recrystallization (30 ml. of water and 5 ml. of ethanol) gave 0.7 g. (47%), m.p. 248–249°. A negative permanganate test indicated that the product was not a salt of 4-vinylpyridine and 5-phenylbarbituric acid.

Anal. Calcd. for $C_{17}H_{15}N_3O_3$: C, 66.0; H, 4.9; N, 13.6. Found: C, 66.5; H, 6.3; N, 13.7.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ILLINOIS, COLLEGE OF PHARMACY]

Pyrazolidines. I. 1,2-Diarylpyrazolidines[1]

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1,2-Diarylpyrazolidines have been prepared by the oxidative cyclization of the related *N,N'*-diaryl-1,3-propanediamines using manganese dioxide. The analogous reaction with two representative *N,N'*-dialkyl-1,3-propanediamines afforded only unchanged diamine.

Although general methods have been developed for the synthesis of pyrazoles, pyrazolines, and pyrazolones,[2] methods for the preparation of the pyrazolidine ring system have not been investigated to any significant extent. Upon occasion, the synthesis of a substituted pyrazolidine has been described, but the scope of the reaction employed was not examined in any detail. In these syntheses, the approach invariably involved hydrazine, or a derivative thereof, and a 1,3-dihalopropane. In this way pyrazolidine,[3,4] 1,5-diazabicyclo[3,3,0]-octane,[3] 1-phenyl-4-allylpyrazolidine,[5] 1,2-diphenylpyrazolidine,[6,7] and 1-phenylpyrazolidine[6,8] have been prepared.

A novel approach to the formation of the pyrazolidine ring system involves closure of a 1,3-propanediamine. Thus Lüttringhaus[9] was able to transform 1,3-propanediamine into pyrazolidine by treating *N*-chloro-1,3-propanediamine with sodium hydroxide and Wittig[10] prepared 1,2-diphenylpyrazolidine from *N,N'*-diphenyl-1,3-propanediamine either by oxidation with manganese dioxide or by treatment with methyllithium followed by iodine.

The 1,2-diarylpyrazolidines described in this paper were prepared by manganese dioxide oxidation of the corresponding *N,N'*-diaryl-1,3-propanediamine. In turn, these diamines were obtained by treating 1,3-dibromopropane with an excess of a primary amine.[11] The latter reaction requires no further comment; the general procedure is given in the experimental section and some specific data are recorded in Table I.

On the other hand, the manganese dioxide oxidation of these diamines provided several noteworthy observations. In common with the experience of other workers, it was found that the oxidation was strongly influenced by the method employed to prepare the manganese dioxide.[12] Material obtained by combining stoichiometric quantities of manganese sulfate and potassium permanganate was *inactive* for ring closure, whereas manganese dioxide[13] like that used by Wittig proved to be satisfactory. Moreover, yields could be increased markedly by using the more active catalyst described by Henbest.[14]

All the *N,N'*-diaryl-1,3-propanediamines were transformed into the corresponding 1,2-diarylpyrazolidines with two exceptions. Firstly, *N,N'*-di-*p*-methoxyphenyl-1,3-propanediamine afforded 4,4'-azoanisole. This type of reaction has been

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[1] This paper represents part of a thesis submitted by Bruce D. Martin to the Graduate College of the University of Illinois, 1959, in partial fulfillment of the requirements for the degree of Master of Science. This work was supported in part by a grant from the Research Board of the Graduate College of the University of Illinois, Grant No. 55-92-32.

(2) T. L. Jacobs, *Heterocyclic Compounds*, Vol. 5, R. C. Elderfield, ed., J. Wiley and Sons, Inc., New York, 1957, p. 45. Although this chapter is entitled "Pyrazoles and Related Compounds," it is noteworthy that the section on pyrazolidines is confined to five lines.

(3) E. L. Buhle, A. M. Moore, and F. Y. Wiselogle, *J. Am. Chem. Soc.*, **65**, 29 (1943).

(4) H. Stetter and H. Spangenberger, *Chem. Ber.*, **91**, 1982 (1958).

(5) M. S. Kharasch and G. Büchi, *J. Org. Chem.*, **14**, 84 (1949).

(6) G. Wittig, *Angew. Chem.*, **53**, 241 (1940).

