4,5,6,7-tetrahydro-7-iminopyrazolo[2,3-*a*]pyridine (XIV), b.p. 123–126° (0.06 mm.). When the viscous distillate was allowed to stand at room temperature, massive crystals of XIV separated.

A sample of this solid was pressed on a clay plate to free it from oil and was crystallized twice from petroleum ether (b.p. 30–60°) and once from hexane to give 4,4-dimethyl-4,5,6,7-tetrahydro-7-iminopyrazolo[2,3-*a*]pyridine (XIV), m.p. 69–71°. The infrared spectrum showed λ_{max}^{KBr} 3.08, 3.22, 3.40, 6.01, and 6.45 μ, but no bands at 4.45 or 5.83 μ.

The n.m.r. spectrum of XIV is summarized in Fig. 1.

Anal. Calcd. for $C_9H_{13}N_3$: C, 66.3; H, 8.04; N, 25.8. Found: C, 66.7; H, 8.10; N, 25.7.

4-[3(5)-Pyrazolyl]-4-methylpentanoic Acid (XV).—A mixture of 169.5 g. of the crude distillate containing XIII and XIV, 92 ml. of concentrated hydrochloric acid, and 250 ml. of water was heated at 90–95° with stirring for 3 hr. The mixture was cooled with stirring, and the solid that crystallized was collected and washed with cold water to give 122.6 g. (62%) of 4-[3(5)-pyrazolyl]-4-methylpentanoic acid (XV), m.p. 157.7–159.0°. The infrared spectrum had λ_{max}^{KBr} 2.98, 3.17, 5.92, 7.18, and 7.30 μ. In another experiment, a sample that had been recrystallized from water had m.p. 155–157° and was analyzed.

Anal. Calcd. for $C_9H_{14}N_2O_2$: C, 59.3; H, 7.75; N, 15.4. Found: C, 59.6; H, 6.00; N, 15.1.

4,4-Dimethyl-4,5,6,7-tetrahydro-7-ketopyrazolo[2,3-*a*]pyridine (X).—An erlenmeyer flask containing 1.0 g. of XV was heated in an oil bath maintained at 200° for 0.25 hr. During the heating period the solid melted, and water distilled out of the melt. The solid obtained when the contents of the flask had cooled was crystallized from hexane to give 0.7 g. (80%) of 4,4-dimethyl-4,5,6,7-tetrahydro-7-ketopyrazolo[2,3-*a*]pyridine (X), m.p. 196.5–198.0°. A sample with the same melting point obtained by recrystallization from heptane was analyzed. The infrared spectrum had λ_{max}^{KBr} 5.72, 6.39, 7.20, and 7.33 μ.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.9; H, 7.38; N, 17.1. Found: C, 66.0; H, 7.33; N, 16.8.

A Synthesis of Cyclopropyl Acetates[1,2]

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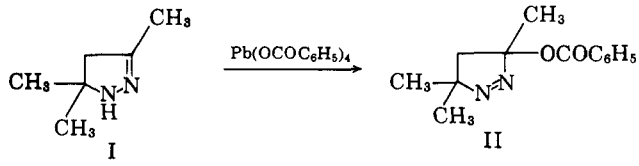
A variety of cyclopropyl acetates may be prepared by pyrolysis of 3-acetoxy-1-pyrazolines which are obtained by the action of lead tetraacetate on 2-pyrazolines. The scope and limitations of the method and the use of n.m.r. spectra for assignment of stereochemistry is discussed.

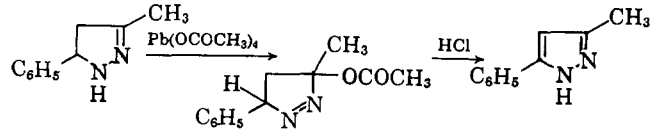
Recent interest in small ring chemistry and in particular that expressed in cyclopropanols[3] prompted an examination of the synthesis and decomposition of 3-acetoxy-1-pyrazolines. The cyclopropyl acetates expected from this decomposition can be cleaved to the desired alcohols.[3] It had been observed in connection with another investigation that 3,5,5-trimethyl-2-pyrazoline (I) could be converted to 3-benzoyloxy-3,5,5-trimethyl-1-pyrazoline (II) by the action of lead



I II

tetrabenzoate.[4] This reaction was an extension of Iffland's hydrazone oxidation reaction[5] to the pyrazoline series.

