groups (2,4-dinitrophenyl and 2-nitro-4-carboxyphenyl) attached to the sulfur atom; while X (Cl or $-OCOCH_3$) is slightly negative, as expected from the electronegativities of these substituent groups. (b) Some degree of stabilization is obtained by attraction between $ArS^{\delta+}$ and $^{\delta-}X$, in view of the partial charges on these groups and the fact (as inferred from models) that the groups can approach one another very closely. (c) Because of the overlapping of the methyl groups in IV (compare models), conformations approaching III will be more likely than those approaching IV. (d) Then, assuming there will be a difference between the energies necessary to raise III to its excited state (as compared for the same process for the less-stabilized IV), it is predicted that the racemate (III) obtained by *trans* addition of ArSX to *cis*-2-butene will require slightly greater energies to be raised to the excited state than will the racemate related to IV. Since the additions of sulfenyl halides to olefins are known to be *trans*,[3,4] and from the knowledge that the adducts as I,I′ and II, II′ undergo acetolysis in a stereospecific manner (involving participation by neighboring sulfur)[3], it follows that the adducts and acetates from *cis*-2-butene are the *threo* forms, related to III, which absorb at shorter wave lengths. Thus, the chemical evidence for the structures of the products agrees with the suggested rationalization of the spectral characteristics of the diastereomeric racemates.

EXPERIMENTAL

The preparations of the compounds of Table I have been previously reported.[3,4] The spectra were measured in absolute methanol solutions, on a Cary recording spectrophotometer.[9]

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Noncatalytic Fischer Indole Synthesis

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Although Wolff in 1912[1] mentioned that distillation of acetophenone phenylhydrazone gave a low yield of 2-phenylindole, it has not been generally realized that no catalyst is necessary in the Fischer indole synthesis. No reference is made to the noncatalytic reaction in the extensive reviews of indole chemistry by Elderfield[2] and Sumpter and Miller.[3] We have found that in general good yields of substituted indoles can be obtained by heating the corresponding phenylhydrazones in a solvent. In many

TABLE I

THERMAL CYCLIZATION OF PHENYLHYDRAZONES

Starting Material	Product	Solvent[a]	Time, Hr.	Yield, %	Method of Isolation and Purification
Methyl ethyl ketone phenylhydrazone	2,3-Dimethylindole	EG	3	70	[b]
Methyl ethyl ketone phenylhydrazone	2,3-Dimethylindole	EG[c]	4	68	[b]
Methyl ethyl ketone phenylhydrazone	2,3-Dimethylindole	TET	17	48	[d]
Acetone phenylhydrazone	2-Methylindole	DEG	3.5	36	[e]
n-Butyraldehyde phenylhydrazone	3-Ethylindole	EG	24	44	[e]
Propionaldehyde *p*-tolylhydrazone	3,5-Dimethylindole	EG	4	..	[b]
Propionaldehyde *N*-methylphenylhydrazone	1,3-Dimethylindole	EG	6	70	[f]
Methyl ethyl ketone *N*-methylphenylhydrazone	1,2,3-Trimethylindole	EG	8	65	[f]
Methyl ethyl ketone *o*-chlorophenylhydrazone	7-Chloro-2,3-dimethylindole[g]	DEG	2	55	[e]
Methyl ethyl ketone 2,5-dichlorophenylhydrazone	4,7-Dichloro-2,3-dimethylindole[h]	EG	6	66	[e]
Butyrophenone phenylhydrazone	3-Ethyl-2-phenylindole	EG	16	50	[b]
Acetophenone phenylhydrazone	2-Phenylindole	EG	48	54	[i]

[a] EG = ethylene glycol; DEG = diethylene glycol; TET = tetralin. [b] Precipitation with water followed by recrystallization from petroleum ether (Darco). [c] Contained 2% sodium hydroxide. [d] Precipitation with petroleum ether followed by recrystallization from petroleum ether (Darco). [e] Steam distillation followed by recrystallization from petroleum ether (Darco). [f] Reduced pressure distillation. [g] Previously unreported compound, m.p. 69–70.5°; nitrogen content: found 7.77%; required 7.80%. [h] Previously unreported compound, m.p. 90–91°; nitrogen content; found 6.66%; required 6.54%. [i] Precipitation with water followed by recrystallization from heptane (Darco).

(9) This is the same instrument, Model 11PMS, as used by Hawthorne and Cram.[5] The kind permission of the faculty of the University of California, Los Angeles, to use this facility, with the assistance of William Netusil, is gratefully acknowledged.

(1) Wolff, *Ann.*, **394**, 107 (1912).

(2) Elderfield, *Heterocyclic Compounds*, John Wiley and Sons, Inc. New York, 1952, Vol. 3, pp. 7–42.

(3) Sumpter and Miller, *The Chemistry of Heterocyclic Compounds*, Interscience Publishers, Inc. New York, 1954, Vol. 8, pp. 3–23.

cases the products are easier to work up because of the absence of an acid catalyst.

