Phenazine Syntheses. VIII.[1] Di-N-Oxides

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In the course of preparing phenazine derivatives for testing against Sarcoma 37, a number of di-N-oxides were synthesized. The compounds were prepared either (1) by the action on the requisite phenazine of a 10% solution of 30% H_2O_2 in glacial acetic acid at 50–55° for 16–20 hours, or (2) by the action at room temperature for 5–10 days of an equilibrium solution of acetylperoxide. The first is the method of Clemo and McIlwain,[2] and the second that of Pachter and Kloetzel.[3] No significant difference in results was shown between the two methods.

Isolation of the oxides was effected by pouring the solutions into about twice their volume of water. In some instances, especially those of room-temperature reactions, it was necessary to initiate precipitation of the product by the addition of a small amount of sodium carbonate.

Recrystallizations were from absolute ethanol, except for 2-chloro-8-ethoxyphenazine 5,10-dioxide, which was recrystallized from glacial acetic acid. The use of this solvent for general recrystallization, however, was abandoned when it was found that the homologous 2-chloro-8-methoxyphenazine 5,10-dioxide, m.p. 187–188° (d),[4] was converted to a monoxide, m.p. 217–220° (d), by recrystallization from boiling acetic acid, as shown by the analysis (see Table II). This resembles the experience of Yoshioka,[5] who obtained 2-methoxyphenazine from its mono-N-oxide when he refluxed the latter with glacial acetic acid. The same phenomenon was exhibited by 2-bromo-8-ethoxyphenazine 5,10-dioxide, m.p. 191–193° (d), which on recrystallization from acetic acid was likewise converted to a monoxide, m.p. 194–222° (d), as shown by the analysis given in Table II.

It is noticeable that the melting points of all the dioxides, save for the one with a free 2-hydroxyl group, are quite closely grouped, falling within the limits of 187–201°. This is likewise close to the m.p. of the unsubstituted phenazine 5,10-dioxide, which is 204° (d).[2] Too much importance should not be attached to the exact m.p. figures, for, as in the instance of the quaternary phenazines,[8] the temperatures are really those of decomposition, and can be caused to undergo considerable variation by changing the rate of heating.

Results are summarized in the following tables:

TABLE I

PROPERTIES OF PHENAZINE 5,10-DIOXIDES

5,10-Dioxide from:	M.p.,[4] °C.	Form	Yield, %	Empirical Formula	Analyses[6] C Calc'd	C Found	H Calc'd	H Found
2-Bromo-8-ethoxyphenazine[7]	191–193(d)	(*a*)	62	$C_{14}H_{11}BrN_2O_3$	50.2	50.2	3.31	3.50
2-Bromo-7-methoxyphenazine[7]	194–196(d)	(*a*)	65	$C_{13}H_9BrN_2O_3$	48.6	49.0	2.82	3.06
2-Bromo-8-methoxyphenazine[7]	189–191(d)	(*a*)	64	$C_{13}H_9BrN_2O_3$	48.6	48.7	2.82	3.01
2-Chloro-7-ethoxyphenazine[9]	190–191(d)	(*a*)	60	$C_{14}H_{11}ClN_2O_3$	57.8	57.8	3.82	4.12
2-Chloro-8-ethoxyphenazine[9]	193–194(d)	(*a*)	68	$C_{14}H_{11}ClN_2O_3$	57.8	57.8	3.82	4.12
2-Chloro-7-methoxyphenazine[9]	195–197(d)	(*a*)	60	$C_{13}H_9ClN_2O_3$	56.6	56.7	3.26	3.63
2-Chloro-8-methoxyphenazine[9]	187–188(d)	(*a*)	76	$C_{13}H_9ClN_2O_3$	56.6	56.5	3.26	3.48
8-Bromo-2-phenazinol[7,10]	Black by 300°, but not melted	(*b*)	45	$C_{12}H_7BrN_2O_3$	47.0	47.0	2.30	2.72
2-Phenazinecarbonitrile[11]	199–201(d)	(*c*)	64	$C_{13}H_7N_3O_2$	65.8	65.7	2.97	3.14

(*a*) Red-orange microcrystals, or small matted needles. (*b*) Brownish-red leaflets. (*c*) Small orange-red flakes, with a golden luster.

TABLE II

PROPERTIES OF PHENAZINE MONOXIDES

Mono-N-oxide from:	M.p., °C.	Empirical Formula	Analyses C Calc'd	C Found	H Calc'd	H Found	Cl Calc'd	Cl Found	N Calc'd	N Found
2-Chloro-8-methoxyphenazine 5,10-dioxide	217–220(d)[a]	$C_{13}H_9ClN_2O_2$	59.9	59.6	3.48	3.71	13.6	13.4	10.7	10.7
2-Bromo-8-ethoxyphenazine 5,10-dioxide	194–222(d)[a]	$C_{14}H_{11}BrN_2O_2$	52.7	52.4	3.47	3.63				

[a] Both of these compounds form very small, matted orange needles.

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(1) Paper VII: *J. Org. Chem.*, **21**, 824 (1956).

(2) Clemo and McIlwain, *J. Chem. Soc.*, 479 (1938).

(3) Pachter and Kloetzel, *J. Am. Chem. Soc.*, **73**, 4958 (1951).

(4) All melting-points are corrected.

(5) Yoshioka, *Jour. Pharm. Soc. Japan*, **72**, 1128 (1952).

