Heterocyclic Studies. 40. Formation and Reactions of 1-Acetyl-3-diazoacetylhydroxypyrazolidines. Conversion to a Diazocyclopentanone[1]

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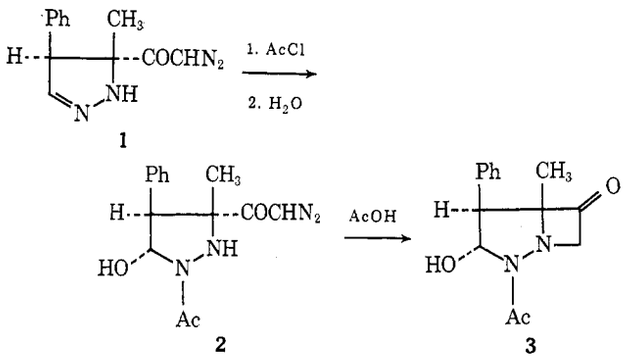
The conversion of two stereoisomeric pairs of 3,4-di-R-3-diazoacetyl-5-pyrazolines to 1-acetyl-5-hydroxy-3,4-di-R-pyrazolidines and subsequent conversion to 2-acetyl-3-*endo*-hydroxy-4,5-di-R-1,2-diazabicyclo[3.2.0]-6-heptanones are described. The reaction of 1-acetyl-3-diazoacetyl-3-methyl-4-phenyl-5-hydroxypyrazolidine with base gives epimers of 2-acethydrazino-2-methyl-3-phenyl-4-hydroxy-5-diazocyclopentanone (**18** and **19**), which were converted to 3-methyl-4-phenyl-3-cyclopentene-1,3-dione (**21**) and the 2-diazo derivative **20**.

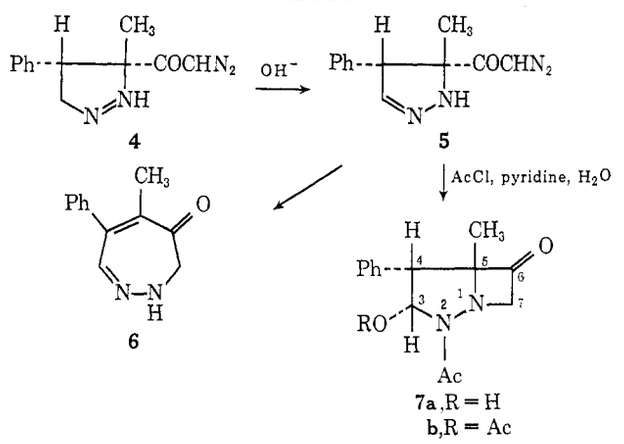
3-Diazoacetyl-Δ^5-pyrazolines undergo cyclization in acid to 1,2-diazabicyclo[3.2.0]heptenones,[2] and are converted by base to pyrazoles.[3] Another reaction of these versatile pyrazolines (*e.g.*, **1**) is the addition



of acetic acid to the C=N bond which occurs on treatment with acetyl chloride followed by water, and leads to 1-acetyl-5-hydroxy derivatives **2**.[4,5] This reaction has now been extended to some additional pyrazolines to provide information on the steric course of the addition, and the chemistry of these acylhydroxypyrazolidines has been studied.

trans-3-Methyl-4-phenyl-Δ^5-pyrazoline **5** was prepared from (*Z*)-α-methylcinnamic acid (α-methyl-*cis*-cinnamic) *via* the mixed anhydride and the Δ^1-pyrazoline **4** (Chart I). The chemistry of **5** paralleled

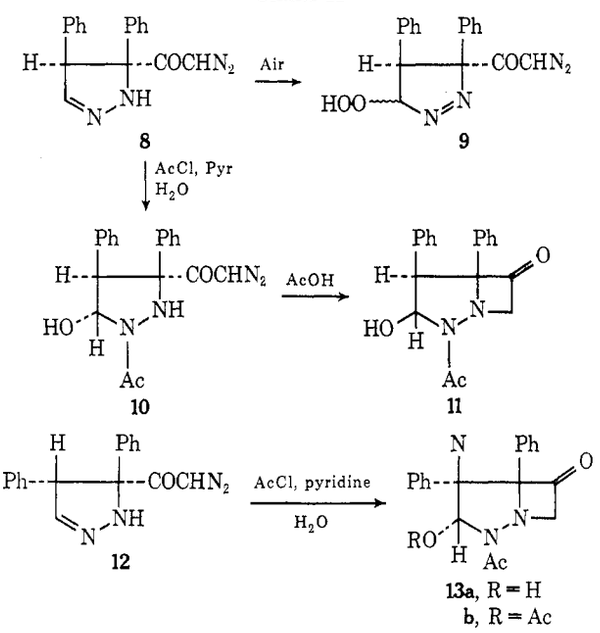
CHART I



that of the isomeric *cis*-pyrazoline **1**; reaction of **4** or **5** with acetic acid gave the diazepinone **6**,[4] and 3-methyl-4-phenylpyrazole was obtained with base.[3] Treatment of the 5-pyrazoline **5** with acetyl chloride–pyridine followed by water gave the 2-acetyl-3-hydroxybicyclic ketone **7a**, which was isolated from the aqueous phase of the reaction mixture. The diazoacetylpyrazolidine analogous to **2** was not detected.

