Acknowledgment. This work was supported by the Department of Energy Office of Basic Energy Sciences under contract no. DE-AC02-81ER10989. The Varian XL-200 spectrometer used in this work was purchased with funds from NSF Grant No. CHE-8004246. This support is gratefully acknowledged.

Registry No. Calcium, 7440-70-2; methylamine, 74-89-5; ethylenediamine, 107-15-3; 2-nonyne, 19447-29-1; 3-nonyne, 20184-89-8; 4-nonyne, 20184-91-2; 4-octyne, 1942-45-6; 1-heptyne, 628-71-7; *trans*-2-nonene, 6434-78-2; *trans*-3-nonene, 20063-92-7; *trans*-4-nonene, 10405-85-3; *cis*-4-nonene, 10405-84-2; *trans*-2-octene, 13389-42-9; *trans*-3-octene, 14919-01-8; *trans*-4-octene, 14850-23-8; *trans*-2-heptene, 14686-13-6; *n*-heptane, 142-82-5; 1-heptene, 592-76-7.

Halogen-Activated Smiles Rearrangement. 2

Diane M. Schmidt and Guido E. Bonvicino*

Department of Chemistry, Long Island University/C. W. Post Center, Greenvale, New York 11548

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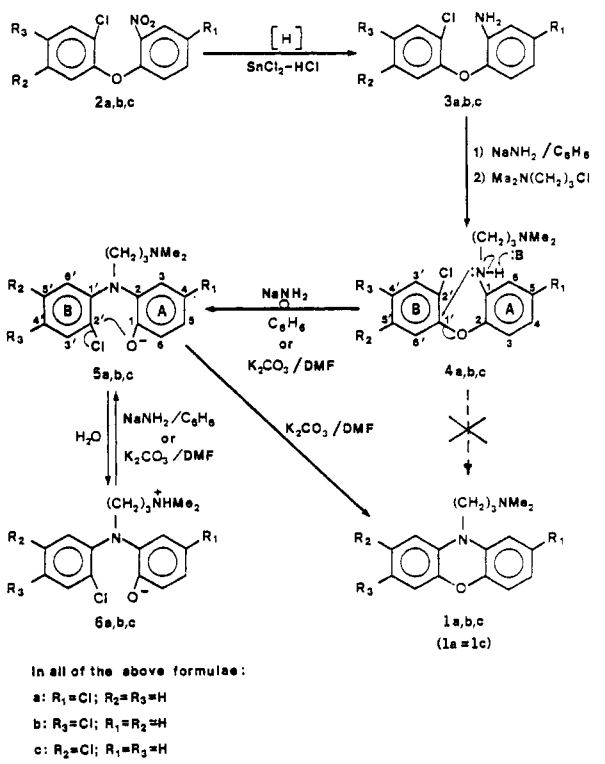
Ring-substituted-10-[3-(dimethylamino)propyl]phenoxazines were previously of interest for pharmacological screening. 2-Chloro-10-[3-(dimethylamino)propyl]phenoxazine (**1a**, $R_1 = R_2 = H$; $R_3 = Cl$) was of special interest since it is isosteric with chloropromazine. The chemistry that developed in the syntheses of **1a** resulted in two papers[1] describing three successful approaches. Two of the routes involved cyclization of an (*o*-halophenoxy)aniline derivative (see **4** → **1**, Scheme I) "directly", and cyclization of a Smiles-rearranged[2] diphenylamine derivative (**6** → **5** → **1**).

The previous experiments did not adequately distinguish the two routes described above. Although we prepared phenoxazine **1a**[1c] "directly" from the *o*-amino-*o'*-bromodiphenyl ether **4a** with K_2CO_3 in DMF, we could not be sure that the diphenylamine **5a**, resulting from Smiles rearrangement of **4a**, was not an intermediate; i.e., **4a** ⟶ [**5a**] → **1a**.[3] All of the previous intermediates (e.g., **4a**)[1c] had substituents on ring A and none on ring B (except for the *o*-bromo group lost on ring closure). Rearrangement occurs on ring B; therefore, evidence for it could only be obtained with the appropriate substituents on ring B.

