reduction in alcohol gave a less pure product and took almost twice as long to complete hydrogen uptake. The much longer reaction time required for the preparation of XII was rather surprising. An examination of a molecular model shows that the starting pyridine makes good contact with the catalyst. However, as hydrogenation proceeds, it appears that there are positions of the molecule where contact with the catalyst is difficult. Under higher pressure, as in reduction with ruthenium,[2] the molecule is apparently forced into the proper configuration to allow uptake of hydrogen to take place rapidly. Under the mild conditions used in this study, there is not enough energy to do the same thing.

Some hydrogenolysis occurred in the preparation of 4-(β-benzylamino) piperidine. From a study of the hydrogen uptake, it seems that debenzylation takes place after the pyridine ring is reduced. In one experiment where the hydrogen uptake was slightly in excess of theoretical, less than 10% of 4-(β-aminoethyl)-piperidine, the product of hydrogenolysis was obtained. In a second run where the uptake of hydrogen was excessive, about 30% of this product was obtained.

The longer reaction time required to obtain XIV and XV is an indication of the inhibiting effect of the basic side chain on the rate of hydrogenation.

From these results, it would appear that the described method should prove useful as a means of carrying out the reduction of most pyridines to a successful conclusion under general laboratory conditions.

EXPERIMENTAL

Selection of catalyst. A solution of 12.3 g. (0.1 mole) of 2-(2-hydroxyethyl)pyridine in 50 cc. of absolute ethyl alcohol was hydrogenated at room temperature under 2.7 atm. pressure in the presence of 2.46 g. of 5% rhodium on carbon.[9] In another run 2.46 g. of 5% rhodium on alumina[9] was used. The two reactions were carried out concurrently in Parr shakers of equal speed for 17 hr. The hydrogen uptake for the experiment with catalyst A was about 70% of theory, for B about 50%. These results were confirmed by vapor phase chromatography which indicated 73% and 54% of I, respectively.

The following is an example of the hydrogenation conditions used, with exceptions noted in the Table.

2-(2-Hydroxyethyl)piperidine. A solution of 12.3 g. (0.1 mole) of 2-(2-hydroxyethyl)pyridine in 50 cc. of absolute ethyl alcohol was hydrogenated under 2.7 atm. pressure at 55–60° with presence of 4.92 g. of 5% rhodium on carbon. The reaction was interrupted at the end of 4 hr. when uptake of hydrogen appeared to be complete. After removal of catalyst the solution was concentrated and the residue identified (see Table I).

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Reaction of α-Diazoacetophenone with *trans*-1,2-Dibenzoylethylene[1a]

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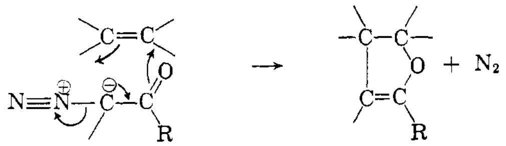
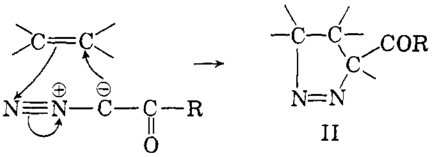
In general there are two possible paths for the uncatalyzed reaction of α-diazo ketones with suitably activated double bonds[2]:



I (1)



II (2)

We have recently shown[3] that the reaction of α-diazoacetophenone with ketenes to give products of type I occurs by route (1) rather than by reaction of the ketene with a species $C_6H_5CO\ddot{C}H$.[4,5] No

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[9] Available from Engelhard Industries, 113 Astor Street, Newark, N. J.

(1)(a) Aliphatic Diazo Compounds VI; for the preceding paper in this series see P. Yates and B. L. Shapiro, *J. Am. Chem. Soc.*, **81**, 212 (1959). (b) National Science Foundation Pre-doctoral Fellow, 1956–59. (c) Present address: Department of Chemistry, University of Toronto.

(2) *Cf.* A. S. Kende, Ph.D. Thesis, Harvard, 1956.

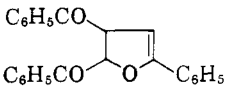
(3) P. Yates and T. J. Clark, *Tetrahedron Letters,* **No. 13,** 435 (1961).