This acylation was also studied with the stereoisomeric diphenylpyrazolines **8** and **12** (Chart II).

CHART II



In repeating the preparation of **8**,[2] the compound was found to undergo rapid air oxidation on recrystallization from ether with formation of a hydroperoxide which is considered to be **9** by analogy to the hydroperoxyazo compounds obtained from hydrazones.[6]

The reactions of the diphenyl-5-pyrazolines **8** and **12** with acetyl chloride and pyridine followed the general pattern seen in the 3-methyl-4-phenyl series. The hydroxyacetylpyrazolidine **10**, analogous to **2**, was isolated in solvated form from **8**. In the reaction of the *trans*-diphenylpyrazoline **12**, the diazoacetylpyrazolidine was observed as an unstable substance which cyclized to **13a** with loss of nitrogen on attempted recrystallization from ether.

(1) Supported in part by the National Science Foundation and the Unidel Foundation.

(2) A. Nabeya, F. B. Culp, and J. A. Moore, *J. Org. Chem.*, **35**, 2015 (1970).

(3) F. B. Culp, A. Nabeya, and J. A. Moore, *ibid.*, **38**, 2949 (1973).

(4) J. A. Moore, F. J. Marascia, R. W. Medeiros, and R. L. Wineholt, *ibid.*, **31**, 34 (1966).

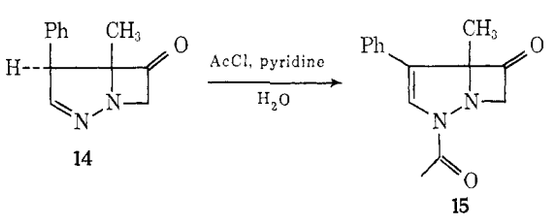
(5) T. Yamauchi and J. A. Moore, *ibid.*, **31**, 42 (1966).

(6) K. N. Pausacker, *J. Chem. Soc.*, 3478 (1950); R. Criegee and G. Lohaus, *Chem. Ber.*, **84**, 219 (1951).

The direct isolation of bicyclic ketones from the trans-3,4-disubstituted pyrazolines **5** and **12** is presumably due to the more rapid cyclization of the intermediate acylhydroxypyrazolidines when the 4-phenyl group is cis to the diazoacetyl chain, perhaps providing orientation for the ring closure. The situation is complex, however, since solubility relationships play a role; pyrazolidines **2** and **10** could be crystallized and extracted, respectively, from the aqueous phase of the reaction mixture, while isolation of products from the other two reaction mixtures required the evaporation of water.

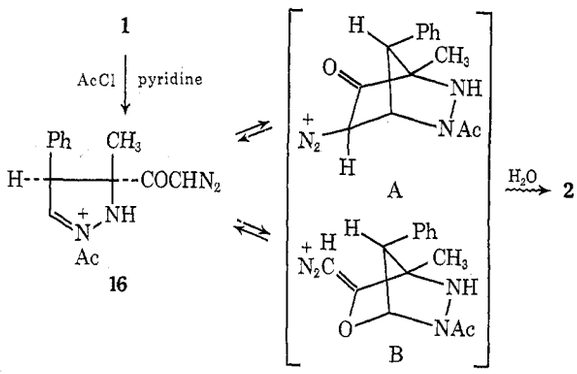
In all of these reactions, the pyrazolidine or bicyclic ketone was obtained as a single stereoisomer. The endo configuration of the hydroxyl group in the *cis*-3-methyl-4-phenylpyrazolidine **2** was assigned on the basis of the nmr spectrum of the derived bicyclic ketone **3**, in which the signals for H-3 and H-4 were broadened singlets ($J_{3,4} \cong$ OHz).[4] The spectra of **7**, **11**, and **13** confirm this stereochemistry and are consistent with an endo hydroxyl in each case. The H-3 and H-4 signals in **7a** and **13a** were doublets, $J_{3,4}$ = 4.2 Hz, appropriate for a cis vicinal coupling, with slightly larger values, 4.7 and 4.5 Hz, for the respective acetates. The corresponding peaks in the spectra of the pyrazolidine **10** and cyclic ketone **11** were singlets. The signals for the 7-CH_2 protons in the hydroxy bicyclic ketones **3** and **7a** are singlets, with the expected equivalence and J_{gem} showing up in the acetates; this relationship is curiously reversed in the endo-phenyl series **13**, with the 7-CH_2 a doublet of doublets in the alcohol and a singlet in the acetate.

As noted previously,[4] the course of these acylation reactions is unexpected; similar treatment of the unsaturated bicyclic ketone **14** with acetyl chloride and aqueous work-up leads cleanly to the acyl enamine system. The pronounced water solubility of the products during the work-up procedure was attributed to the intermediacy of a pyridinium salt intermediate in the formation of **2**, but this does not account for the absence of products analogous to **15**, nor the consistent formation of endo hydroxy derivatives from both C-4 epimers.