1-Pyrazolines.—This reaction, now employing lead tetraacetate, is a general one for pyrazolines even for those bearing a hydrogen atom at position 5. It might have been expected that these compounds would be oxidized to pyrazoles based upon the report that 5-ethylpyrazoline is converted to 5-ethylpyrazole by this reagent.[6] Under the mild conditions employed in the present work the pyrazolines were not aromatized nor were the 1-pyrazolines isomerized to 2-pyrazolines during the lead tetraacetate reaction. However, it was possible to isomerize and aromatize 3-acetoxy-3-methyl-5-phenyl-1-pyrazoline (III) to 3-methyl-5-phenylpyrazole by heating it in dilute ethanolic hydrochloric acid. This isomerization also occurred upon standing or upon warming below the decomposition

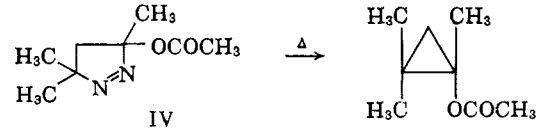


III

point. For best results, the thermal decomposition of the crude pyrazolines was conducted immediately after their preparation.

In some cases the intermediate 1-pyrazolines were isolated and characterized. However, those bearing α-phenyl substituents appeared to be particularly prone to decomposition and little effort was made to purify them. The 1-pyrazolines were characterized by a band at 1565 cm.$^{-1}$ in their infrared spectra which may be attributed to the *cis*-azo function and by low intensity absorption at 330 mμ in the ultraviolet. Other 1-pyrazolines are characterized by similar spectral properties.[7]

Cyclopropyl Acetates.—Preliminary efforts to decompose pyrazoline IV with ultraviolet light[7] indicated that this method was effective but slow. However, by simply heating the compound under reflux, nitrogen



IV

(1) This research was carried out under Army Ordnance Contract DA-01-021 ORD-11878.

(2) A preliminary report of this work has been published: J. P. Freeman, *J. Org. Chem.*, **28**, 885 (1963).

(3) C. H. DePuy, L. R. Mahoney, and K. L. Eilers, *ibid.*, **26**, 3616 (1961); C. H. DePuy, R. A. Klein, and G. M. Dappen, *ibid.*, **27**, 3742 (1962).

(4) J. P. Freeman, *Tetrahedron Letters*, **No. 21**, 749 (1961).

(5) D. C. Iffland, L. Salisbury, and W. R. Schafer, *J. Am. Chem. Soc.*, **83**, 747 (1961).

(6) R. Kuhn and K. Henkel, *Ann.*, **549**, 279 (1941). An azoacetate may have been involved in this aromatization, since an intermediate impure product was further treated with acid dichromate to obtain the pyrazole.

(7) K. L. Rinehart, Jr., and T. V. Van Auken, *J. Am. Chem. Soc.*, **84**, 3736 (1962).