(7) J. W. Reesor and G. F. Wright, *J. Org. Chem.*, **22**, 325 (1957).

(8) A. Michaelis and O. Lampe, *Ann.*, **274**, 316 (1893).

(9) A. Lüttringhaus, J. Jander, and R. Schneider, *Naturwissenschaften*, **44**, 442 (1957).

(10) G. Wittig, W. Joos, and P. Rathfelder, *Ann.*, **610**, 180 (1957).

(11) (a) A. Hanssen, *Ber.*, **20**, 781 (1887); (b) M. Scholtz, *Ber.*, **22**, 2251 (1899); (c) W. L. Veer, *Rec. trav. chim.*, **57**, 989 (1938); (d) F. B. Zienty, *J. Am. Chem. Soc.*, **68**, 1388 (1946); (e) S. L. Shapiro, *J. Am. Chem. Soc.*, **80**, 3734 (1958); (f) W. R. Boon, *J. Chem. Soc.*, 307 (1947).

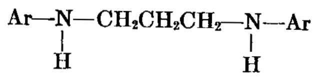
(12) R. M. Evans, *Quart. Rev.*, **13**, 61 (1959) discusses this point in some detail.

(13) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1104 (1952).

(14) H. B. Henbest, E. R. H. Jones, and T. C. Owen, *J. Chem. Soc.*, 4909 (1957).

TABLE I

N,N'-DIARYL-1,3-PROPANEDIAMINES

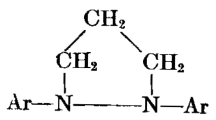

$Ar{-}\underset{H}{N}{-}CH_2CH_2CH_2{-}\underset{H}{N}{-}Ar$

Ar	Amine, $ArNH_2$ Moles (G.)	1,3-Dibromopropane, Moles (G.)	Methanol, Ml.	Yield, %	M.P.	Recryst. Solv.	Empirical Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
								Calcd.	Found	Calcd.	Found	Calcd.	Found
C_6H_5—	5.14 (478)	1.03 (208)	425	68	[a]		$C_{15}H_{18}N_2$	79.60	79.26	8.02	7.68	12.38	12.61
p-CH_3—C_6H_4—	2.57 (275)	0.515 (104)	240	50	69–70[b]	Hexane	$C_{17}H_{22}N_2$	80.26	79.97	8.72	9.09	11.02	10.90
m-CH_3—C_6H_4—	2.57 (275)	0.515 (104)	240	57	[c]		$C_{17}H_{22}N_2$	80.26	80.63	8.72	8.58	11.02	11.10
o-CH_3—C_6H_4—[d]	2.57 (275)	0.515 (104)	240	68.5	50–51	Ethanol	$C_{17}H_{22}N_2$	80.26	80.55	8.72	8.45	11.02	10.90
p-CH_3O—C_6H_4—	1.38 (170)	0.27 (52)	250	54	96–96.5	Methanol	$C_{17}H_{22}N_2O_2$	71.30	71.39	7.74	7.59	9.79	9.69
o-CH_3O—C_6H_4—	2.57 (316)	0.515 (104)	225	68	45–46	Methanol	$C_{17}H_{22}N_2O_2$	71.30	70.99	7.74	7.71	9.79	10.20
p-C_2H_5O—C_6H_4—	2.57 (352)	0.515 (104)	250	48	79–80	Methanol	$C_{19}H_{26}N_2O_2$	72.57	72.61	8.34	8.60	8.91	8.77

[a] B.p. 161–163° at 0.14 mm.; n_D^{20} 1.6193. [b] Lit.[11c] m.p. 69–70°. [c] B.p. 166–168° at 0.4 mm.; n_D^{20} 1.6013; dihydrochloride, m.p. 215–216°; *Anal.* Calcd. for $C_{17}H_{24}Cl_2N_2$: C, 62.38; H, 7.39; N, 8.56. Found: C, 62.16; H, 7.25; N, 8.62. [d] See ref. 11b.