Rearrangements of **4** to **5** were the first examples[1b] of a Smiles rearrangement in which only a halogen-atom activated ring B (Scheme I). The diphenylamine **5a** with K_2CO_3 in *N,N*-dimethylformamide (DMF) afforded the phenoxazine **1a**, which was also obtained "directly" from

Scheme I



the diaryl ether **4a**.[1c] The latter reaction could proceed either via the diphenylamine intermediate **5a**[1c] or by direct cyclization of **4a**.[1c] The latter course (with K_2CO_3 in DMF) was favored since carbonate was considered to be a weak base incapable of generating the anilino-nitrogen's conjugate base of **4a**, considered essential for the Smiles rearrangement to occur.

Similar rearrangements, derived from our earlier study,[1b] have appeared in the literature. Since the rearranged isomers were not reported, they apparently were not isolated.[4,5]

We now report that the phenoxazines **1b** and **1c** prepared "directly" from the *o*-aminophenyl phenyl ethers **4b** and **4c** containing chloro substituents on ring B must indeed be formed via the "Smiles-rearranged" diphenylamine isomers **5b** and **5c**, respectively. The substrates chosen in this study were *N,N*-dimethyl-*N'*-[2-(2,4-dichlorophenoxy)phenyl]-1,3-propanediamine (**4b**, $R_3 = Cl$; $R_1 = R_2 = H$) and *N,N*-dimethyl-*N'*-[2-(2,5-dichlorophenoxy)-phenyl]-1,3-propanediamine (**4c**, $R_2 = Cl$; $R_1 = R_3 = H$). They were prepared by transformations analogous to those reported.[1] The preparation of the diphenyl ether intermediates **2** by the Ullmann reaction was greatly improved. Coupling[6] of the appropriate sodium phenolate and aryl halide in Me_2SO at 140 °C eliminated the cumbersome pyrolytic condensations. The products (**2**) were obtained in better than 80% yields. Reduction of **2** as previously described[1] gave the corresponding *o*-phenoxyanilines **3**, isolated as the hydrochlorides.

The key intermediates **4b** and **4c** (Scheme I) were prepared from the appropriate *o*-phenoxyanilines **3b** and **3c**, respectively, as previously described.[1] Intermediates **4b** and **4c** both rearranged in benzene and $NaNH_2$ to the corresponding *o*-anilinophenols (**4** ⟶ **5**), i.e., **4b** rearranged to 2-[2,4-dichloro-*N*-[3-(dimethylamino)-

(1) (a) Bonvicino, G. E.; Yogodzinski, L. H.; Hardy, R. A., Jr. *J. Org. Chem.* **1961**, *26*, 2797. (b) *Ibid.* **1962**, *27*, 4272. (c) A bromine atom was at the 2'-position of ring B of intermediates **2–6**, instead of a chlorine atom as shown in Scheme I.

(2) (a) Smiles, S.; et al. *J. Chem. Soc.* **1931**, 914 and succeeding papers. (b) Bunnett, J. F.; Okamoto, T. *J. Am. Chem. Soc.* **1956**, *78*, 5363. (c) Bunnett, J. F. *Q. Rev. Chem. Soc.* **1958**, *12*, 1. (d) Shine, H. J. "Aromatic Rearrangements"; Elsevier: Amsterdam, 1967; pp 307–316. (e) Truce, W. E.; Kreider, E. M.; Brand, W. W. "Organic Reactions"; Wiley: New York, 1970; Vol. XVIII, Chapter 2. (f) Stevens, T. S.; Watts, D. W. "Selected Molecular Rearrangements"; Van Nostrand Reinhold: New York, 1973; pp 120–124.

(3) The notation **4** ⟶ [**5**] means that **4** rearranges to **5** and that **5** was not isolated; **4** ⟶ **5** means that **4** rearranges to **5** and that **5** was isolated. (b) See: Grundmann, C.; Grunanger, P. "The Nitrile Oxides"; Springer-Verlag: Berlin, Heidelberg, 1971; p 7.

(4) Grundon, M. F.; Matier, W. L. *J. Chem. Soc. B* **1966**, 266.

(5) Nodiff, E. A; Hausman, M. *J. Org. Chem.* **1964**, *29*, 2453.

(6) Schmutz, J.; Kunzle, F.; Hunziker, F.; Burki, A. *Helv. Chim. Acta* **1965**, *48*, 336–347; *Chem. Abstr.* **1967**, *62*, 14681*b*.

