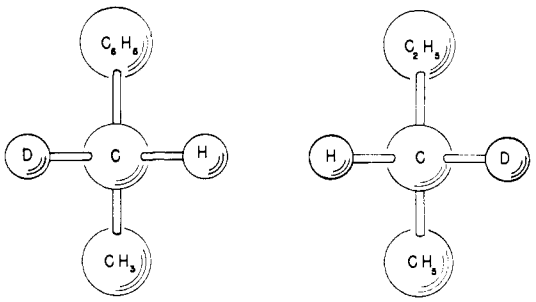
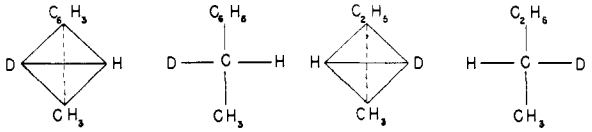
bond. Quantum mechanical calculations[10] assign the positive sign to β' as does a consideration of the known sign of α' and the relative magnitudes of α' and β'.

The optical rotation of the enantiomorph of α-deuteroethylbenzene shown was calculated from Eq. (4). The angle ϕ defining the internal conformation is taken to be zero when the methyl group lies in the plane corresponding to the plane of symmetry of ethylbenzene, and to increase positively as the phenyl group is rotated so as to increase the distance from deuterium to the plane of the ring.





The potential function for the internal conformation can be estimated roughly from the work of Pitzer and Scott on the xylenes.[11] The ethyl group is assumed to have the staggered configuration and to be free to rotate relative to the ring until its hydrogens approach van der Waals contact with those of the ring. The simplified potential function is thus taken to be

$$V(\phi) = 0 \quad \text{for} \quad -30° \leq \phi \leq 30°$$
$$V(\phi) = 0 \quad \text{for} \quad 150° \leq \phi \leq 210°$$
$$V(\phi) = \infty \quad \text{otherwise}$$

The calculated optical rotation is then $[\alpha]^{25}D$ $+0.41°$ for a medium of refractive index 1.50, corresponding to the pure liquid. The experimental value for the pure liquid enantiomorph prepared by deuteride reduction of (−)-phenylmethylcarbinol is $[\alpha]^{25}D$ $-0.30°$. The relative configuration of the carbinol is known.[12] If the deuteride reduction is accompanied by inversion, as is probably the case, then the (−)-α-deuteroethylbenzene has a spatial configuration opposite to that for which the calculations were made, in agreement with the Fischer convention regarding absolute configuration, and consistent with the findings for 2,3-epoxybutane and 1,2-dichloropropane.[5,13]

(10) M. N. Adamov, *Doklady Akad. Nauk. S.S.S.R.*, **62**, 461 (1948), *C. A.*, **43**, 1264 (1949); J. O. Hirshfelder, *J. Chem. Phys.*, **3**, 555 (1935); J. G. Kirkwood, *Physik. Z.*, **33**, 257 (1932).

(11) K. S. Pitzer and D. W. Scott, THIS JOURNAL, **65**, 803 (1943).

(12) W. A. Cowdry, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1260 (1937); P. A. Levene and S. H. Harris, *J. Biol. Chem.*, **113**, 55 (1936); P. A. Levene and P. G. Stevens, *ibid.*, **89**, 471 (1930).

(13) W. Fickett, H. K. Garner and H. J. Lucas, THIS JOURNAL, **73**, 5063 (1951).

A calculation for 2-deuterobutane was also carried out, although as far as is known the optically active compound has not been prepared. The problem of internal conformation was treated in terms of three isomers: two "bent" forms of equal energy and one "straight" form, corresponding to the terminology of Szasz, Sheppard and Rank,[14] who determined the equilibrium concentrations of the two forms from the temperature dependence of the infrared spectrum. The calculated optical rotation for the enantiomorph shown is $[\alpha]^{25}D$ $+1.1°$ for a medium of refractive index 1.33, corresponding to the pure liquid.

The author wishes to thank Professor J. G. Kirkwood for his help and advice throughout this investigation and Professor Verner Schomaker for a helpful discussion of the internal conformation of ethylbenzene.

(14) G. J. Szasz, N. Sheppard and D. H. Rank, *J. Chem. Phys.*, **16**, 705 (1948).

CONTRIBUTION NO. 1620 FROM THE
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Some 10-Substituted Phenothiazines

BY HENRY GILMAN, R. DAVID NELSON AND JOHN F. CHAMPAIGNE, JR.