The reaction of **2** with base, described below, suggested that interaction of the diazoacetyl group with C-5 might be responsible for these apparently anomalous acylations. Evidence for participation of the diazo group was found when the reaction of **1** with acetyl chloride was quenched with D_2O; the signal for the CHN_2 proton was absent in the nmr spectrum of the resulting **2**. The reaction of **1** and acetyl chloride was then observed in the nmr spectrometer, and the CHN_2 signal disappeared immediately on addition of acetyl chloride. Hydrolysis with H_2O led to **2** with the CHN_2 signal intact. That these observations were not due to acylation of the $COCHN_2$ group and subsequent hydrolysis of a diazo diketone was established by carrying out the experiment with the 3-diazoacetyl-Δ^1-pyrazoline. The spectrum was unchanged, with no diminution of the CHN_2 peak on addition of acetyl chloride. The nmr spectrum of the reaction mixture of **1** with acetyl chloride underwent a series of changes on standing, but only **2** has been isolated under various work-up times and conditions.

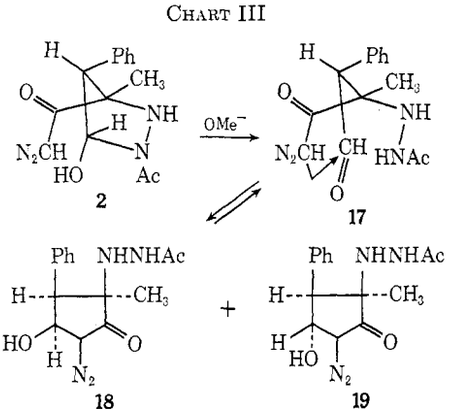
These observations clearly indicate that the $COCHN_2$ group has a role in the acylation of **1** and probably also the other diazoacetylpyrazolines. Interaction of this group with the C=N bond could lead *via* **16**



to the bicyclic intermediates A and/or B. Formation of A would explain loss of diazomethyl proton; hydrolysis of the enol derivative B would lead directly to the observed endo-hydroxy product.[7]

In addition to the extremely facile acid-catalyzed cyclization, the hydroxydiazoacetylpyrazolidines are quite sensitive to base; this reaction was examined in detail with the 3-methyl-4-phenyl compound **2**. On standing in dilute methanolic methoxide, **2** was converted to two products, which were separated by chromatography and found to be isomeric with the starting material. The ir spectra of both compounds showed the presence of a diazocarbonyl system (ν 2080 cm^{-1}) but the nmr spectra contained no signals for diazomethyl protons; peaks were present in both for three exchangeable protons and two mutually coupled methine protons. These data and several chemical transformations establish the structures of these base products as the stereoisomeric hydroxydiazocyclopentanones **18** and **19** (Chart III).

CHART III



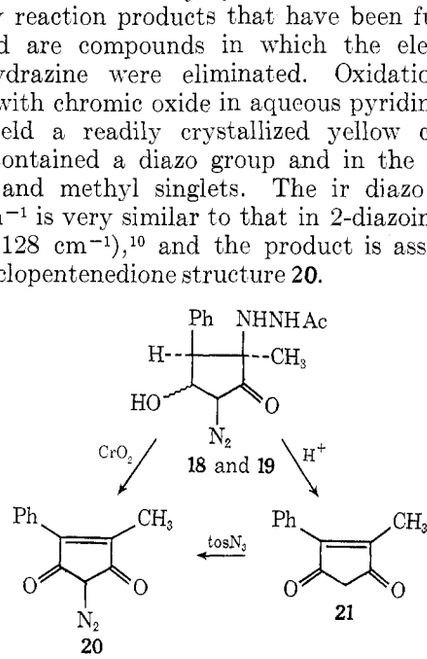
The cyclic diazo ketone structures can be derived readily from the diazoacetylpyrazolidine by ring open-

(7) We are grateful to a reviewer for this suggestion.

ing of the carbinol amide system as in **17** and recyclization by aldol condensation of the diazomethyl group. Comparable condensations have been observed with diazo esters or diazo ketones and aldehydes[8a] or reactive ketones,[8b] and a few intramolecular condensations have also been reported.[9] The steric configuration at C-2 and C-3 in **18** and **19** is based on the known stereochemistry of **2**, the position of the 3-methyl group relative to phenyl ring being inverted in the process.

The hydroxyl configurations in the carbinols are assigned on the basis of the values of $J_{3,4}$ for the two isomers. Epimer **18**, with the OH group cis to the phenyl and acethydrazide groups, was obtained in somewhat larger amount, but the isomers are equilibrated in base, and the product ratio presumably reflects the relative stabilities and not conformational preference in the condensation.

The reactions of **18** and **19** are complicated by the additional sensitive acylhydrazine substituent and the only reaction products that have been fully characterized are compounds in which the elements of acetylhydrazine were eliminated. Oxidation of **18** and **19** with chromic oxide in aqueous pyridine gave in 22% yield a readily crystallized yellow compound which contained a diazo group and in the nmr only phenyl and methyl singlets. The ir diazo band at 2124 cm^{-1} is very similar to that in 2-diazoindandione ($\nu_{N\equiv N}$ 2128 cm^{-1}),[10] and the product is assigned the diazocyclopentenedione structure **20**.