TABLE I
PROPERTIES OF CYCLOPROPYL ACETATES

Compound	B.p., °C. (mm.)	$n^{20}D$	Yield, %[a]	Anal., % C Calcd.	C Found	H Calcd.	H Found
1,2,2-Trimethyl (V)	46 (20)	1.4141	62,[d] 36[c]	67.57	67.34	9.92	10.28
cis-2-Phenyl[b] (VII)	64 (0.8)	1.5160	10[d]	74.97	74.22	6.86	7.12
trans-2-Phenyl[b] (VIII)	64 (0.8)	1.5179		74.97	75.05	6.86	7.07
1-Phenyl-2,2-dimethyl (IX)	70–72 (0.5)	1.4990	42[d]	76.44	76.04	7.90	7.87
cis-2-Phenyl-1-methyl[b] (X)	70 (0.35)	1.5081	61[d]	75.76	76.06	7.42	7.57
trans-2-Phenyl-1-methyl[b] (XI)	70 (0.35)	1.5060		75.76	75.35	7.42	7.60
cis-1,2-Diphenyl (XII)[e]	53–53.5 (m.p.)		30[d]	80.92	80.66	6.39	6.34
1,2-Diethyl-2-methyl (XIII)[f]	42 (5)	1.4256	64[c]	70.55	70.37	10.66	10.76
1-Phenyl (XIV)	68–70 (0.4)	1.5232	20[d]	74.97	75.21	6.87	6.99
trans-2-Methyl-1-phenyl (XV)[b]	110 (1.2)	1.5071	60[d]	75.76	75.64	7.42	7.70
cis-2-Methyl-1-phenyl (XVI)[b]	110 (1.2)	1.5100		75.76	75.42	7.42	7.45
1-Cyclopropyl-2-phenyl (XVII)[f]	96–98 (0.8)	1.5180	62[d]	77.75	77.95	7.46	7.89

[a] Over-all yield based on starting 2-pyrazoline. [b] The boiling point and yields recorded are for the mixture of isomers which were separated by gas chromatography on a Carbowax M–Chromosorb column operating at 180°. The *cis* isomers were eluted first. *cis* and *trans* refer to the relation of phenyl and acetate groups except for XII. [c] Prepared by method A, Experimental section. [d] Prepared by method B, Experimental section. [e] The *trans*-1,2-diphenyl isomer was a high boiling oil which could not be entirely freed of *cis* isomer. Its yield is not included in this table but may be found in the Experimental section. [f] Mixture of *cis* and *trans* isomers.

was evolved rapidly and 1,2,2-trimethylcyclopropyl acetate was produced in 60% yield. The properties of the cyclopropyl acetates prepared in this manner are summarized in Table I. The reaction proceeds best when there is no hydrogen at positions 3 or 5 of the pyrazolines and fails altogether with mono- or dialkylated pyrazolines. For example, it has not yet been possible to convert either the 5-methyl- or 3,5-dimethyl-3-acetoxy-1-pyrazolines to their respective cyclopropyl acetates by either light or heat. Monoaryl pyrazolines yielded cyclopropanes but in lower yield. It is tempting to relate the decomposition of the pyrazolines to the stability of the presumed intermediate biradical. When the intermediate radical is primary or secondary, and thus formed more difficultly, isomerization becomes competitive and no nitrogen evolution occurs. While small amounts of the corresponding pyrazoles were obtained from these compounds, these do not appear to be the major products; this side reaction is under investigation. It is interesting that cyclopropane formation is favored over pyrazole formation with 3-acetoxy-1-pyrazolines in view of the predominance of the latter with 3-sulfonyl-[8a] and 3-nitro-1-pyrazolines.[8b]

Other methods of obtaining cyclopropyl esters include the addition of diazo compounds[9] or iodomethylzinc iodide[2] to enol esters, the reaction of Grignard reagents with epichlorohydrins in the presence of iron salts,[2,10] and the oxidation of methyl cyclopropyl ketones with peroxytrifluoroacetic acid.[2,11] Since pyrazolines are among the most accessible and versatile starting materials required for these various cyclopropane syntheses, the presently described method provides a simple route to a variety of cyclopropyl acetates.

Since stereochemistry of the decomposition of 1-pyrazolines is unknown, it is not possible to determine whether the pyrazoline–lead tetraacetate reaction is stereospecific. However, one or the other of the two reactions is highly stereoselective, since in those cases where isomers were possible a *trans* arrangement of the bulkier groups at C-1 and C-2 predominated. If it may be assumed that the decomposition of 1-pyrazolines is predominantly stereospecific,[7,12] then it appears that the acetoxylation reaction occurs predominantly by approach of the acetate group (whether by an ionic or radical mechanism) to the least hindered side of the pyrazoline ring thus becoming oriented *trans* to the bulkier group at position 5. Such selectivity seems quite reasonable. 3-Phenyl-5-methylpyrazoline yielded a nearly equimolar mixture of *cis*- and *trans*-2-methyl-1-phenylcyclopropyl acetates showing that there was little difference between orientation of the methyl group with the phenyl or acetate groups. In the case of 3-methyl-5-phenylpyrazoline, *trans*-2-phenyl-1-methylcyclopropyl acetate predominated by a ratio of at least 6:1.