0022-3263/84/1949-1664$01.50/0

propyl]anilino]phenol (**5b**, R_3 = Cl; R_1 = R_2 = H) and **4c** rearranged to 2-[2,5-dichloro-*N*-[3-(dimethylamino)-propyl]anilino]phenol (**5c**; R_2 = Cl; R_1 = R_3 = H). The rearranged intermediates **5b** and **5c** were isolated in their zwitterionic forms **6b** (R_3 = Cl, R_1 = R_2 = H) and **6c** (R_2 = Cl, R_1 = R_3 = H), respectively.

Treating **4b** *or* **6b** with K_2CO_3 in DMF, as previously described,[1b] yielded 3-chloro-10-[3-(dimethylamino)-propyl]phenoxazine (**1b**, R_3 = Cl; R_1 = R_2 = H) in 86% yield from **4b** and in 96% yield from **6b**, identical to the product obtained by a modified Turpin reaction (route B) previously reported.[1b] Cyclization of either **4c** or **6c** under the same conditions gave 2-chloro-10-[3-(dimethylamino)propyl]phenoxazine (**1c**, R_2 = Cl; R_2 = R_3 = H) in 95% yield from **4c** and 97% yield from **6c**, identical in every respect with the product (**1a**) prepared from **4a** and **6a** (R_1 = Cl; R_2 = R_3 = H), following the sequence **2a** → **3a** → **4a** ——⊖→ [**5a**] → **1a** and **4a** ——⊖→ [**5a**] → **6a** → [**5a**] → **1a**, i.e., from the isosteric intermediates (a chlorine atom instead of a bromine atom at the 2′-position of ring B);[1c] **1a** and **1c** were identical and so were their hydrochlorides.

Therefore the "direct" cyclization of **4** to **1** involves the critical rearranged intermediates **5** (isolated as **6**); i.e., the sequence is **4** ——⊖→ [**5**] → **1**. The isolation and cyclization of the diphenylamines **6** (from the Smiles rearrangement of isomers **4**) confirms that the syntheses of the phenoxazines **1** are unambiguous and show that direct cyclization of the diaryl ethers **4** do not occur under the conditions of the reactions.

Experimental Section

Melting Points. Melting points are uncorrected and were determined on a Fisher–Johns apparatus.[7]

Yields were determined after purification of the products either by chromatography, distillation, and/or recrystallization.

***o*-Halophenyl *o*-Nitrophenyl Ethers 2.** The pyrolytic condensations of a sodium *o*-halophenolate and a 1-chloro-2-nitrobenzene were eliminated.[1a,b] A better procedure, in terms of convenience, purity of product, and yields, is a modification of the one reported by Schmutz et al.[6]

***o*-Chlorophenyl 4-chloro-2-nitrophenyl ether (2a)**: mp 61–63 °C (lit.[8a] mp 59–61 °C; lit.[8b] mp 61–63 °C), recrystallized from MeOH, 82% yield. The elemental analyses were within acceptable limits.

2,4-Dichlorophenyl *o*-nitrophenyl ether (2b): mp 58–59.5 °C (lit.[9] mp 58 °C), recrystallized from MeOH, 80% yield. The previously used pyrolytic fusion procedure[1a,b] gave a 50% yield. The elemental analyses were within acceptable limits.

2,5-Dichlorophenyl *o*-nitrophenyl ether (2c): mp 69–69.5 °C (lit.[6] mp 67–68 °C), recrystallized from MeOH, 70% yield. The elemental analyses were within acceptable limits.

The above intermediates all had similar IR spectra; the ether absorption band at 1240 cm^{-1} is split into two closely adjacent bands due to the substituents ortho to the ether oxygen atom. "The symmetrical stretching vibration of the *o*-nitro group at 1345 cm^{-1} is much less intense than is that of its *p*-isomer because of the interference of the neighboring aromatic nucleus."[8]

***o*-(2-Halophenoxy)anilines 3.** These intermediates were prepared by a general procedure previously described[1a,b] and improved.