Treatment of the epimeric alcohols with acetic acid in the presence of copper bronze gave a mixture of at least four products. The least polar component was isolated in 5–10% yield by chromatography and sublimation. This compound was a yellow solid, $C_{12}H_{10}O_2$, with nmr showing phenyl and methyl singlets plus a CH_2 peak [δ 3.03 (s, 2)]. These properties suggested the cyclopentene-1,3-dione structure **21**. The compound appeared to be more stable to base than the parent dione reported by DePuy;[11] brief treatment of **21** with NaOD in D_2O caused disappearance of the CH_2 peak without appreciable decomposition. A pK_a of about 12 was indicated spectrophotometrically. Reinforcement of the structure of the 1,3 dione and of the diazo diketone **20** as well was provided by conversion of **21** to **20** by a diazo transfer reaction with tosyl azide.

(8) (a) E. Wenkert and C. A. MacPherson, *J. Amer. Chem. Soc.*, **94**, 8084 (1972); (b) B. Eistert and P. Donath, *Chem. Ber.*, **102**, 1725 (1969).

(9) T. Burkoth, *Tetrahedron Lett.*, 5049 (1969).

(10) M. Regitz and G. Heck, *Chem. Ber.*, **97**, 1482 (1964).

(11) C. H. DePuy and E. F. Zaweski, *J. Amer. Chem. Soc.*, **81**, 4920 (1959); C. H. DePuy and P. R. Wells, *ibid.*, **82**, 2909 (1960).

Experimental Section

(*Z*)-α-Methylcinnamic Acid ("α-Methyl-*cis*-cinnamic").[12,13]—A solution of 10 g of the *E* ("α-methyl-*trans*") acid[17] [δ ($CDCl_3$) 6.85 ppm (d, J = 1 Hz)] in 40 ml of ethanol was irradiated in a quartz tube surrounded by ten 15-W 2537-Å sterilizing lamps. After 24 hr the solution was evaporated to dryness. The mixture of stereoisomeric acids was dissolved in sufficient concentrated aqueous ammonia to produce a clear solution. To this solution was added excess saturated $BaCl_2$ solution. The insoluble barium salt of the *E* (trans) acid was collected and the *E* acid was recovered by acidification.

The filtrate was treated with additional $BaCl_2$ to confirm that precipitation of the *E* salt was complete, and the solution was then cooled and acidified. The resulting precipitate of the *Z* acid ("α-methyl-*cis*") was collected, washed with water, and dried. The nmr spectrum indicated a negligible amount of *E* acid. Recrystallization from $CHCl_3$–petroleum ether (bp 30–60°) gave 1.7 g of the *Z* acid: mp 90–91° (lit.[14] mp 91°); δ^{CDCl_3} 2.06 (d, 3, J = 1 Hz), 6.85 (d, 1, J = 1 Hz), 7.30 (s, 5).

***r*-3-Diazoacetyl-3-methyl-*c*-4-phenyl-1-pyrazoline (4).**—A solution of 6.48 g of (*Z*)-α-methylcinnamic acid and 4.34 g of ethyl chloroformate in 180 ml of anhydrous ether was treated dropwise at 0° with 4.04 g of triethylamine. After stirring for 1 hr the amine hydrochloride was collected by filtration and the solution of the mixed anhydride was concentrated to a thin oil. This oil was added to a solution of diazomethane prepared (with distillation) from 36 g of bis(*N*-methyl-*N*-nitroso)terephthalamide. The solution stood for 2 days at 25° and was then evaporated *in vacuo*. The yellow solid residue was washed with hexane and collected to give 7.21 g (79%) of crude **4**. Recrystallization from ether–petroleum ether gave pale yellow needles: mp 106° dec; ν^{KBr} 2110, 1620 cm^{-1}; δ^{CDCl_3} 1.47 (s, 3), 3.1–3.25 (four lines of X part of ABX, δ_X^{calcd} 3.17, H-4), 4.35–5.25 (eight lines of AB part of ABX, δ_B^{calcd} 4.67, δ_A^{calcd} 5.00, J_{AX} = 2.5, J_{BX} = 7.8, J_{AB} = −18.0 Hz, 5-CH_2), 5.68 (s, 1, CHN_2), 6.7–7.3 (m, C_6H_5).

Anal. Calcd for $C_{12}H_{12}N_4O$: C, 63.14; H, 5.30; N, 24.55. Found: C, 62.77; H, 5.23; N, 24.11.

A solution of 1.5 g of **4** in 15 ml of acetic acid was heated at 85° for 2 hr. Evaporation and crystallization from methanol gave 0.8 g of 2,3-dihydro-5-methyl-6-phenyl-4*H*-1,2-diazepin-4-one (**6**).

***r*-3-Diazoacetyl-3-methyl-*c*-4-phenyl-5-pyrazoline (5).**—To a solution of 2.25 g of the 1-pyrazoline **4** in 60 ml of methanol at 0° was added 1 ml of 1 *N* KOH. After 4 hr, tlc showed **4** to be absent. The solution was treated with solid CO_2 and evaporated to a solid residue which was extracted with ether. Concentration of the ether gave 1.95 g (86%) of pale yellow solid. Recrystallization from ether gave 1.5 g of **5**: mp 102° dec; ν^{KBr} 3400, 3200, 2110, 1620 cm^{-1}; δ^{CDCl_3} 1.54 (s, 3), 3.97 (d, H-4, J = 1.5 Hz), 5.51 (s, 1, CHN_2), 5.67 (br, 1, NH), 6.85 (d, H-5, J = 1.5 Hz), 6.9–7.35 (m, 5).