TABLE II

1,2-DIARYLPYRAZOLIDINES



Ar	Diamine, Moles (G.)	Carbon Tetrachloride, Ml.	Manganese Dioxide, G.	Yield, %	M.P.	Recryst. Solv.	Empirical Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
								Calcd.	Found	Calcd.	Found	Calcd.	Found
C_6H_5—	0.022 (5)	250	50	45	98.5–99[a]	Ethanol	$C_{15}H_{16}N_2$	80.32	80.59	7.18	6.84	12.50	12.30
p-CH_3—C_6H_4—	0.039 (10)	500	70	20[b]	74–75	Ethanol	$C_{17}H_{20}N_2$	80.91	81.18	7.99	7.88	11.10	10.60
m-CH_3—C_6H_4—	0.039 (10)	450	100	13.5[c]	172–173	Acetone	$C_{17}H_{20}N_2$	80.91	80.39	7.99	7.68	11.10	10.41
o-CH_3O—C_6H_4—	0.018 (5)	250	50	5	125–126	Methanol	$C_{17}H_{20}N_2O_2$	71.80	71.63	7.09	6.94	9.86	10.20
				26	160–161	Methanol	$C_{17}H_{20}N_2O_2$	71.80	71.82	7.09	6.87	9.86	10.07
p-C_2H_5O—C_6H_4—	0.016 (5)	400	35	10	128–129	30–60° Pet. ether	$C_{19}H_{24}N_2O_2$	73.04	72.39	7.74	7.53	8.97	9.25

[a] Lit.[10] m.p. 96–98°. [b] An 80% recovery of starting material was obtained. [c] A 66% recovery of starting material was obtained.

reported by Henbest[15]; manganese dioxide oxidation of *N*-methylaniline, *N*-ethylaniline, or *N,N*-diethylaniline provided small yields of azobenzene. It is noteworthy that *N,N'*-di-*p*-ethoxyphenyl-1,3-propanediamine afforded the expected pyrazolidine.

Secondly, oxidation of *N,N'*-di-*o*-tolyl-1,3-propanediamine afforded no 1,2-di-*o*-tolylpyrazolidine, and starting material was recovered. This was in contrast to the *meta* and *para* isomers which underwent ring closure and yielded the corresponding pyrazolidine. Thus, it is probable that the failure experienced with the *ortho* isomer arises from steric requirements involved in ring closure and not from a resonance or an inductive effect.

Although *N,N'*-diaryl-1,3-propanediamines could be converted into the related pyrazolidines, the *N,N'*-dialkyl-1,3-propanediamines resisted ring closure under the conditions of the oxidation and were recovered. If the initial step in the cyclization involves removal of the hydrogen atom on a nitrogen atom as a hydride ion, then it is not unlikely that the arylamino compounds would react with greater facility since they can provide resonance stabilization for the cation that is produced.

One further observation requires comment: oxidation of *N,N'*-di-*o*-methoxyphenyl-1,3-propanediamine yielded two solids each giving analytical data consistent with that expected for 1,2-di-*o*-methoxyphenylpyrazolidine. It is possible that these are isomeric compounds arising from restricted rotation about the bonds between the aryl groups and the nitrogen atoms. This area is being investigated further.

EXPERIMENTAL[16]

N,N'-Diaryl-1,3-propanediamines. A solution of 5 moles of the primary amine in methanol was heated to 70–80° and, with mechanical stirring, 1 mole of 1,3-dibromopropane was added at the rate of 1 drop per second. The reaction mixture was kept at that temperature for 10 to 12 days to complete the reaction. The black mixture was made alkaline (*p*H 11) with 30% aqueous sodium hydroxide and steam distilled to remove the methanol and recover excess volatile primary amine. The oily organic phase in the distilling flask was separated; the aqueous layer was extracted with four 100-ml. portions of benzene and the extracts combined with the oil. This solution was dried with anhydrous sodium sulfate, filtered, and the filtrate concentrated by flash evaporation. The dark viscous residue was fractionally distilled *in vacuo*. When the distillate solidified, it was recrystallized from methanol or ethanol. Freshly distilled material is colorless but becomes amber rapidly at room temperature; this occurs more slowly under refrigeration. Data relevant to these preparations are recorded in Table I.

In the preparation of *N,N'*-di-*p*-tolyl-1,3-propanediamine the oily residue obtained upon steam distillation solidified into a red pasty mass which was isolated by filtration and purified by sublimation and recrystallization from hexane.