2-(*o*-Chlorophenoxy)-5-chloroaniline (3a) and Hydrochloride. The free base was isolated as an oil[10] (lit.[11] mp 167 °C) in 89% yield. The hydrochloride, mp 118–120 °C, recrystallized from MeOH, 77% yield. Anal. Calcd for $C_{12}H_9Cl_2NO$·HCl: C, 49.6; H, 3.47; Cl, 36.6; N, 4.82. Found: C, 49.2; H, 3.59; Cl, 36.2; N, 4.99.

***o*-(2,4-Dichlorophenoxy)aniline (3b) and Hydrochloride.** 2,4-Dichlorphenyl *o*-nitrophenyl ether (**2b**) was reduced as described.[1a,b] The free base (93% yield) was converted to the hydrochloride as previously described,[1a,b] mp 146–149 °C, in 85% yield. This salt readily hydrolyzes in water (the free base is weaker than water). This is an advantage in the isolation of intermediate **4b** made from it. Anal. Calcd for $C_{12}H_9Cl_2NO$·HCl: C, 49.6; H, 3.47; Cl, 36.6; N, 4.82. Found: C, 49.4; H, 3.49; Cl, 36.4; N, 4.65.

***o*-(2,5-Dichlorophenoxy)aniline (3c) and Hydrochloride.** The free base, bp 133–138 °C (0.1 torr) (lit.[6] bp 130–135 °C (0.07 torr), and the hydrochloride, mp 152–155 °C, recrystallized from MeOH, 83% yield. Anal. Calcd for $C_{12}H_9Cl_2NO$·HCl: C, 49.6; H, 3.47; Cl, 36.6; N, 4.82. Found: C, 49.3; H, 3.41; Cl, 36.2; N, 4.73.

***N*,*N*-Dimethyl-*N*′-[2-(*o*-chlorophenoxy)phenyl]-1,3-propanediamines 4.** These intermediates were prepared by treating appropriately substituted 2-(*o*-chlorophenoxy)anilines **3** with 1 molar equiv of $NaNH_2$[12] and 3-chloro-*N*,*N*-dimethylpropylamine[13] in anhydrous benzene. They were purified by partition chromatography using a *n*-heptane–methyl Cellosolve system and Celite 545 as previously described.[1a]

***N*,*N*-Dimethyl-*N*′-[2-(*o*-chlorophenoxy)-5-chlorophenyl]-1,3-propanediamine (4a).** From a mixture of 13.4 g of 2-(*o*-chlorophenoxy)-5-chloroaniline (**3a**), 2.34 g of $NaNH_2$ and 7.39 g of 3-chloro-*N*,*N*-dimethylpropylamine, **4a** was obtained in 87% yield as an amber oil: bp 185–190 °C (0.5 torr); n^{25}_D 1.600. Anal. Calcd for $C_{17}H_{20}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 59.9; H, 5.89; Cl, 21.0; N, 7.98.

***N*,*N*-Dimethyl-*N*′-[2-(2,4-dichlorophenoxy)phenyl]-1,3-propanediamine (4b).** From a mixture of 4.12 g of *o*-(2,4-dichlorophenoxy)aniline (**3b**), 0.74 g of $NaNH_2$ and 2.07 g of 3-chloro-*N*,*N*-dimethylpropylamine, **4b** was obtained in 92% yield as an amber oil: bp 183–188 °C (0.5 torr); n^{25}_D 1.595. Anal. Calcd for $C_{17}H_{20}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 59.9; H, 5.90; Cl, 21.0; N, 8.31.

***N*,*N*-Dimethyl-*N*′-[2-(2,5-dichlorophenoxy)phenyl]-1,3-propanediamine (4c).** From a mixture of 13.3 g of *o*-(2,5-dichlorophenoxy)aniline (**3c**), 2.15 g of $NaNH_2$ and 6.44 g of 3-chloro-*N*,*N*-dimethylpropylamine, **4c** was obtained in 91% yield as an amber oil: bp 180–185 °C (0.5 torr); n^{25}_D 1.588. Anal. Calcd for $C_{17}H_{20}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 60.5; H, 5.90; Cl, 21.2; N, 8.01.