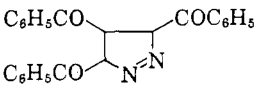
(4) The *copper-catalyzed* reaction of diazoketones with olefinic compounds, producing cyclopropane derivatives [J. Novák, J. Ratusky, V. Sneberg, and F. Šorm, *Collection Czechoslov. Chem. Communs.*, **22**, 1836 (1957); R. J. Mohrbacher and N. H. Cromwell, *J. Am. Chem. Soc.*, **79**, 401 (1957)]; undoubtedly proceeds *via* an intermediate formed by interaction of the diazo compound with the catalyst [*cf.* P. Yates, *J. Am. Chem. Soc.*, **74**, 5376 (1952); W. von E. Doering and L. H. Knox, *J. Am. Chem. Soc.*, **78**, 4947 (1956); P. S. Skell and R. M. Etter, *Chem. & Ind. (London)*, 624 (1958); K. R. Kopecky, G. S. Hammond, and P. A. Leermakers, *J. Am. Chem. Soc.*, **83**, 2397 (1961)]. The uncatalyzed reaction of α-diazo-4-phenylacetophenone with styrene to give cyclopropane derivatives (R. J. Mohrbacher and N. H. Cromwell, *loc. cit.*) may well proceed *via* pyrazoline formation.

(5) The related thermal reaction of diazoöxides with ketenes proceeds by attack at the carbonyl rather than the ethylenic double bond of the ketene: P. Yates and E. W. Robb, *J. Am. Chem. Soc.*, **79**, 5760 (1957). However, no evidence is available in this instance which distinguishes between attack on the ketene by diazoöxide or by a species $RCO\ddot{C}H$.

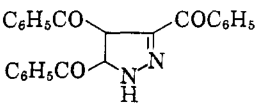
evidence was obtained which indicated any reaction of type (2) in this instance. Very few reactions of this type, which are common in the case of diazo hydrocarbons[6] and α-diazo esters,[6,7] have been reported. Guha and Muthanna prepared a pyrazoline by the reaction of diazoacetone with ethyl α-isopropylacrylate,[8] and Diels and König found that 3-diazo-2-butanone undergoes a vigorous reaction with diethyl acetylenedicarboxylate to give a pyrazole and reacts with cyclopentadiene dimer to give a product containing nitrogen.[9]

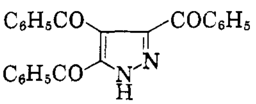
We considered it of interest to determine whether in the case of α-diazoacetophenone the two types of reaction path are competitive when the activated double bond is of a kind different from the unusually reactive ketene double bond. To this end the reaction of α-diazoacetophenone with *trans*-1,2-dibenzoylethylene was studied; reaction by pathway (1) would give the dihydrofuran III, while the reaction course (2) would give the pyrazoline IV.


III


IV

A solution of α-diazoacetophenone and a small excess of *trans*-1,2-dibenzoylethylene in carbon tetrachloride was boiled under reflux. Within four hours 95% of the diazoketone had reacted. From the reaction mixture there was isolated by fractional crystallization a small amount of *trans*-1,2,3-tribenzoylcyclopropane (V)[10] and, as the major product, a compound, $C_{24}H_{18}N_2O_3$, m.p. 157–159°. This compound has bands in its infrared spectrum at 2.95, 5.91–5.95, 6.10, and 11.60 μ and is clearly 3,4,5-tribenzoyl-2-pyrazoline (VI), formed from IV by a prototropic shift.[11] This structural assignment


VI


VII

was confirmed by the formation of V, albeit in low yield, when VI was heated in decanol at 190°, and by the facile oxidation of VI with *N*-bromosuccinimide to a compound, $C_{24}H_{16}N_2O_3$, m.p. 167–168°, with infrared bands at 2.92, 6.02, and 11.00 μ, which is considered to be the corresponding pyrazole, VII.[12] None of the dihydrofuran III was isolated from the reaction mixture and infrared spectral examination of the mother liquors gave no indication of its presence. Thus the reaction of α-diazoacetophenone with *trans*-1,2-dibenzoylethylene proceeds exclusively by pathway (2), unlike the reaction with diphenylketene which proceeds by pathway (1). It is probable that the latter course is favored in the case of ketenes because of appreciable stabilization of the transition state by resonance in the developing lactone function.

