Experimental Section

General (Caution).—The polynitro compounds described in this paper are explosives and should be handled with due care. In particular, reactions, should be run on a small scale (1 or 2 g) behind adequate shielding with careful attention to temperature control. Handling of hot reaction vessels should be strictly avoided. Personnel should be equipped with full face masks, heavy rubber gloves, and fire-retardant laboratory coats.

Pmr spectra were obtained in deuteriochloroform solution with tetramethylsilane as the internal standard using a Varian HA-100 spectrometer. Infrared spectra were obtained in 1,2-dichloroethane solution using a Beckman IR-4 spectrometer. Melting points are uncorrected.

General Directions for Preparing *N*,*N*-Bis(2-fluoro-2,2-dinitroethyl)amides.—The reactants in the proportions given in Table I were combined in a stoppered flask and stirred magnetically until the amine **1** was dissolved. The flask was then allowed to stand at ambient temperature for the indicated time, while samples were withdrawn periodically to monitor the course of the reaction by tlc. For reactions run at higher temperatures the flask was equipped with a reflux condenser topped with a drying tube filled with calcium sulfate.

After the indicated time had elapsed, the crude mixture was taken up in methylene chloride and washed consecutively with water, 0.4 *N* NaOH, and water. After drying with magnesium sulfate and filtering, volatiles were removed *in vacuo*. If crystallization did not occur spontaneously, the crude product was purified by column chromatography on silica gel (G. Frederick Smith Co., 50–200 mesh). Benzene was used as the eluent. Recrystallization was from methylene chloride or methylene chloride–carbon tetrachloride mixtures.

Registry No.—**2**, 35666-43-4; **3**, 35666-44-5; **4**, 35666-45-6; **5**, 35666-46-7; **6**, 35666-47-8; **7**, 35666-48-9; **8**, 35666-49-0.

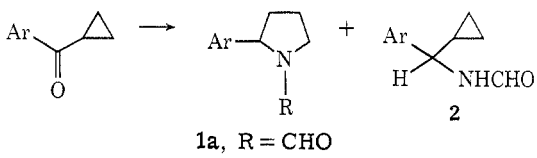
The Synthesis of *cis*- and *trans*-1-Methyl-2,5-diphenylpyrrolidines by the Leuckart Reaction of 1-Benzoyl-2-phenylcyclopropane[1]

ELI BREUER* AND DAVID MELUMAD

Department of Pharmaceutical Chemistry, The Hebrew University School of Pharmacy, Jerusalem, Israel

Received March 8, 1972

Previously we reported that the Leuckart reaction of cyclopropyl aryl ketones with formamide gives predominantly the rearranged products 1-formyl-2-arylpyrrolidines (**1a**), in addition to small amounts of the



1a, R = CHO
b, R = CH_3 **2**

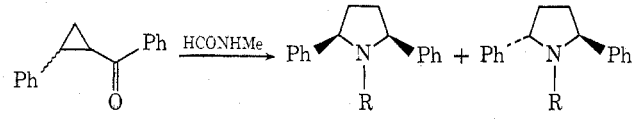
normal products (**2**).[2] Subsequently we observed that the reaction of *N*-methylformamide with cyclopropyl phenyl ketone, which proceeds considerably more slowly than that of the formamide, occurs with exclusive rearrangement, giving in high yield 1-methyl-2-phenylpyrrolidine (**1b**, Ar = Ph).[3] Using this reaction we achieved a one-step synthesis of nicotine (**1b**, Ar = 3-pyridyl) from cyclopropyl 3-pyridyl ketone.[3]

In this paper we wish to describe results obtained from the Leuckart reaction of 1-benzoyl-2-phenylcyclopropane with *N*-methylformamide. This work was undertaken to study the direction of the cyclopropane ring opening and the stereochemistry of the reaction.

Results

A mixture of *cis*- and *trans*-1-benzoyl-2-phenylcyclopropane (**3**) was obtained from the reaction of benzalacetophenone and dimethylsulfoxonium methylide.[4] This mixture of stereoisomeric ketones was heated to 180° with *N*-methylformamide in the presence of catalytic amounts of magnesium chloride for 25 hr. After this period of time gas chromatographic analysis indicated the absence of ketone and the presence of two products in the ratio of 2:1, in a total yield of 50%.

The products were separated by chromatography on silica gel. The major component was identified as *cis*-1-methyl-2,5-diphenylpyrrolidine (**4b**), while the minor component was found to be the trans isomer (**5b**).



3 **4a**, R = H **5a**, R = H
b, R = Me **b**, R = Me

These structure assignments were confirmed by independent syntheses. Thus we have prepared *cis*- and *trans*-2,5-diphenylpyrrolidine[5] (**4a** and **5a**, respectively), which were converted to the respective *N*-methyl derivatives (**4b** and **5b**) by formic acid–formaldehyde. The *cis*- and *trans*-1-methyl-2,5-diphenylpyrrolidines so obtained were found identical in every respect with the products obtained in our reaction. Nmr data are given in Table I.