2-[*N*-[3-(Dimethylamino)propyl]-*o*-chloroanilino]phenols 6. These compounds were produced together with the isomeric *N*,*N*-dimethyl-*N*′-[2-(*o*-chlorophenoxy)phenyl]-1,3-propanediamines **4** when employing 2 or more molar equiv of $NaNH_2$. Alternately, the anilinophenols **6** were prepared from **4** with 1 or more equiv of $NaNH_2$ in benzene.[1b]

2-[*o*-Chloro-*N*-[3-(dimethylamino)propyl]anilino]-4-chlorophenol (6a). The product, 16.3 g (**6a**) obtained from a reaction mixture of 13.4 g of 2-(*o*-chlorophenoxy)-5-chloroaniline (**3a**), 4.33 g of $NaNH_2$ (2 equiv), and 7.39 g of 3-chloro-*N*,*N*-dimethylpropylamine, was recrystallized from 95% EtOH in 81% yield, mp 148–150 °C. Anal. Calcd for $C_{17}H_{10}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 60.5; H, 5.90; Cl, 20.9; N, 8.31.

2-[2,4-Dichloro-*N*-[3-(dimethylamino)propyl]anilino]-phenol (6b). The product, 7.25 g (**6b**) obtained from a reaction mixture of 11.4 g of *o*-(2,4-dichlorophenoxy)aniline (**3b**), 3.86 g

(7) Purchased from Fischer Scientific Co., Pittsburgh, PA.

(8) (a) Matsui, K.; Oda, K.; Seino, J. *Yuki Gosei Kagaku Kyokai Shi* **1956**, *14*, 401–406; *Chem. Abstr.* **1957**, *51*, 10415*b*. (b) Mason, G. W.; Brooker, E. G. *Proc. N. Z. Weed Pest Control Conf.* **1968**, *21*, 163–172; *Chem. Abstr.* **1969**, *70*, 77494*s*. (This compound is incorrectly abstracted in this entry; it is abstracted as *o*-chlorophenyl 4-chloro-3-nitrophenyl ether.)

(9) Dahlgard, M.; Brewster, R. Q. *J. Am. Chem. Soc.* **1958**, *80*, 5861–5863; *Chem. Abstr.* **1959**, *53*, 8804*d*.

(10) Chemical Abstracts lists[11] this compound as a solid. We were unable to crystallize our preparation. The isomers **3b** and **3c** are also oils. The hydrochloride of **3a** gave a satisfactory elemental analysis as noted. The IR spectra of the hydrochloride of **3a** was consistent with the IR spectra of the hydrochlorides of **3b** and **3c**.

(11) Yamashiro, S.; Matsueda, S. *Nippon Kagaku Zasshi* **1954**, *75*, 399–401; *Chem. Abstr.* **1957**, *51*, 11300*i*.

(12) The sodium amide used was: "Sodium Amide. (Gray Powder)", S-677; lot 762097, purchased from Fisher Scientific Co, Chemical Manufacturing Division, Fair Lawn, NJ 07410.

(13) Marxer, A. *Helv. Chim. Acta* **1941**, *24*, 209E.

of $NaNH_2$ (2 equiv), and 5.59 g of 3-chloro-*N*,*N*-dimethylpropylamine, was recrystallized from 95% EtOH in 42% yield, mp 168–170 °C. Anal. Calcd for $C_{17}H_{20}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 60.3; H, 5.95; Cl, 20.5; N, 8.42.

The IR spectra of the above material and the product obtained by the isomerization of **4b** with 1 equiv of $NaNH_2$ in anhydrous benzene were absolutely identical. A mixture melting point was not depressed.

2-[2,5-Dichloro-*N*-[3-(dimethylamino)propyl]anilino]-phenol (6c). The product, 14.9 g (**6c**) obtained from a mixture of 13.3 g of *o*-(2,5-dichlorophenoxy)aniline (**3c**), 5.10 g of $NaNH_2$ (2 equiv), and 6.44 g of 3-chloro-*N*,*N*-dimethylpropylamine, was recrystallized from 95% EtOH in 60% yield, mp 161–163 °C. Anal. Calcd for $C_{17}H_{20}Cl_2N_2O$: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 60.4; H, 5.73; Cl, 21.0; N, 8.33.

2-Chloro- and 3-Chloro-10-[3-(dimethylamino)propyl]-phenoxazines (1a = 1c and 1b).[14] These compounds were prepared by cyclization of the new "phenoxyaniline" intermediates **4a**, **4c**, and **4b** and/or the isomeric "anilinophenol" intermediates **6a**, **6c**, and **6b**.