N.m.r. Spectra.—At the beginning of this investigation n.m.r. spectra were run routinely in order to follow the course of the pyrolysis of pyrazoline to cyclopropane. This was done in the case of compounds V and XIII by observing the appearance of the typical high-field cyclopropane ring hydrogen resonance. It soon became apparent that phenyl substitution greatly affected this high-field resonance to the extent that its absence cannot be taken as evidence that the cyclopropane ring is not present. In the case of compound IX, for example, the ring protons are found near τ 8.9 compared with τ 9.5 in the aliphatic cyclopropane V. This effect of phenyl groups on the cyclopropane proton resonance has recently been commented upon.[13] It would be of interest to know whether this effect is due to paramagnetic shielding or to a change in hybridization within the cyclopropane ring.

However, n.m.r. analysis was quite helpful in an unanticipated way in the assignment of configuration to geometric isomers of this series. It has been shown by Curtin and co-workers[14] that the *cis–trans* isomers of 1,2-diphenylcyclopropane may be distinguished by the

(8) (a) W. E. Parham, H. G. Braxton, Jr., and D. R. Theissen, *J. Org. Chem.*, **27**, 2632 (1962); (b) W. E. Parham and J. L. Bleasdale, *J. Am. Chem. Soc.*, **73**, 4664 (1951).

(9) I. A. D'Yakonov., *J. Gen. Chem. USSR*, **20**, 2385 (1950).

(10) C. W. Stahl and D. L. Cottle, *J. Am. Chem. Soc.*, **65**, 1782 (1943).

(11) W. D. Emmons and G. B. Lucas, *ibid.*, **77**, 1187 (1955).

(12) C. G. Overberger and J. P. Anselme, *ibid.*, **84**, 869 (1962). Controversy on this point still rages, but it appears that thermal decompositions, although not so specific as photochemical decompositions, largely maintain the stereochemistry of the pyrazoline.

(13) J. D. Graham and M. T. Rogers, *ibid.*, **84**, 2249 (1962).

(14) D. Y. Curtin, H. Gruen, Y. G. Hendrickson, and H. E. Knipmeyer, *ibid.*, **83**, 4838 (1961); D. Y. Curtin, H. Gruen, and B. A. Shoulders, *Chem. Ind.* (London), 1205 (1958).

TABLE II

PROTON N.M.R. SPECTRA OF CYCLOPROPYL ACETATES

Compound	Group chemical shift, τ[a] 1-CH_3	2-CH_3	CH_3CO_2-
1,2,2-Trimethyl (V)	8.52	8.95, 8.88	8.08
1-Methyl (VI)[b]	8.53	...	8.12
cis-2-Phenyl (VII)	...	...	8.30
trans-2-Phenyl (VIII)	...	...	8.12
1-Phenyl-2,2-dimethyl (IX)	...	9.20, 8.70	8.10
cis-2-Phenyl-1-methyl (X)	8.35	...	8.35
trans-2-Phenyl-1-methyl (XI)	8.80	...	8.03
cis-1,2-Diphenyl (XII)	...	...	8.13
1,2-Diethyl-2-methyl (XIII)[c]	...	8.98, 8.95	8.12
1-Phenyl (XIV)	...	...	8.12
trans-2-Methyl-1-phenyl (XV)	...	9.18	8.13
cis-2-Methyl-1-phenyl (XVI)	...	8.74	8.02

[a] Spectra were measured on Varian Associates V-4300B 40-Mc. and A-60 spectrometers on dilute (5–10%) solutions in carbon tetrachloride, tetramethylsilane internal standard. We are indebted to Mrs. Carolyn Haney for measurement of the spectra. [b] We are indebted to Dr. C. H. DePuy for the spectrum of this material. [c] Mixture of *cis*–*trans* isomers.