In order to study the possible influence of the stereochemistry of starting material, we have prepared pure *cis*-1-benzoyl-2-phenylcyclopropane.[6] Reaction of this ketone with *N*-methylformamide yielded a mixture of **4b** and **5b** in the same yield and ratio as those obtained in the previous reaction.

The absence of 2,4-diphenylpyrrolidines was confirmed by comparison of the product mixture with samples prepared by a known reaction.[7]

The formation of products **4b** and **5b** can be rationalized by assuming that attack of *N*-methylformamide upon the carbonyl group of **3** produces a hydroxyformamide type intermediate[8] which dissociates to an

(1) A preliminary account of this study was presented at the 39th Meeting of the Israel Chemical Society, Jerusalem, Sept 29–Oct 1, 1969. E. Breuer and D. Melumad, *Israel J. Chem.*, **7**, 31 (1969).
(2) E. Breuer and Y. Stein, *ibid.*, **6**, 901 (1968).
(3) E. Breuer and D. Melumad, *Tetrahedron Lett.*, 3595 (1969).
(4) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).
(5) C. G. Overberger, M. Valentine, and J. P. Anselme, *ibid.*, **91**, 687 (1969).
(6) H. M. Walborsky and L. Plonsker, *ibid.*, **83**, 2138 (1961).
(7) M. C. Kloetzel, *ibid.*, **69**, 2271 (1947).
(8) M. L. Moore, *Org. React.*, **5**, 301 (1949).

TABLE I

NMR DATA OF *cis*- AND *trans*-2,5-DIPHENYLPYRROLIDINES AND THEIR *N*-METHYL DERIVATIVES[a]

Compd	Aromatic (10 H)	Benzylic (2 H)	*N*-Methyl (3 H)
4a	7.27	4.25	
5a	7.23	4.43	
4b	7.31	3.34	1.98
5b	7.22	4.10	1.88

[a] Given in δ values; $CDCl_3$ solution with TMS as internal standard.

immonium–carbonium ion that is capable of rearranging to a pyrroline derivative.[9,10] The latter is reduced *in situ* by formic acid to products **4b** and **5b**.[11] The predominant formation of the cis product **4b** is in agreement with what is known concerning the stereochemistry of the Leuckart reaction.[12]

Experimental Section[13]

1-Benzoyl-2-phenylcyclopropane (**3**) (a mixture of isomers) was prepared by the action of dimethylsulfoxonium methylide on benzalacetophenone,[4] mp 45–50° (lit.[4] mp 45.5–50.0°). The spectral properties of the material were in agreement with those published.[4]

***cis*-1-Benzoyl-2-phenylcyclopropane** was prepared by the action of phenyllithium on *cis*-2-phenylcyclopropanecarboxylic acid, mp 68–70° (lit.[6] mp 69–70°).

Reaction of *N*-Methylformamide with 1-Benzoyl-2-phenylcyclopropane.—A mixture of 5.5 g (0.025 mol) of ketone, 9 g of *N*-methylformamide, and 0.32 g (0.0025 mol) of $MgCl_2 \cdot 2H_2O$ was heated in an oil bath at 180° for 24 hr under N_2. The reaction mixture was dissolved in dilute hydrochloric acid and extracted several times with ether. The aqueous acidic solution was made alkaline by the addition of sodium hydroxide, and extracted five times with ether. After drying, the ether was evaporated to give a residue (2.5 g). This mixture was separated by chromatography on silica gel. Elution with benzene gave pure *cis*-1-methyl-2,5-diphenylpyrrolidine (**4b**), mp 60° (1.6 g). The compound was further purified by collecting a sample by preparative gas chromatography.

Anal. Calcd for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90. Found: C, 86.47; H, 8.04; N, 5.75.

The picrate had mp 152° from ethanol.

Anal. Calcd for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75; N, 12.01. Found: C, 59.45; H, 4.94; N, 12.29.

Further elution with benzene–chloroform (1:1) provided pure *trans*-1-methyl-2,5-diphenylpyrrolidine (**5b**) as a colorless oil (0.8 g). Purification by preparative gas chromatography gave an analytical sample.

Anal. Calcd for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90. Found: C, 86.05; H, 7.86; N, 6.04.

The picrate had mp 175° from ethanol.

Anal. Calcd for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75; N, 12.01. Found: C, 59.35; H, 5.04; N, 12.08.

2,4-Diphenylpyrrolidine was prepared according to Kloetzel by hydrogenation of 4-nitro-1,3-diphenyl-1-butanone,[7] bp 165° (1.5 mm) [lit.[7] bp 182.5° (3.8 mm)]. The product gave a benzamide, mp 122° (lit.[7] mp 122–124°).