As *p*-anisidine does not steam distill, it was removed from the crude reaction mixture by extraction with hot water. The remaining oil was fractionated and the product, *N,N'*-di-*p*-methoxyphenyl-1,3-propanediamine, distilled at 212° at 0.1 mm.

p-Phenetidine does not steam distill so that the crude reaction mixture was subjected to a fractional distillation. The *N,N'*-di-*p*-ethoxyphenyl-1,3-propanediamine boiled at 210–215° at 0.09 mm.

N,N'-Di-t-butyl-1,3-propanediamine. To a solution of 73.14 g. (1.0 mole) of *t*-butylamine and 40.38 g. (0.2 mole) of 1,3-dibromopropane was added 10.81 g. of water. The temperature rose steadily to 63° within 30 min. The reaction mixture was stirred at 60° for 13 hr. and allowed to stand at room temperature for 2 days. The semisolid mass was treated with a cold solution of 150 g. of potassium hydroxide in 175 ml of water and extracted with 400 ml. of ether followed by two 100-ml. portions of ether. The combined ethereal extracts were dried with potassium hydroxide, filtered, and concentrated by distillation. The residue was distilled through a short column (b.p. 93–95° at 19 mm.), and 29.86 g. (80%) of a white solid was obtained m.p. 40–41°. The substance form a hydrate, m.p. 72–73°.

A *dihydrochloride* m.p. 269° dec., was prepared and recrystallized from ether–absolute alcohol.

Anal. Calcd. for $C_{11}H_{28}Cl_2N_2$: C, 50.96; H, 10.89; N, 10.80. Found: C, 50.70; H, 10.70; N, 10.20.

N,N'-Di-n-butyl-1,3-propanediamine. This compound was prepared as described in the literature[11d] and distilled at 150–153° at 20 mm. The hydrate melted at 44–45° (lit.[11d] m.p. 44–45°).

A *dihydrochloride* was prepared and recrystallized from ether: methanol and melted at 323° dec.

Anal. Calcd. for $C_{11}H_{28}Cl_2N_2$: C, 50.96; H, 10.89; N, 10.80. Found: C, 51.52; H, 10.66; N, 10.80.

1,2-Diarylpyrazolidines. The diamine was dissolved in carbon tetrachloride, cooled to −20 to −10° in Dry Ice-ethanol bath and the active manganese dioxide[13] was added in one portion. After stirring the mixture for 2 to 3 hr. at −20 to −10°, the manganese dioxide was removed by filtration and washed with three 30-ml. portions of carbon tetrachloride. The combined organic layers were concentrated *in vacuo*, and the red oil was taken up in petroleum ether (b.p. 60–90°) and passed through a 1.5 cm. × 40 cm. column of F-20 alumina (Alcoa). Unchanged diamine was present in the initial fractions. The product, isolated from the intermediate fractions, was purified by recrystallization. The data pertinent to these preparations are recorded in Table II.

The first eluate obtained in the preparation of 1,2-di-*o*-methoxyphenylpyrazolidine afforded a colorless solid melting at 125–126° after recrystallization from methanol. Intermediate fractions yielded a yellow solid melting at 160–161° after recrystallization from methanol.

Attempts to synthesize 1,2-di-*o*-tolylpyrazolidine afforded only a 15% recovery of the starting diamine, m.p. and mixed m.p. 50–51°.

Attempts were made to prepare 1,2-di-*n*-butylpyrazolidine and 1,2-di-*t*-butylpyrazolidine by this method. In all attempts, the starting diamine was recovered and characterized as the dihydrochloride. No evidence of other products could be found.

When the oxidation was carried out with *N,N'*-di-*p*-methoxyphenyl-1,3-propanediamine, a deep yellow solid was eluted from the alumina (12% yield). Recrystallization from methanol gave 4,4'-azoanisole as yellow needles, m.p. 163–164°, (lit.[17] m.p. 164.6–165°).

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[15] H. B. Henbest and A. Thomas, *J. Chem. Soc.*, 3032 (1957).

[16] All melting points and boiling points are uncorrected.

[17] D. Vorlander, *Ber.*, 40, 1422 (1897).