RECEIVED MARCH 15, 1952

There is a discrepancy in the literature concerning the melting point of 10-benzylphenothiazine. Desai[1] reported that this compound, m.p. 90.5–91°, was formed by heating a mixture of benzyldiphenylamine and sulfur at 220° for 8 hours. Finzi[2] stated that this particular phenothiazine derivative was obtained by heating phenothiazine and benzyl chloride at 140–145° for 2 hours. However, his product melted at 130°. In connection with the cleavage of some alkoxy heterocycles by compounds containing the imino group, it has been found[3] that the reaction of 2-benzyloxyquinoline with phenothiazine, in refluxing cumene, gave a 90% yield of 2-hydroxyquinoline and a 34% yield of a product melting at 91–92°. The latter compound analyzed for a benzylphenothiazine. A repetition[3] of Finzi's preparation gave a small amount of crystals, m.p. 132–134°. Therefore, the following procedure was attempted in order to prepare the benzyl derivative.[3] A mixture of benzyl chloride and 10-lithiophenothiazine (prepared from phenothiazine and phenyllithium) in a benzene–ether solution and under a nitrogen atmosphere was stirred for one day at room temperature and then one hour at reflux temperature. No pure product has as yet been isolated.

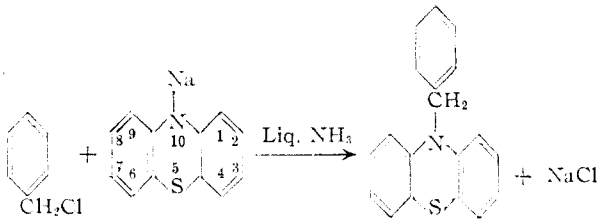
Various 10-(dialkylaminoalkyl)-phenothiazines have been prepared by refluxing in xylene (or similar solvent) a mixture of a dialkylaminoalkyl chloride and phenothiazine in the presence of the

(1) R. D. Desai, *J. Indian Inst. Sci.*, **7**, 235 (1924) [*C. A.*, **19**, 2645 (1925)].

(2) C. Finzi, *Gazz. chim. ital.*, **62**, 175 (1932) [*C. A.*, **26**, 4338 (1932)].

(3) H. Gilman, I. Zarember and J. A. Beel, THIS JOURNAL, **74**, 3177 (1952).

condensing agent, sodamide.[4] Therefore this type of reaction was used to prepare 10-benzylphenothiazine. The product obtained, in a 15.5% yield, from the reaction of benzyl chloride, phenothiazine and sodamide in refluxing xylene melted at 90–90.5°. The mixed melting point with the phenothiazine derivative, m.p. 91–92°, obtained from the cleavage reaction involving 2-benzyloxyquinoline[3] was undepressed. Since the compound, m.p. 91–92°, gave the correct analysis for a benzylphenothiazine, both products are considered to be 10-benzylphenothiazine. In addition, their infrared spectra were identical. The compound also was prepared, in a 66.3% yield, by allowing benzyl chloride to react with 10-sodiophenothiazine in liquid ammonia. Thus, liquid ammonia is the more satisfactory solvent for this reaction.



Abnormal rearrangements have been noted in the reaction of benzylmagnesium chloride with certain carbonyl compounds. These observations[5] suggested the possibility that rearrangement may have occurred in the reaction of benzyl chloride with 10-sodiophenothiazine. Consequently, 10-(*p*-tolyl)- and 10-(*o*-tolyl)-phenothiazine were prepared in order to compare them with 10-benzylphenothiazine. They were found to be different on the basis of the melting points and the infrared analyses.

The sodamide-condensation type of reaction was also applied to the preparation of 10-ethylphenothiazine from phenothiazine and an ethyl halide. In this case it was found that the reaction proceeded much more satisfactorily in liquid ammonia than in refluxing benzene. An almost quantitative yield of the desired compound was obtained by using liquid ammonia as the solvent.

Experimental

10-Benzylphenothiazine. (A) Preparation in Xylene.—Nineteen and nine-tenths grams (0.1 mole) of phenothiazine was added with mechanical stirring to a suspension of 0.12 mole of sodamide[6] (prepared from 3.0 g. of sodium and liquid ammonia) in 80 ml. of dry xylene. The brown mixture was refluxed for 40 minutes and then a solution of 19 g. (0.15 mole) of benzyl chloride in 20 ml. of xylene was added dropwise over a period of 2.5 hours. The mixture was refluxed for another 0.5 hour. The color changed from brown to black. The mixture was filtered while hot to remove the inorganic material. The solvent was removed and the residue distilled under reduced pressure giving 10 g. of yellow oil, b.p. 195–205° (0.02–0.03 mm.) with the heating bath at 270–290°. The oil was dissolved in benzene and the solution chromatographed on a 38 × 120 mm. column of alumina.[7] From the eluate there was obtained 4.5 g. (15.5%) of white crystals, m.p. 88.5–90°. This solid was recrystallized from ethanol giving small white platelets, m.p. 90–90.5°. The mixed melting point with the phenothiazine derivative, m.p. 91–92°, obtained from the cleavage reaction involving 2-benzyloxyquinoline[3] was undepressed.