different chemical shifts of the benzylic hydrogens; there is increased shielding of these protons in the *trans* isomer by the adjacent benzene ring. It appears that the benzene ring may shield other functional groups *cis* to it in cyclopropanes.[15] As model compounds we have used 1-methylcyclopropyl acetate,[2] 1,2,2-trimethylcyclopropyl acetate, *trans*-2-phenylcyclopropyl acetate,[2] and *cis*- and *trans*-1-phenyl-2-methylcyclopropane.[16] From the data summarized in Table II the following τ values may be assigned to the various "unperturbed" methyl groups: 1-methyl, τ 8.5; 2-methyl, 8.9; acetate methyl, 8.1. The effect of a *cis*-phenyl group on the 2-methyl resonance may be gaged from *cis*-1-phenyl-2-methylcyclopropane in which the methyl group appears at much higher field (τ 9.2)[16] than in the model compounds. In compound IX one of the methyl groups appears at τ 9.2 and is thus the one *cis* to the phenyl group.[18] One of the two isomers (XV) of 2-methyl-1-phenylcyclopropyl acetate also has a signal at τ 9.2, and it is assigned the structure with the phenyl and methyl groups *cis*.

In the case of the isomers of 2-phenyl-1-methylcyclopropyl acetate (X and XI), the methyl resonance of XI appears at τ 8.80, higher than expected upon the basis of models V and VI. On this basis, XI is assigned the structure in which the methyl group is *cis* to the adjacent phenyl group. In the minor product the 1-methyl group and the acetate methyl group have the same chemical shifts. Thus the 1-methyl group is in the normal region, but the acetate methyl group has shifted to higher field. That this shift is related to its *cis* orientation to the phenyl group is shown by the spectra of *cis*- and *trans*-2-phenylcyclopropyl acetates in which the acetate methyl group appears in the normal region in the *trans* isomer but at the higher field position in the *cis* isomer. This diamagnetic shielding of the acetate methyl group is a rather striking example of long range shielding.

Because of the complexity of the ring hydrogen signals no attempts have been made to correlate their chemical shifts and coupling constants with the configuration of the ring.

(15) While this manuscript was being prepared, a report appeared in which the stereochemistry of several cyclopropanes was assigned on the basis that the group *cis* to the phenyl group was shifted to higher fields while that *trans* to the phenyl group was shifted to lower fields: G. L. Closs, R. A. Moss, and J. J. Coyle, *J. Am. Chem. Soc.*, **84**, 4986 (1962). These results are in complete accord with the results reported here.

(16) An authentic sample of *trans*-1-phenyl-2-methylcyclopropane was prepared by the Simmons–Smith reaction[17] on *trans*-propenylbenzene. Surprisingly, this same isomer was obtained by sodium reduction of the reported *cis*-1-phenyl-2-methyl-3,3-dichlorocyclopropane.[18] It could be shown that this latter compound was actually the *trans* isomer and sodium reduction of its authentic *cis* isomer yielded *cis*-1-phenyl-2-methylcyclopropane. The methyl proton signal of the *cis* isomer was found at τ 9.20 and that of the *trans* isomer at τ 8.87. Details of these preparations may be found in the Experimental section. In line with this reassignment of the Graham and Rogers dichlorocyclopropane[18] as the *trans* isomer, it was found that the vicinal proton n.m.r. coupling constant of authentic *cis* isomer (J = 11.5 c.p.s.) was larger than that reported by Graham and Rogers for their product (J = 8.28 c.p.s.). Vicinal proton coupling constants of *cis* cyclopropanes are consistently larger than those of the *trans* isomers.[18] The rather large values for the coupling constants in these two dichlorocyclopropanes may reflect the dependence of coupling constants upon substituents. [For a recent discussion of this phenomenon, see K. L. Williamson, *J. Am. Chem. Soc.*, **85**, 516 (1963).]

(17) H. E. Simmons and R. D. Smith, *ibid.*, **81**, 4256 (1959).