2-Chloro-10-[3-(dimethylamino)propyl]phenoxazine (1a and 1c)[14] and Hydrochloride. From 4a. Treatment of 7.33 g of **4a** and 6.10 g of K_2CO_3 in 200 mL of DMF for 18 h, under reflux using the previously described procedure including partition chromatography,[1a,b] gave 6.33 g 95% yield of **1a** as a viscous oil, bp 175–180 °C (0.5 torr); (lit.[1b] bp 176–180 °C (0.5 torr)). The hydrochloride melted at 220–222 °C. The IR spectra of **1a** was identical with that of a sample isolated from the hydrochloride preparation previously prepared[15] and reported.[1b] Elemental analyses were within acceptable limits.

From 4c. A mixture of 8.48 g of **4c** with 7.00 g of K_2CO_3 that was allowed to react as previously desribed and including partition chromatography, yielded 7.19 g (95%) of **1c** as a viscous oil. Distillation gave 5.25 g, 69% yield, of a light amber oil: bp 175–180 °C (0.5 torr); n^{25}_D 1.614 (lit.[1b] bp 176–180 °C (0.5 torr); n^{25}_D 1.614). A portion of this base was converted to the hydrochloride, mp 220–222 °C, 93% yield. A mixtur melting point of the hydrochlorides of **1a** and **1c** was not depressed, mp 220–222 °C (lit.[1a,b] mp 220–222 °C). Anal. Calcd for $C_{17}H_{19}ClN_2O$·HCl: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 60.4; H, 5.98; Cl, 20.9; N, 8.03.

From 6c. A mixture of 8.48 g of **6c** and 7.00 g of K_2CO_3 was allowed to react as described above. After similar workup, including partition chromatography, 7.36 g (97% yield) of **1c** was obtained as an oil; **1a** (identical with **1c**) was also prepared (in 90% yield) from **6a** by employing this procedure. The IR spectra of **1a**, prepared from **4a** and **6a**, and the IR spectra of **1c**, prepared from **4c** and **6c**, were absolutely identical, and so were the IR spectra of the corresponding hydrochlorides, mp 220–222 °C. Needless to say, mixture melting points were not depressed. Elemental analyses were within acceptable limits.

3-Chloro-10-[3-(dimethylamino)propyl]phenoxazine (1b) and Hydrochloride. From 4b. From a mixture of 4.60 g of **4b** and 2.82 g of K_2CO_3 in 50 mL of DMF, and purification of the product by partition chromatography as previously reported,[1a] 4.07 g of **1b** was obtained in 86% yield; bp 176–180 °C (0.4 torr); n^{25}_D 1.601 (lit.[1b] bp 176–180 °C (0.4 torr); n^{25}_D 1.601) (route B). The hydrochloride of **1b** was obtained in 82% yield, mp 184–185 °C (lit.[1b] mp 183–184 °C). Elemental analyses were within acceptable limits.

From 6b. From a mixture of 5.25 g of **6b** and 8.82 g of K_2CO_3 in 50 mL of DMF, and after the usual workup described above, including partition chromatography, 4.50 g (96% yield) of **1b** was obtained as an oil: bp 175–180 °C (0.4 torr); n^{25}_D 1.601 (lit.[1b] 176–180 °C (0.4 torr); n^{25}_D 1.601). The IR spectra of **1b**, prepared from **4b** and **6b**, and by route B,[1b] were identical and so were the corresponding IR spectra of the hydrochlorides, mp 184–185 °C (lit.[1b] mp 183–184 °C). A mixture melting point with a sample prepared from **4b** was not depressed. Anal. Calcd for $C_{17}H_{19}ClN_2O$·HCl: C, 60.2; H, 5.94; Cl, 20.9; N, 8.26. Found: C, 59.9; H, 5.99; Cl, 21.2; N, 7.95.

(14) In this paper 2-chloro-10-[3-(dimethylamino)propyl]phenoxazine is prepared from two separate routes and is designated **1a** and **1c** according to the designations in Scheme I of the intermediates from which it was prepared. 3-Chloro-10-[3-(dimethylamino)propyl]phenoxazine is analogously designated **1b**.