EXPERIMENTAL

Reaction of α-diazoacetophenone with trans-1,2-dibenzoylethylene. Formation of 3,4,5-tribenzoyl-2-pyrazoline (VI). A solution of 2.85 g. (12.1 mmoles) of *trans*-1,2-dibenzoylethylene and 1.65 g. (11.3 mmoles) of α-diazoacetophenone in 35 ml. of carbon tetrachloride was boiled under reflux for 2 hr. The solution was cooled in ice and the crystals collected by filtration. Fractional crystallization from ethanol (under nitrogen) afforded 0.1 g. of *trans*-1,2,3-tribenzoylcyclopropane and 2.40 g. (6.28 mmoles) of 3,4,5-tribenzoyl-2-pyrazoline (VI), m.p. 157.4–158.6°. Infrared spectrum (methylene dichloride): 2.95, 5.91–5.95, 6.10, 11.60 μ; ultraviolet spectrum $\lambda_{max}^{C_2H_5OH}$ 251 mμ (log ϵ 4.49).

Anal. Calcd. for $C_{24}H_{18}N_2O_3$: C, 75.38; H, 4.74; N, 7.33. Found: C, 75.25; H, 4.67; N, 7.51.

Infrared spectral analysis of the mother liquors showed the presence of diazoacetophenone, *trans*-1,2-dibenzoylethylene, and 3,4,5-tribenzoyl-2-pyrazoline.

Formation of trans-1,2,3-tribenzoylcyclopropane (V) *from* VI. A solution of 24 mg. of VI in 5 ml. of decanol was heated at 190° for 1.5 hr. The solution was cooled to room temperature and the crystals which separated were collected by filtration. Recrystallization from ethanol afforded *trans*-1,2,3-tribenzoylcyclopropane (15%), m.p. 215–217° (lit.[10] m.p. 217–218°); infrared spectrum (chloroform): 5.92 (sh), 5.97 μ.

Oxidation of VI. *Formation of 3,4,5-tribenzoylpyrazole* (VII). To a solution of 0.430 g. (1.12 mmoles) of VI in 35 ml. of carbon tetrachloride was added 0.240 g. (1.34 mmoles) of *N*-bromosuccinimide. The solution was boiled under reflux for 1 hr. and at the end of this period was deep red. The solution was shaken with aqueous potassium iodide, aqueous sodium thiosulfate, and water. The solvent was removed under reduced pressure and the red, gummy residue was dissolved in benzene and chromatographed on 30 g. of silica gel. In fractions eluted with 1:100 ether-benzene there was found 40 mg. of VI and from fractions eluted with 1:25 ether-benzene there was isolated 0.267 g. (0.70 mmole) of 3,4,5-tribenzoylpyrazole (VII). Recrystallization from benzene-cyclohexane afforded pure VII, m.p. 167.0–167.8°; infrared spectrum (methylene dichloride): 2.92, 6.02, 11.00 μ; ultraviolet spectrum $\lambda_{max}^{C_2H_5OH}$ 259 mμ (log ϵ 4.57).

Anal. Calcd. for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.37. Found: C, 75.71; H, 4.11; N, 7.26.

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(6) R. Huisgen, *Angewandte Chemie*, **67**, 439 (1955); T. L. Jacobs, *Heterocyclic Compounds*, R. C. Elderfield, ed., Vol. 5, John Wiley, New York, 1957, p. 45.

(7) However, a product of type I is formed in the reaction of ethyl diazoacetate with diphenylketene: A. S. Kende, *Chem. & Ind.* (*London*), 1053 (1956).

(8) P. C. Guha and M. S. Muthanna, *Ber.*, **71**, 2665 (1938).

(9) O. Diels and H. König, *Ber.*, **71**, 1179 (1938).

(10) C. Grundmann, *Ann.*, **536**, 29 (1938); J. F. Neumer, Ph.D. Thesis, Chicago, 1957.

(11) K. v. Auwers and E. Cauer, *Ann.*, **470**, 284 (1929); K. v. Auwers and O. Ungemach, *Ber.*, **66**, 1198 (1933).

(12) A strong band at *ca.* 11 μ is a characteristic feature of the infrared spectra of nitrogen heterocycles with a benzoyl substituent: D. G. Farnum, Ph.D. thesis, Harvard, 1959.