.4–2.7 (m, 4, (NCH$_2$)$_2$), 3.71 (d, 1, *J* = 7.5 Hz, NCH), 7.2-7.7 (m, 5, aromatic H's).

Anal. Calcd for $C_{19}H_{25}ON_3$: C, 73.28; H, 8.09. Found: C, 73.59; H, 8.07.

β-Hydroxy Esters (18). A mixture of 3.24 g of diazo ester **2a** and 50 mg of 5% palladium/charcoal in 20 ml of ethanol was hydrogenated at 3 atm for 12 hr. It was filtered, water added to the filtrate, and the latter extracted with chloroform. Evaporation of the extract gave 2.34 g of liquid ethyl β-hydroxybutyrate (**18a**)[26]: ir (neat) 2.84 (m, OH), 5.77 μ (s C=O); pmr δ 1.09 (d, 3, *J* = 7.0 Hz, Me), 1.25 (t, 3, *J* = 7.5 Hz, ethyl Me), 2.40 (d, 2, *J* = 6.5 Hz, CH$_2$), 4.13 (q, 3, *J* = 7.5, 7.0 Hz, OCH$_2$ and OCH).

A mixture of 1.00 g of diazo ester **3a** and 50 mg of 5% palladium/charcoal in 10 ml of ethanol was hydrogenated at 3 atm for 12 hr. Work-up as for **18a** gave 803 mg of liquid ethyl β-hydroxy-β-phenylpropionate (**18b**)[26]: ir (neat) 2.84 (m, OH), 5.79 (s, C=O), 6.22 μ (w, C=C), 6.30 μ (w, C=C); pmr δ 1.10 (t, 3, *J* = 7.5 Hz, Me), 2.52 (d, 2, *J* = 7.0 Hz, CH$_2$), 3.98 (q, 2, *J* = 7.5 Hz, OCH$_2$), 4.98 (t, 1, *J* = 7.0 Hz, OCH), 7.18 (s, 5, aromatic H's).

Ethyl Acetoacetate. A solution of 603 mg of **2a** in 10 ml of benzene was refluxed for 48 hr. Evaporation of the solvent under vacuum gave 376 mg of ethyl acetoacetate, identical in all physical properties with an authentic sample.

Ester **2a**, 0.70 g, was added to 10 ml of 10% sulfuric acid solution. Upon cessation of gas evolution the mixture was diluted with 20 ml of water and extracted with chloroform. Evaporation of the extract yielded 0.48 g of ethyl acetoacetate.

Ethyl Benzoylacetate (19a). A solution of 649 mg of **3a** in 10 ml of benzene was refluxed for 48 hr. Evaporation of the solvent under vacuum gave 556 mg of **19a**, identical in all respects with an authentic sample.

Benzoylacetone (19b). A solution of 1.2 g of diazo ketone **5a** and 20 ml of benzene was refluxed for 34 hr. Evaporation of the solvent gave 1.0 g of **19b**, mp 54–56°, spectra identical with those of an authentic specimen.

Diester 19c. A solution of 614 mg of diazo ester **10a** in 10 ml of benzene was refluxed for 72 hr. Evaporation of the solvent afforded 524 mg of diester **19c**;[27] molecular ion *m/e* 264.1026 (calcd for $C_{14}H_{16}O_5$ 264.0998).

A solution of 400 mg of the product in 10 ml of 10% aqueous potassium hydroxide was kept at room temperature for 12 hr. Acidification with 10% hydrochloric acid and extraction with benzene gave 167 mg of a solid, mp 74–76°, identical in all respects with authentic phenylacetic acid.

Ethyl Cycloheptanone-α-carboxylate. A solution of 931 mg of diazo ester **13c** and 1 ml of sulfuric acid in 10 ml of water was heated at 70° for 1 hr. It then was extracted with ether and the extract dried and evaporated under vacuum. The residue, 457 mg, was indistinguishable spectrally from authentic 2-carboethoxycycloheptanone.[28]

(26) J. Cure and M. Gaudemar, *Bull. Soc. Chim. Fr.*, 2471 (1969).

(27) H. Schinz and M. Hinder, *Helv. Chim. Acta*, 30, 1349 (1947).

(28) S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spangler, and M. J. Urbigkit, *Tetrahedron*, **19**, 1625 (1963).