(18) All the methyl groups *trans* to phenyl groups appear at lower field than those in the model compounds. This shift to lower field is apparently due to deshielding by the phenyl groups.[15]

Experimental

Reagents.—The lead tetraacetate was obtained from Arapahoe Chemical Company, Boulder, Colorado. Apparently some batches of this material contain substantial amounts of acetic anhydride. This material is detrimental since it reacts with the pyrazolines to form N-acetyl derivatives which reduce the yields of cyclopropanes and complicates their purification. This side reaction could be substantially reduced or completely eliminated by recrystallizing the lead tetraacetate from acetic acid immediately preceding its use.

The pyrazolines were prepared by standard literature methods as indicated. 3-Phenyl-5,5-dimethylpyrazoline was prepared from β,β-dimethylacrylophenone[19] and 90% hydrazine in ethanol solution. The pyrazoline was not purified, but rather the crude product was oxidized directly.

3,5,5-Trimethylpyrazoline,[20] 3,5-dimethylpyrazoline,[21] 3,5-diphenylpyrazoline,[22] 3-methyl-5-phenylpyrazoline,[22] 3-phenyl-5-methylpyrazoline,[21] 5-phenylpyrazoline,[22] and 3-cyclopropyl-5-phenylpyrazoline[23] were prepared from the corresponding α,β-unsaturated carbonyl compounds and hydrazine. 3-Phenylpyrazoline[22] was prepared from β-dimethylaminopropiophenone and hydrazine. 3,5-Diethyl-5-methylpyrazoline was prepared by the cyclization of methyl ethyl ketazine with formic acid.[24]

Synthesis of Azoacetates. Preparation of 3-Acetoxy-3,5,5-trimethyl-1-pyrazoline.—A solution of 11.2 g. (0.1 mole) of 3,5,5-trimethylpyrazoline in 25 ml. of methylene chloride was added over a 15-min. period at 10–15° to a solution of 50 g. (0.11 mole) of lead tetraacetate in 200 ml. of methylene chloride. The mixture was stirred at 20–25° for 30 min. Water (200 ml.) was added and the solution was filtered. The organic layer was separated and washed with water and 10% sodium bicarbonate solution until it was free of acid. The organic extracts were dried over magnesium sulfate, concentrated *in vacuo*, and distilled to yield a pale yellow oil, b.p. 72–76° (3 mm.), $n^{20}D$ 1.4422, yield 10.6 g. (62%).

Anal. Calcd. for $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.40; H, 8.38; N, 16.76.

Infrared spectrum: ν_{CO} 1750 cm.$^{-1}$, $\nu_{N=N}$ 1570 cm.$^{-1}$; ultraviolet spectrum: λ_{max} 330, ϵ_{max} 196 (ethanol).

3-Acetoxy-3,5-diethyl-5-methyl-1-pyrazoline.—The same procedure was followed using 13.4 g. (0.11 mole) of 3,5-diethyl-5-methylpyrazoline. Distillation yielded a yellow oil, b.p. 74° (1 mm.), $n^{20}D$ 1.4514, yield 11.5 g. (53%).

Anal. Calcd. for $C_{10}H_{18}N_2O_2$: C, 60.57; H, 9.15; N, 14.14. Found: C, 60.39; H, 9.06; N, 14.47.

(19) L. I. Smith and V. A. Engelhardt, *J. Am. Chem. Soc.*, **71**, 2671 (1949).

(20) S. Curtius and B. Wirsing, *J. prakt. Chem.*, [2]**50**, 548 (1894).

(21) K. von Auwers and P. Heimke, *Ann.*, **458**, 186 (1927).

(22) S. G. Beech, J. H. Turnbull, and W. Wilson, *J. Chem. Soc.*, 4686 (1952).

(23) L. I. Smith and E. R. Rogier, *J. Am. Chem. Soc.*, **73**, 3840 (1951).

(24) A. N. Kost and I. I. Grandberg, *J. Gen. Chem. USSR*, **26**, 1925 (1956).