(6) Microanalyses by the Microanalytical Laboratory of the National Institutes of Health, under the direction of Dr. W. C. Alford.

(7) Vivian, Hartwell, and Waterman, *J. Org. Chem.*, **19**, 1136 (1954).

(8) Vivian, *J. Org. Chem.*, 21, 822 (1956).

(9) Vivian, Greenberg, and Hartwell, *J. Org. Chem.*, **16**, 1 (1951).

(10) Purified by solution in KOH, filtration, and reprecipitation. Additional analysis: N, Calc'd: 9.12. Found: 9.03.

(11) Vivian, Hartwell, and Waterman, *J. Org. Chem.*, **20**, 797 (1955).

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The Addition of Alkanols to 1,1,2-Trichloro-3,3,3-trifluoropropene—Some Corrective Data

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We[1] had previously reported the addition of alkanols to $CF_3CCl{=}CCl_2$ in the presence of a base. The principal product was identified as an unsaturated fluorochloroether. However, an examination of the infrared spectrogram taken of these vinyl ethers revealed the presence of an impurity having a characteristic carbonyl absorption peak. This work was repeated in order to obtain pure samples of these vinyl fluorochloroethers and to isolate and identify this carbonyl-containing compound and any other by-products.

Methyl, ethyl, *n*-propyl, and *n*-butyl alcohols were added to $CF_3CCl{=}CCl_2$ in the presence of a base and ethers of the structure of $CF_3CCl{=}CClOR$ were isolated, R being the methyl, ethyl, *n*-propyl, or *n*-butyl group.

Infrared spectrograms of these compounds were quite similar and showed them to be practically free of carbonyl-containing impurities.

As a further proof, the dibromide $CF_3CClBrCClBrOCH_3$ was prepared by the addition of bromine to $CF_3CCl{=}CClOCH_3$. This compound was a solid and easily purified by sublimation at near room temperatures under reduced pressure. The carbon, hydrogen, chlorine, and bromine analyses compared closely with the theoretical values calculated for the above structure.

The dibromides of the higher members of this series of ethers were liquids. No attempts were made to purify and identify them.

As a further proof, these vinyl ethers were hydrolyzed according to the method of Tarrant and Young[2,3] to the corresponding saturated esters by treatment with 90 per cent sulfuric acid. This method is similar to the acid hydrolysis[4] of $CHCl{=}CClOC_2H_5$ to $CH_2ClCO_2C_2H_5$.

The methyl, ethyl, *n*-propyl, and *n*-butyl esters of $CF_3CHClCO_2H$, are new compounds and were identified by analyses and by the conversion of the methyl and ethyl members of the series to the amide, $CF_3CHClCONH_2$ by the usual method.

The carbonyl-containing compounds which were present as impurities in the previous chlorofluorovinyl alkyl ethers[1] were isolated by careful fractionation on a modified Todd precision column with a platinum spiral. These compounds had exactly the same physical and chemical properties as the series of esters prepared by the hydrolysis of the ethers, $CF_3CCl{=}CClOR$ to the corresponding esters CF_3CHCO_2R where R is the methyl, ethyl, *n*-propyl, and *n*-butyl group. One other by-product proved to be $CF_3CHClC(OCH_3)_3$.

TABLE I

PHYSICAL PROPERTIES OF SUBSTITUTED TRIFLUOROPROPENE DERIVATIVES

Compound	B.p., °C.	Mm.	d_4^{20}	n_D^{20}	M.R. Exptl.	M.R. Calc'd	AF_f	Magnetic Susceptibility[a] Calc'd	Magnetic Susceptibility[a] Obsd.
$CF_3CHClCO_2CH_3$	104.0	628	1.4170	1.3588	27.42	27.19	1.18	− 95.2	− 83.4
$CF_3CHClCO_2C_2H_5$	119.0	620	1.3215	1.3634	32.06	31.81	1.18	−107.1	− 98.2
$CF_3CHClCO_2C_3H_7$	135.0	629	1.2678	1.3733	36.74	36.43	1.20	−118.9	−108.9
$CF_3CHClCO_2C_4H_9$	156.0	627	1.2275	1.3803	41.26	41.03	1.18	−130.8	−118.0
$CF_3CHCl(OCH_3)_3$	150.0	626	1.3311	1.3842	39.09	39.70	0.92	—	—
$CF_3CCl{=}CClOCH_3$	115.0	626	1.4981	1.4070	32.06	31.57	1.26	−100.4	− 93.5
$CF_3CCl{=}CClOC_2H_5$	130.0	612	1.3945	1.4058	36.98	36.19	1.36	−112.3	−106.7
$CF_3CCl{=}CClOC_3H_7$	74.5	43	1.3330	1.4123	41.64	40.81	1.38	−124.1	−121.6
$CF_3CCl{=}CClOC_4H_9$	81.0	29	1.2581	1.4180	47.24	45.70	1.70	−136.0	−138.6

[a] Determined by the Quincke method.

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(1) Park, Halpern, and Lacher, *J. Am. Chem. Soc.*, **74**, 4104–4105 (1952).

(2) Young and Tarrant, *J. Am. Chem. Soc.*, **72**, 1860 (1950).

(3) Young and Tarrant, *J. Am. Chem. Soc.*, **71**, 2432 (1949).

(4) Imbert, German Patent 210,502; *Chem. Zent.*, **II**, 78 (1909).