Anal. Calcd for $C_{12}H_{12}N_4O$: C, 63.14, H, 5.30; N, 24.55. Found: C, 63.36; H, 5.30; N, 24.65.

3-Methyl-4-phenylpyrazole.—A solution of 0.45 g of the 5-pyrazoline **5** in 20 ml of methanol was treated with 2 ml of 1 *N* KOH and was stirred at room temperature for 36 hr; tlc still showed the presence of some **5**. The solution was neutralized with acid and evaporated to a tan solid residue which was washed with water and recrystallized from methanol to give 130 mg of 3-methyl-4-phenylpyrazole, mp 143–145°.

(12) We are greatly indebted to Dr. Aiko Nabeya for carrying out this preparation in the laboratories of the University of Tokyo.

(13) The preparation of this acid ("*allo*-cinnamic acid") by irradiation of the "normal" trans acid (*E*) was described by Stoermer.[14] The *Z* acid was isolated in unspecified yield by a complex fractional crystallization procedure, and was characterized by crystal form and melting point; the structure was confirmed by H_2SO_4-catalyzed cyclization to 2-methylindenone. The acid has subsequently appeared in the literature,[15,16] with ultraviolet data, but the isolation procedure and other physical characterization were not given. The situation is further obscured by the report of three crystalline forms of the *E* acid[17] and the description of two crystalline modifications of the *Z* acid having different melting points and spectra (in solution).[16] To clarify matters we describe the preparation and isolation in detail. It will be noted that the acid with β-H and CO_2H cis (*E*) has a more deshielded β-H and less soluble barium salt than the isomeric *Z* acid, as found with other isomeric α-substituted cinnamic acids.[2]

(14) R. Stoermer and G. Voht, *Justus Liebigs Ann. Chem.*, **409**, 51 (1915).

(15) A. Mangini and F. Montanari, *Gazz. Chim. Ital.*, **88**, 1081 (1958).

(16) Y. Ushibara and M. Hirota, *Nippon Kagaku Zasshi*, **82**, 354 (1961).

(17) J. R. Johnson, *Org. React.*, **1**, 251 (1942).

2-Acetyl-3-*endo*-hydroxy-5-methyl-4-*endo*-phenyl-1,2-diazabicyclo[3.2.0]heptan-6-one (7a).—A solution of 0.84 g of 5-pyrazoline **5** in 10 ml of methylene chloride was treated with 0.6 ml of pyridine and 0.3 ml of acetyl chloride. After stirring at 0° for 20 min, ice water and 0.22 g of Na_2CO_3 were added. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers were washed twice with water. After drying, the CH_2Cl_2 solution was evaporated to give 0.35 g of tan solid; the ir spectrum of this material had a strong band at 2100 cm^{-1}. No pure compound could be isolated from this fraction; tlc showed the presence of starting **5** and another compound which was not the product **7a**. The aqueous phase (original layer plus washings) was then concentrated at 30° to 20 ml volume; at this point solid began to crystallize. This material (0.60 g) was collected; tlc showed one compound. Recrystallization from ether gave 0.52 g of colorless, granular **7a**: mp 156–158°; ν^{KBr} 3250, 1800, 1630 cm^{-1}; δ ($CDCl_3$) 1.48 (s, 3), 2.18 (s, 3, $COCH_3$), 3.24 (d, J = 4.2 Hz, H-4), 4.77 (s, 2, 7-CH_2), 5.01 (d, J = 3 Hz, 1, in D_2O exchanges), 6.20 (m, 1, H-3, in D_2O → d, J = 4.2 Hz), 7.2–7.4 (m, 5).

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.70. Found: C, 64.85; H, 6.35; N, 10.69.

For conversion to the acetate **7b**, 0.3 g of alcohol **7a** was treated at 25° with 2 ml of acetic anhydride and 0.8 ml of pyridine. After 12 hr, water was added and the resulting white crystals were collected, dried, and recrystallized from ether to give 0.22 g of **7b**: mp 159–161°; ν^{KBr} 1800, 1755, 1660 cm^{-1}; δ ($CDCl_3$) 1.52 (s, 3, 5-CH_3), 1.87 (s, 3, OAc), 2.25 (s, 3, NAc), 3.53 (d, J = 4.7 Hz, H-4), 4.39–5.06 (four lines AB dd, δ_B^{calcd} 4.82, J_{AB} = 17.8 Hz, 7-CH_2), 7.15–7.45 (m, 6, C_6H_5 + H-3).

Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.59; H, 5.97; N, 9.05.

3-Diazoacetyl-*cis*-3,4-diphenyl-5-hydroperoxy-1-pyrazoline (9).—On several occasions attempts to recrystallize the pyrazoline **8** gave a sparingly soluble product. In a typical case, 1.2 g of **8**[2] was dissolved in 100 ml of ether and 400 ml of hexane was added. On standing (exposed to air) overnight, 0.75 g of well-formed needles separated from the solution. Recrystallization from ether–pentane gave colorless needles: mp 119–121° dec; ν^{KBr} 3200, 2100, 1630 cm^{-1}; δ^{DMSO} 4.3 (d, 1, J = 3 Hz), 5.4 (br, 1), 6.00 (s, 1), 7.12–7.24 (m, 10).