Infrared spectrum: ν_{CO} 1750 cm.$^{-1}$, $\nu_{N=N}$ 1565 cm.$^{-1}$; ultraviolet spectrum: λ_{max} 330, ϵ_{max} 180 (ethanol).

3-Acetoxy-3,5-dimethyl-1-pyrazoline.—By the same procedure using 4.9 g. (0.05 mole) of 3,5-dimethylpyrazoline, a bright yellow oil, b.p. 72–76° (0.3 mm.), $n^{20}D$ 1.4545, was obtained.

Anal. Calcd. for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.75; N, 17.94. Found: C, 55.05; H, 8.17; N, 17.97.

Infrared spectrum: ν_{CO} 1750 cm.$^{-1}$; $\nu_{N=N}$ 1568 cm.$^{-1}$; ultraviolet spectrum: λ_{max} 330, ϵ_{max} 186 (ethanol).

Synthesis of Cyclopropyl Acetates. A. From Azoacetates. 1,2,2-Trimethylcyclopropyl Acetate.—3,5,5-Trimethyl-3-acetoxy-1-pyrazoline (5.0 g., 0.03 mole) was heated under reflux (*ca.* 200°) until nitrogen evolution ceased (1 hr.). The residue was distilled to yield 2.5 g. (63%) of 1,2,2 trimethylcyclopropyl acetate (Table I).

B. From 2-Pyrazolines. 2-Phenyl-1-methylcyclopropyl Acetate.—A solution of 8.0 g. (0.05 mole) of crude 3-methyl-5-phenylpyrazoline in 25 ml. of methylene chloride was added to 25 g. (0.056 mole) of lead tetraacetate in 200 ml. of methylene chloride at 10–15° with good stirring. After the addition the mixture was allowed to warm to room temperature and stirred there for an hour. The mixture was diluted with water, the organic layer separated, and the aqueous layer extracted with two 50-ml. portions of methylene chloride. The combined organic extracts were washed with water and 5% sodium bicarbonate solution until the aqueous layer was free of acid. The organic extracts were dried over magnesium sulfate and concentrated. The residue was heated under reflux until gas evolution ceased. The crude product (8.9 g.) was distilled through a Holzman column to yield 5.8 g. (61%) of 2-phenyl-1-methylcyclopropyl acetate, b.p. 70° (0.35 mm.).

Vapor chromatography of the material on a Carbowax 20 M on Chromosorb column at 180° using an Aerograph Model 90 gas chromatograph resolved it into two components. The smaller component eluted first proved to be 1-methyl-*cis*-2-phenylcyclopropyl acetate; the predominant product was the *trans* isomer; ratio of isomers, 1:6 (Table I).

1,2-Diphenylcyclopropyl Acetate.—The crude pyrazoline prepared from 20.8 g. (0.1 mole) of benzalacetophenone and 40 ml. of 90% hydrazine was diluted with 50 ml. of methylene chloride and added at 10–15° to 49 g. (0.11 mole) of lead tetraacetate in 300 ml. of methylene chloride. The work-up procedure was the same as described for 2-phenyl-1-methylcyclopropyl acetate. The residual oil (20 g.) was induced to partially crystallize by addition of hexane. By further crystallizations of the oil a total of 7.5 g. (30%) of *cis*-1,2-diphenylcyclopropyl acetate, m.p. 52–53° (hexane) was obtained. The residual oil was distilled at 125° (0.4 mm.) to yield 8.8 g. (35%) of a viscous oil whose n.m.r. spectrum indicated that it was mainly the *trans* isomer, but which still contained substantial amounts of the *cis* isomer.