(15) We thank Dr. R. A. Hardy, Jr., of the Medical Research Division, Lederle Laboratories, American Cyanamid Company, Pearl River, NY, for samples of **1a** prepared as previously described.[1b,c]

Summary

Cyclization of (*o*-halophenoxy)anilines **4** with K_2CO_3 in DMF to form phenoxazines **1** proceeds via Smiles rearrangements of **4** to the isomeric (*o*-haloanilino)phenols **6** which cyclize to **1**.

The (*o*-haloanilino)phenol intermediates **6** were isolated and converted to the corresponding phenoxazines **1**. *N*,*N*-Dimethyl-*N*′-[2-(2,4-dichlorophenoxy)phenyl]-1,3-propanediamine (**4b**) heated with K_2CO_3 in DMF gave 3-chloro-10-[3-(dimethylamino)propyl]phenoxazine (**1b**). The intermediate in this transformation, 2-[2,4-dichloro-*N*-[3-[(dimethylamino)propyl]anilino]phenol (**6b**) was prepared from **4b** and $NaNH_2$ in benzene. Cyclization of **6b** with K_2CO_3 in DMF also gave **1b**. *N*,*N*-Dimethyl-*N*′-[2-(2,5-dichlorophenoxy)phenyl]-1,3-propanediamine (**4c**) heated with K_2CO_3 in DMF yielded 2-chloro-10-[3-(dimethylamino)propyl]phenoxazine (**1c**). The intermediate in this transformation, 2-[2,5-dichloro-*N*-[3-(dimethylamino)propyl]anilino]phenol (**6c**), prepared from **4c** and $NaNH_2$ in benzene also gave **1c** with K_2CO_3 in DMF. 2-[*o*-Chloro-*N*-[3-(dimethylamino)propyl]-anilino]-4-chlorophenol (**6a**) was prepared by the Smiles rearrangement of *N*,*N*-dimethyl-*N*′-[2-(*o*-chlorophenoxy)-5-chlorophenyl]-1,3-propanediamine (**4a**) with $NaNH_2$ in benzene. Both **4a** and **6a** gave 2-chloro-10-[3-(dimethylamino)propyl]phenoxazine (i.e., **1a** = **1c**) also, when heated with K_2CO_3 in DMF.

Acknowledgment. This research was partially supported by a grant from the Long Island University/C. W. Post Center Research Committee, which we acknowledge with gratitude. We thank Dr. R. A. Hardy, Jr., of the Medical Research Division, Lederle Laboratories, American Cyanamid Company, Pearl River, NY, for help in obtaining some of the NMR spectral data and for his critical reading of the manuscript and constructive comments. We thank Maria Falasca and William E. Topazio for the drawings of the chemical formulae.

Registry No. **1a**, 4418-46-6; **1a**·HCl, 89279-25-4; **1b**, 89279-24-3; **1b**·HCl, 89279-26-5; **2a**, 22544-02-1; **2b**, 38461-29-9; **2c**, 3169-76-4; **3a**, 56966-48-4; **3a**·HCl, 89279-15-2; **3b**, 26306-64-9; **3b**·HCl, 89279-16-3; **3c**, 3169-77-5; **3c**·HCl, 89279-17-4; **4a**, 89279-18-5; **4b**, 89279-19-6; **4c**, 89279-20-9; **6a**, 89279-21-0; **6b**, 89279-22-1; **6c**, 89279-23-2; 3-chloro-*N*,*N*-dimethylpropylamine, 109-54-6.

Preparation of Chirally Deuterated *N*-(Trifluoroacetyl)-β-alanine and Related Compounds

Richard K. Hill,* Shimoga R. Prakash, and Thomas M. Zydowsky

Chemistry Department, University of Georgia, Athens, Georgia 30602

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Isotopically labeled amino acids containing a hydrogen isotope at a prochiral carbon have proven valuable for the investigation of the stereospecificity of enzymatic reactions.[1]

(1) (a) Hill, R. K. In "Bioorganic Chemistry"; van Tamelen, E. E., Ed.; Academic Press: New York, 1978; Vol. II, Chapter 5. (b) Parry, R. J. ref 1a, Chapter 10.

0022-3263/84/1949-1666$01.50/0