Anal. Calcd for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.38; N, 17.38. Found: C, 62.97, 63.18; H, 3.83, 4.37; N, 17.26.

The spectra indicate retention of the CHN_2 and PhCH groups and the presence of an OH group. These data and the incorporation of O_2 led to the assignment of the hydroperoxide structure **9**. Application of the compound to starch–iodide paper moistened with acetic acid caused immediate appearance of a deep violet color. Attempts to obtain transformation products of **9** with acid, base, or reducing agents gave complex mixtures.

1-Acetyl-*r*-3-diazoacetyl-3,*t*-4-diphenyl-*c*-5-hydroxypyrazolidine (10).—To a solution of 0.58 g of the *cis*-diphenylpyrazoline **8** in 10 ml of CH_2Cl_2 at 0° was added 0.4 ml of pyridine and 0.2 ml of acetyl chloride. After 15 min the clear solution was treated with ice water containing 0.15 g of sodium carbonate. The CH_2Cl_2 phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic solution was dried and evaporated; benzene was added and evaporated to remove traces of pyridine. The residual solid was washed with cyclohexane to remove oily material, giving 0.63 g of light yellow solid. Recrystallization from ether gave 0.37 g of **10** as white needles: mp 123–124° dec; ν^{KBr} 3250, 2100, 1640 cm^{-1}; δ (DMSO-d_6) 2.38 (s, 3), 4.44 (s, 1, H-4), 5.50 (br d, in D_2O → br s, H-5), 6.20 (br s, in D_2O exchanges), 6.57 (s, 1, CHN_2), 6.90 (s, in D_2O exchanges), 7.1–7.2 (m, 10). The compound could not be obtained free of solvent despite exhaustive drying.

Anal. Calcd for $C_{19}H_{18}N_4O_3$: C, 65.13; H, 5.18; N, 15.99. Found (dried at 56°, 10 hr, 0.1 mm): C, 64.57; H, 5.55; N, 14.97.

2-Acetyl-3-*endo*-hydroxy-4-*exo*,5-diphenyl-1,2-diazabicyclo[3.2.0]-6-heptanone (11).—A solution of 1.08 g of the pyrazolidine **10** in 10 ml of acetic acid was stirred at 25° for 45 min; visible gas evolution ceased after 30 min. The solution was concentrated *in vacuo* to give 0.83 g of brown solid which was recrystallized from benzene to give 0.43 g of colorless crystals of **11**: mp 165–167°; ν^{KBr} 3200, 1800, 1630 cm^{-1}; δ^{CDCl_3} 2.45 (s, 3), 4.26 (s, 1, H-4), 4.88 (s, 2, 7-CH_2), 5.72 (s, 1 in D_2O exchanges), 6.26 (s, 1, H-3), 7.4–7.66 (m, 10).

Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.83; H, 5.32; N, 8.51.

2-Acetyl-3-*endo*-hydroxy-4-*endo*,5-diphenyl-1,2-diazabicyclo[3.2.0]-6-heptanone (13a).—A solution of 0.58 g of the *trans*-diphenylpyrazoline **12** in 10 ml of CH_2Cl_2 was treated with 0.6 ml of pyridine and then 0.2 ml of acetyl chloride. A significant amount of white precipitate appeared and then redissolved during 15 min of stirring. Ice water containing Na_2CO_3 was added and, after separation and extraction, the combined CH_2Cl_2 layers were evaporated to give 0.23 g of oily residue which solidified on adding petroleum ether; the ir spectrum of this material showed strong absorption at 2100 cm^{-1}.

The combined aqueous layers from the extraction and washing were concentrated at reduced pressure to 10 ml volume, and 0.36 g of white crystalline solid separated. This material showed strong ir bands at 3200 (br), 2100, and 1630 cm^{-1} (br), and is assumed to be the diazoacetylpyrazolidine. On attempted recrystallization from ether, gas evolution occurred before all of the solid had dissolved; after 20 min of heating, the solution was filtered to remove a trace of solid. Evaporation of the ether and recrystallization of the residue gave 0.3 g of white needles of the bicyclic ketone **13**: mp 185–187° dec; ν^{KBr} 3300, 1800, 1640 cm^{-1}; δ^{CDCl_3} 2.36 (s, 3, NAc), 3.36 (d, J = 4.2 Hz, H-4), 4.57–5.17 (eight lines of 7-CH_2 Ab dd further split by H-3, δ_A^{calcd} 4.77, δ_B^{calcd} 4.97, J_{AB} = 17, J_{3-7A} = 0.7, J_{3-7B} = 0.7 Hz), 6.29 (m, J = 3 Hz, in D_2O → d, J = 4.2 Hz, H-3), 7.25–7.38 (m, 10).

Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.49; H, 5.60; N, 8.79.

The acetate **13b** was obtained in the usual way (Ac_2O, pyridine): mp 181° dec; ν^{KBr} 1800, 1760, 1670 cm^{-1}; δ ($CDCl_3$) 1.97 (s, 3, OAc), 2.42 (s, 3, NAc), 3.65 (d, J = 4.5 Hz, H-4), 4.83 (s, 2, 7-CH_2), 7.3–7.4 (m, 10), 7.46 (d, J = 4.5 Hz, H-3).

Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.40; H, 5.65; N, 7.60.