***trans*-1-Phenyl-2-methylcyclopropane.**—To a solution of iodomethylzinc iodide[17] prepared from 13.4 g. (0.05 mole) of methylene iodide, 0.05 g. of iodine, and the zinc–copper couple (4 g. of zinc) in 50 ml. of anhydrous ether was added 11.8 g. (0.1 mole) of *trans*-propenylbenzene[25] in 25 ml. of anhydrous ether. After stirring under reflux overnight, the mixture was worked up and the organic product distilled through a spinning-band column to yield 3.0 g. (53%) of *trans*-1-phenyl-2-methylcyclopropane, b.p. 76° (19 mm.), $n^{20}D$ 1.5215. From a mixture of *cis*- and *trans*-propenylbenzene, Simmons and Smith[17] obtained a mixture of phenylmethylcyclopropanes, b.p. 78–79° (20 mm.), $n^{25}D$ 1.5204. Since reduction of the reported[13] 1-phenyl-2-methyl-3,3-dichlorocyclopropane yielded *trans*-1-phenyl-2-methylcyclopropane, it must have the *trans* configuration.

***cis*-1-Phenyl-2-methyl-3,3-dichlorocyclopropane.**—A mixture of 18.2 g. (0.1 mole) of sodium trichloroacetate, 65 g. (0.5 mole) of *cis*-propenylbenzene,[26] and 75 ml. of ethylene glycol dimethyl ether was heated under reflux overnight. The dichlorocyclopropane was isolated by distillation, b.p. 60–62° (0.5 mm.), $n^{20}D$ 1.5405, yield 12.1 g. (61%).

Anal. Calcd. for $C_{10}H_{10}Cl_2$: C, 59.73; H, 5.01. Found: C, 59.65; H, 5.22.

***cis*-1-Phenyl-2-methylcyclopropane.**—A solution of 10 g. (0.05 mole) of *cis*-1-phenyl-2-methyl-3,3-dichlorocyclopropane in 200 ml. of ether was reduced with 23 g. (1 g.-atom) of sodium and 150 ml. of methanol containing 5 ml. of water. Distillation of the ether extracts yielded 2.4 g. (36%) of *cis*-1-phenyl-2-methylcyclopropane, b.p. 78–80° (20 mm.), $n^{20}D$ 1.5201.

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(25) *trans*-Propenylbenzene of high purity may be obtained from Columbia Organic Chemicals Company. Their product was purified by gas chromatography on a Dow 710 silicone-on Chromosorb column at 125°. The properties of the purified material agreed in detail with those reported: R. Y. Mixer, R. F. Heck, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **75**, 4094 (1953).

(26) W. R. R. Park and G. F. Wright, *J. Org. Chem.*, **19**, 1435 (1954).

Factors Influencing the Separation of 4-Hydroxyproline Diastereomers by Ion-Exchange Chromatography

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On a preparative scale 4-hydroxy-DL-proline and allo-4-hydroxyproline were separated on ion-exchange resin. By working in alcoholic buffer systems, optimal conditions for accurate and rapid separation were elaborated. The method was applied to the preparation of pure diastereomers from mixtures obtained by two different synthetic pathways. The ratios of crystalline hydroxyproline to allohydroxyproline were 1:2 in the *intra*molecular cyclization of 2-amino-4-hydroxy-5-bromopentanoic acid, and 7:5 in the *inter*molecular reaction of 2,5-dichloro-γ-valerolactone with ammonia.

In the previous study[1] we reported on the preparation, separation, and quantitative determination of the diastereomers of hydroxyproline. The subject of this paper is the manipulation of the variables in the ion-exchange technique and an improved method for the rapid and quantitative separation of hydroxyproline diastereomers.

Reviewing the literature on the separation of the diastereomers of hydroxyamino acids, one notices that DL-threonine and DL-allothreonine[2] have been separated on Dowex 50 by elution with 1.5 *N* hydrochloric acid, the diastereomers of hydroxylysine by a buffer system of pH 5.0,[3] the diastereomers of β-hydroxy-DL-aspartic acid on Dowex 1 with dilute

(1) N. Izumiya and B. Witkop, *J. Am. Chem. Soc.*, **85**, 1835 (1963).

(2)(a) A. T. Shulgin, O. G. Lien, Jr., E. M. Gal, and D. M. Greenberg, *ibid.*, **74**, 2427 (1952); (b) throughout this paper the use of the name hydroxyproline refers to 4-hydroxy-DL-proline and its diastereomer.

(3) P. G. Hamilton and R. A. Anderson, *J. Biol. Chem.*, **213**, 249 (1955).