The method is widely applicable. 2-Phenylindole, 2,3-dimethylindole, 2-methyl-3-ethylindole, 3,5-dimethylindole, 1,3-dimethylindole, 1,2,3-trimethylindole, 7-chloro-2,3-dimethylindole, 4,7-dichloro-2,3-dimethylindole and 3-ethyl-2-phenylindole have all been made in fair to good yields. The optimum reaction conditions have not been determined for most of these compounds. With some, reaction is complete after two to three hours in boiling ethylene glycol; others require refluxing 24 hr. or more. In some cases the reaction rate is accelerated by the higher temperature obtained in refluxing diethylene glycol. The polarity of the solvent is not critical; tetralin works about as well as the glycols.

No theory has been formulated about the mechanism of the reaction. Robinson and Robinson's widely accepted mechanism[4,5] for the Fischer synthesis involving an acid-catalyzed benzidine type rearrangement does not appear to be adequate, since the cyclization takes place even in the presence of small amounts of alkali.

Reaction conditions and yields are given in Table I. All reactions were carried out by refluxing a solution of the phenylhydrazone in the specified solvent. Products were isolated by steam distillation, reduced pressure distillation, or precipitation, and purified by recrystallization or distillation.

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(4) Robinson and Robinson, *J. Chem. Soc.*, **113**, 639 (1918).

(5) Robinson and Robinson, *J. Chem. Soc.*, **125**, 827 (1924).

Preparation and Reactions of Some Aralkyl Cyanoacetic Esters

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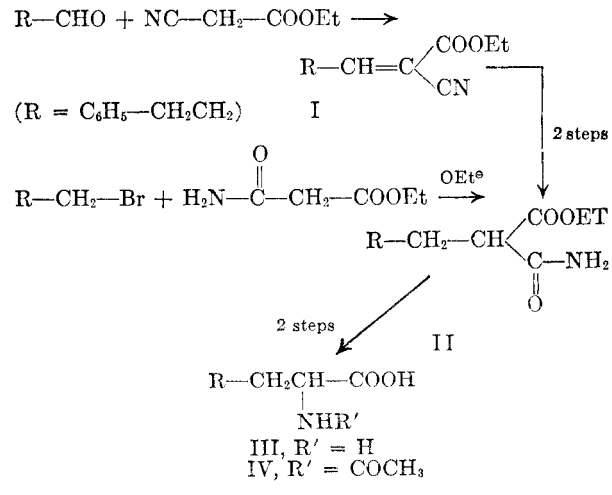
The occurrence in nature of cyclic structures possessing the acetamido function prompted an investigation of cyclization reactions of some aralkyl acids containing amine or acetamido functions.[1] The problem was twofold, that of synthesis of appropriate α-acetamido aralkyl acids and that of cyclizing such substances to the corresponding ketones without alteration of the substituent. Moreover, it was required that only those methods be considered which could be easily adapted to the use of variously substituted starting materials.

(1) One such cyclization using polyphosphoric acid has been reported. W. J. Horton and G. Thompson, *J. Am. Chem. Soc.*, 76, 1909 (1954).

α-Amino-δ-phenylvaleric acid (III) was prepared from hydrocinnamaldehyde by the sequence shown. Condensation of the aldehyde with ethyl cyanoacetate, by the general Knoevenagel[2] reaction using piperidine–acetic acid as a catalyst[3] gave I which was then converted by hydrogenation to ethyl α-cyano-δ-phenylvalerate. Hydrolysis of this cyano ester to α-carbethoxy-δ-phenylvaleramide (II) was effected by treatment with polyphosphoric acid.[4,5] The final conversion to the amine (III) was made by the Hofmann method.[6] Alternatively, II was prepared by the base-catalyzed condensation of 1-bromo-3-phenylpropane with ethyl malonamate.

Several attempts to cyclize the amino acid (III) or its acetyl derivative (IV) with polyphosphoric acid gave only recovered starting material. The carbethoxy amide (II) was equally resistant to cyclization by this reagent.

Another series of compounds of interest appeared to be obtainable by application of the above described sequence of reactions to *p*-hydroxybenzaldehyde. Thus, ethyl α-cyano-β-(*p*-hydroxyphenyl)-propionate (V, R = H) and the acetate (R = $COCH_3$) were prepared and the former converted to the amide (VI, R = H) *via* the imino ester hydrochloride. The use of polyphosphoric acid in this instance (R = H or $COCH_3$) was unsuccessful. Repeated attempts to prepare the corresponding amino acid from VI by the Hofmann method were unsuccessful. It has been reported that the corresponding methyl ether compound failed to undergo this reaction.[6] The failure of the Hofmann reaction as a general method appears to be a definite limitation in this approach to the α-amino acids.



(2) J. Scheiber and F. Meisel, *Ber.*, **48**, 257 (1915).

(3) A. C. Cope, U. S. Patent 2,655,526; *Chem. Abstr.*, **48**, P11484 (1954).

(4) H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **76**, 3039 (1954).

(5) C. R. Hauser and C. J. Eby, *J. Am. Chem. Soc.*, **79**, 725 (1957).

(6) See for example R. Gaudry, *Can. J. Research*, 23B, 234 (1954).