Methylation of 2,4-diphenylpyrrolidine was carried out according to Icke, *et al.*,[14] using 1.56 g of 2,4-diphenylpyrrolidine, 1.75 ml of formic acid, and 1.60 ml of a 30% solution of formaldehyde. After work-up 1.0 g of product was isolated by distillation, bp 120° (0.5 mm).

Anal. Calcd for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90. Found: C, 86.25; H, 8.23; N, 5.88.

The nmr spectrum of the product showed the aromatic protons at δ 7.5–7.1 (m, 10 H), the N–Me protons as two singlets in the ratio of approximately 1:3 at 2.25 and 2.18, respectively, and the rest of the protons as multiplets at 3.7–1.6.

Registry No.—*cis*-**3**, 1145-91-1; *trans*-**3**, 1145-92-2; **4a**, 22147-83-7; **4b**, 35657-63-7; **4b** picrate, 35657-64-8; **5a**, 22147-84-8; **5b**, 35657-66-0; **5b** picrate, 35657-67-1; 1-methyl-2,4-diphenylpyrrolidine, 35657-68-2.

(9) J. B. Cloke, *J. Amer. Chem. Soc.*, **51**, 1174 (1929).

(10) Rearrangement of the cyclopropyl ketimine to a pyrroline by a concerted mechanism does not seem likely, as no 2,4-diphenylpyrrolidines were found in the product mixture.

(11) For similar reductions of enamines see N. J. Leonard and R. R. Sauers, *J. Amer. Chem. Soc.*, **79**, 6210 (1957).

(12) In all known examples of this reaction the product resulting from the approach of the reducing agent from the least hindered side predominates: (a) D. G. Hey, G. D. Meakins, and T. L. Whateley, *J. Chem. Soc. C*, 1509 (1967); (b) M. Davis, E. W. Parnell, and D. Warburton, *ibid.*, 1688 (1966); (c) D. S. Noyce and F. W. Bachelor, *J. Amer. Chem. Soc.*, **74**, 4577 (1952); (d) P. F. Coe, B. C. Uff, and J. W. Lewis, *J. Chem. Soc. C*, 2265 (1968); (e) R. R. Sauers, *J. Amer. Chem. Soc.*, **80**, 4721 (1958).

(13) All boiling points and melting points are uncorrected. Nmr spectra were measured by a Jeol C-60H instrument in $CDCl_3$; all chemical shifts are given in parts per million downfield from TMS. All gas chromatographic work was carried out on an F & M Model 720 dual column programmed temperature gas chromatograph on a 6 ft × 0.25 in., 10% diethylene glycol succinate on Chromosorb W column. Microanalyses were carried out by the Hebrew University Microanalytical Laboratory.

(14) R. N. Icke, B. B. Wisegarver, and G. A. Alles, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 723.

Structure and Proton Magnetic Resonance Study of 3-(*N'*-Aziridinyl)succinimides[1a]

P. JOSEPH-NATHAN,* V. MENDOZA, AND E. GARCÍA G.[1b]

Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, P. O. Box 14-740, México 14, D.F., México.

Received May 30, 1972

In an earlier communication,[2] it was shown that reaction of N-substituted maleimides with ethereal solutions of diazomethane gave instantaneously the corresponding pyrazolines in high yields. Extending further the studies on the reactivity of maleimides, we describe now the results obtained with aziridine.[3]

Mild treatment of N-substituted maleimides with aziridine gave solid adducts whose elemental composition corresponded to the combination of equimolecular amounts of aziridine and of the maleimide.

The adducts showed an infrared absorption band at 1720 cm^{-1} corresponding to the imide carbonyl groups. Their 100-MHz pmr spectra showed, in addition to the signals of the N substituent, the presence of an ABX system (δ_A 3.01, δ_B 2.90, and δ_X 2.59 ppm; J_{AB} = 18, J_{AX} = 7.5, and J_{BX} = 4.5 Hz) attributable to a $-CH_2-CH-$ moiety on a five membered ring. The CH signal is found at higher fields than the AB signals of the methylene group. In the high field region there is a strongly coupled four-proton system, which even at 220 MHz remained complex. It showed signals at 2.036 (1 H), ~1.873 (2 H), and 1.359 (1 H) ppm. In view of these results, and considering that N-substituted

(1) (a) Presented at the VII Congreso Mexicano de Química Pura y Aplicada, Morelia, Mich., México, April 1972. (b) This work is part of the M.S. thesis of E. G. G. who receives a CoNaCyT (México) scholarship (1970–1972).

(2) V. Mendoza, P. Joseph-Nathan, and C. Perez, *Rev. Soc. Quim. Mex.*, **15**, 103 (1971).

(3) O. C. Dermer and G. E. Man, "Ethylenimine and Other Aziridines," Academic Press, New York, N. Y., 1969, Chapter 3.