5-Diazo-*r*-2-(2-acethydrazido)-*r*- and -*t*-4-hydroxy-2-methyl-*c*-3-phenylcyclopentanone (18 and 19).—A solution of 6.3 g of the acetylpyrazolidine **2** in 125 ml of methanol was flushed with nitrogen and 44 ml of 0.5 *N* sodium methoxide in methanol was added slowly with stirring at 25°. The solution was allowed to stand at room temperature for 1 day and was then neutralized with Dry Ice and concentrated at reduced pressure. The residue was extracted with three 30-ml portions of boiling chloroform. The organic solution was washed with two 15-ml portions of 10% NH_4Cl and once with water and was then dried over $MgSO_4$. Concentration of the solution to a small volume and addition of benzene precipitated a pale yellow powder containing both isomers of the product. The melting point of the isomer mixture varied from 107° to 138°, depending on the composition. Slow recrystallization from CH_2Cl_2–ether gave a mixture (mp 138–142°) containing 80–85% of **19**. Complete separation was achieved by chromatography over a silicic acid column, using 85:15 chloroform–benzene as eluent for **19** and chloroform for **18**. Recrystallization from CH_2Cl_2–ether gave the pure isomers.

Alcohol **18** had mp 165–167°; ν^{KBr} 3130, 2080, 1650 cm^{-1}; δ^{CD_3OD} 1.21 (s, 3), 1.81 (s, 3), 3.13 (d, 1, J = 7.8 Hz, H-3), 5.88 (d, 1, J = 7.8 Hz, H-4), 7.4 ppm (s, 5).

Anal. Calcd for $C_{14}H_{16}O_3N_4$: C, 58.32; H, 5.59; N, 19.44. Found: C, 58.34; H, 5.75.

Alcohol **19** had mp 144–147°; ν^{KBr} 3130, 2080, 1650–1630 cm^{-1}; δ^{CD_3OD} 1.18 (s, 3), 1.87 (s, 3), 3.18 (d, 1, J = 4.6 Hz, H-3), 5.37 (d, 1, J = 4.6 Hz, H-4), 7.1–7.8 ppm (m, 5).

Anal. Found: C, 58.42; H, 5.72; N, 19.18.

The acetate was prepared from 147 mg of **19** with 5 ml of Ac_2O and 0.2 ml of pyridine. The reaction mixture was warmed briefly to dissolve the solid and was then allowed to stand at 26 for 30 min. The solution was poured into iced 1 *N* KOH solution, stirred thoroughly, and extracted with three portions of CH_2Cl_2. After removal of the solvent and addition of a few drops of ether, 92 mg (55%) of yellow solid, mp 143–146°, was obtained. Recrystallization from ether–pentane gave a yellow, chalky solid: mp 144–145°; ν^{KBr} 3200–3100, 2090, 1725, 1690–1640 cm^{-1}; δ^{CDCl_3} 1.24 (s, 3), 1.90 (s, 3), 212 (s, 3), 3.37 (d, 1, J = 5 Hz, H-3), 5.72 (br, 1, in D_2O exchanges), 6.08 (d, 1, J = 5 Hz, H-4), 7.2–7.6 (m, 6).

Anal. Calcd for $C_{16}H_{18}O_4N_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.18; H, 5.48; N, 16.91.

2-Diazo-4-methyl-5-phenyl-4-cyclopentene-1,3-dione (20).—A solution of 0.235 g of chromium trioxide in 1.5 ml of water and 22 ml of pyridine was slowly added to a magnetically stirred solution of 0.507 g (1.75 mmol) of a mixture of **18** and **19** in 30 ml of pyridine. The dark red reaction mixture was stirred at room temperature for 24 hr, treated with 30 ml of water, and extracted with

ether. After drying, the solvent was evaporated to a yellow solid. Recrystallization from ethanol–water gave 64 mg (22%) of yellow needles of **20**: mp 114–115°; ν^{KBr} 2120, 1690, 1378 cm^{-1}; λ_{max}^{MeOH} 238 mμ (ε 25,500), 278 (15,300), 355 (1290); δ^{CDCl_3} 2.20 (s, 3), 7.50 (s, 5).

Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.93; H, 3.73; N, 13.03.

Reaction of 18 and 19 in Acetic Acid.—To a solution of 2.0 g of the mixed alcohols **18** and **19** in 50 ml of glacial acetic acid was added about 100 mg of copper powder. The solution was stirred at 45° until gas evolution became very slow (1 hr). The mixture was filtered and the acetic acid was evaporated. The residual greenish-brown syrup was dissolved in CH_2Cl_2 and washed with water to remove copper salts. The organic phase was dried and concentrated and the residue (1.47 g) was chromatographed on 40 g of silicic acid. The first two fractions, eluted with chloroform, gave 190 mg of dark yellow oil which was distilled in short-path apparatus to give 140 mg (10%) of yellow crystals of methylphenylcyclopentene-1,3-dione (**21**): mp 117–118°; ν^{KBr} 1740, 1705, 1385 cm^{-1}; λ_{max}^{MeOH} 224 mμ (ε 10,000), 286 (7800); δ^{CDCl_3} 2.18 (s, 3), 3.03 (s, 2), 7.49 (s, 5).

Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.34; H, 5.47.

Conversion of 21 to 20.—To a solution of 61 mg (0.33 mmol) of dione **21** and 71 mg (0.35 mmol) of *p*-toluenesulfonyl azide in 2 ml of acetonitrile was added 0.15 ml of triethylamine. The yellow solution darkened rapidly and tlc examination after 30 min showed no starting material remaining. The orange solution was diluted with 20 ml of ether, washed with water, dried, and concentrated to a dark, noncrystalline residue. Chromatography over a short silicic acid column (85:15 chloroform–benzene eluent) gave 39 mg of an orange oil which crystallized on addition of a few drops of benzene. Recrystallization from benzene–hexane gave 30 mg (43%) of orange needles, mp 112–114°, mixture melting point with **20** prepared by oxidation, 112–114°. The ir spectra of the two samples matched in all peaks.

Registry No.—**2**, 40704-62-9; **4**, 40704-63-0; **5**, 40704-64-1; **6**, 1706-26-9; **7a**, 40704-65-2; **7b**, 40704-66-3; **8**, 24302-15-6; **9**, 40704-14-1; **10**, 40704-68-5; **11**, 40704-69-6; **12**, 24302-17-8; **13a**, 40704-16-3; **13b**, 40704-17-4; **18**, 40704-18-5; **19**, 40704-19-6; **19** acetate, 40704-20-9; **20**, 40674-82-6; **21**, 40704-21-0; (*Z*)-α-methylcinnamic acid, 15250-29-0; diazomethane, 334-88-3; bis(*N*-methyl-*N*-nitroso)terephthalamide, 133-55-1; 3-methyl-4-phenylpyrazole, 13788-84-6.

Heterocyclic Studies. 41. The Conversion of 3-Diazoacetylpyrazolines to Pyrazoles *via* Pyrazolo[1,5-*c*]-*v*-triazines[1]

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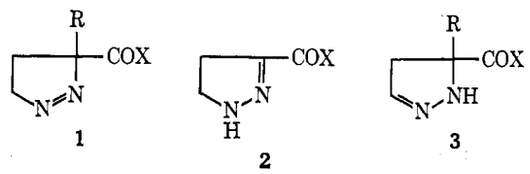
3-Diazoacetyl-4-methoxycarbonyl-3-methyl-1-pyrazoline (4) is converted by base to the pyrazolotriazinone **6**. Further reaction of **6** with base leads to the pyrazole **8** and methyl glyoxylate hydrazone (**9**). The hydrazone was also isolated, together with pyrazoles, from the reaction of several related diazoacetylpyrazolines in base, but triazinone intermediates were not detected. *cis*- and *trans*-3,4-di(methoxycarbonyl)-3-methyl-1-pyrazolines (**17** and **18**) were found to epimerize at C-4 on conversion to the 5-pyrazolines, suggesting that the triazinone **6** is isolable because of the rapid isomerization of the double bond in the presumed intermediate **7**.

The 1-pyrazolines **1** (R = H) that are initially formed in the 1,3-dipolar addition of diazomethane to α,β-unsaturated carbonyl systems containing no α substituent are highly labile and rapidly isomerize to the conjugated 2-pyrazoline **2**. With a 3-alkyl or aryl substituent (**1**, R ≠ H) the 1-pyrazolines are more stable, but isomerization with acid or base under mild conditions leads to the 5-pyrazoline **3**.[2] In the preparation of diazabicyclo[3.2.0]heptenones from 3-diazoacetylpyrazolines (**1** X = CHN_2), milder acid conditions can be used for the cyclization if base-catalyzed isomerization to **3** is carried out prior to the



cyclization step.[3] It has been found, however, that longer exposure of a 3-diazoacetyl-5-pyrazoline to base leads to formation of a pyrazole.[2a] The reactions of these compounds with base have now been further examined, and the nature of this unusual elimination reaction has been clarified.

In the attempted tautomerization of the 4-methoxycarbonylpyrazoline **4**[3] with base, an isomer was obtained which was not the diazoacetyl-5-pyrazoline. The ir spectrum contained no diazo band; the nmr spectrum contained peaks for two NH protons and two singlet vinyl protons at δ 6.61 and 6.81 as well as CH_3 signals at δ 1.31 and 3.88 (OCH_3). The uv spectrum had λ_{max} 330 nm (ε 6000). The mass spectrum contained a small parent ion peak at *m/e* 210 and two more intense peaks at *m/e* 141 and 109, corresponding to loss of a C_2HN_2O fragment and further loss of CH_3O. These data, particularly the nmr values, define the bicyclic triazinone structure **6**, resulting from isomerization of the pyrazoline, nucleophilic attack of N-2 at the terminus of the diazocarbonyl group, and tautomerization (Chart I).

A number of reactions have been observed in which the diazo group in $COCHN_2$ and $COCN_2CO$ systems coordinates various nucleophiles, including HSO_3^-, CN^-, amines, phosphines, and hydrazine.[4] In the last case, the intermediate tetrazene breaks down to give an azide.[5] A chain of four contiguous nitrogen atoms has previously been obtained in this type of coupling only with arenediazonium ions and hydrazines or pyrazoles,[6] and with these products the coupling is reversed in acid. The pyrazolotriazinone **6** was relatively stable in acid, and did not give the 1,2-

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