(B) Preparation in Liquid Ammonia.—Sodamide[6] was prepared by adding 2.6 g. (0.11 mole) of sodium to 500 ml. of liquid ammonia. Nineteen and nine-tenths grams (0.1 mole) of phenothiazine was added in small portions, with stirring, to the sodamide in liquid ammonia giving a dark red mixture. The red color was probably due to 10-sodiophenothiazine dissolved in liquid ammonia, since phenol thiazine, itself, was found to be slightly soluble in liquid ammonia giving a green solution.[8] Because of the intensity of the red color, it was difficult to determine by visual inspection alone whether or not the 10-sodiophenothiazine was completely in solution; however, it appeared to be so. The mixture was stirred for 2 hours. Nineteen grams (0.15 mole) of benzyl chloride was added over a period of 20 minutes. The color of the mixture changed from red to brown. The stirring was continued for an additional 90 minutes. The ammonia was then allowed to evaporate and the residue extracted with 150 ml. of hot benzene. After filtration, the solution was chromatographed on a 38 × 180 mm. column of alumina (Alcoa, F-20). A yellow oil was obtained from the eluate. Recrystallization from ethanol gave 19.2 g. (66.3%) of crystals, m.p. 90.5–91.5°. The mixed melting point with the compound prepared by the foregoing procedure was undepressed.

10-(*p*-Tolyl)-phenothiazine.—A mixture of 10.9 g. (0.05 mole) of *p*-iodotoluene, 10 g. (0.05 mole) of phenothiazine, 0.2 g. of copper bronze powder, 7.5 g. of anhydrous potassium carbonate, 10 ml. of xylene and 50 ml. of nitrobenzene was heated at 155–165° (internal temperature) with stirring for 17 hours. The mixture was filtered while still hot and the residue was washed with about 40 ml. of hot xylene. The solvent was removed under reduced pressure, the dark red liquid which remained solidified on cooling. The crude product was dissolved in 350 ml. of benzene and the solution chromatographed on a 38 × 150 mm. column of alumina[7] giving 4.6 g. (32%) of light yellow solid, m.p. 128–134°. The product was recrystallized from petroleum ether (b.p. 60–70°) to give 2.2 g. (15%) of yellow crystals, m.p. 135–136°.

Anal. Calcd. for $C_{19}H_{15}NS$: N, 4.85. Found: N, 4.76.

10-(*o*-Tolyl)-phenothiazine.—A mixture of 16.4 g. (0.075 mole) of *o*-iodotoluene, 10 g. (0.05 mole) of phenothiazine, 0.2 g. of copper bronze powder, 7.5 g. of anhydrous potassium carbonate, 50 ml. of nitrobenzene and 5 ml. of xylene was heated at 165–175° (internal temperature) with stirring for 23 hours. The inorganic material was removed by filtration of the hot mixture and washed with hot xylene. The solvent was then removed by distillation under reduced pressure. The dark red residue was dissolved in 350 ml. of benzene and the resulting solution chromatographed on a 38 × 185 mm. column of alumina.[7] The eluate was collected in approximately 125-ml. portions. Removal of the solvent left residues totaling 12.4 g. (86%) and melting at 80–95°. The crude material was purified by recrystallization from petroleum ether (b.p. 60–70°) and methanol, respectively, giving 7.5 g. (52%) of light brown needles, m.p. 101–101.5°. The mixed melting point with 10-benzylphenothiazine was depressed to 70–72°.

Anal. Calcd. for $C_{19}H_{15}NS$: N, 4.85. Found: N, 4.77.

10-Ethylphenothiazine.[9] **(A) Preparation in Benzene.**—Nineteen and nine-tenths grams (0.1 mole) of phenothiazine was added with mechanical stirring to 0.113 mole of sodamide[6] in 200 ml. of liquid ammonia. After 15 minutes, 120 ml. of dry benzene was slowly added and the mixture par-

(4) P. Charpentier, *Compt. rend.*, **225**, 306 (1947); W. B. Reid, Jr., J. B. Wright, H. G. Kolloff and J. H. Hunter, THIS JOURNAL, **70**, 3100 (1948); R. Dahlbom, *Acta Chem. Scand.*, **3**, 247 (1949) [*C. A.*, **44**, 1515 (1950)]; Société des usines chimiques Rhône-Poulenc, British Patent 608,208, Sept. 10, 1948 [*C. A.*, **43**, 2647 (1949)]; P. Charpentier, U. S. Patent 2,526,118, Oct. 17, 1950 [*C. A.*, **45**, 2511 (1951)] and U. S. Patent 2,530,451, Nov. 21, 1950 [*C. A.*, **45**, 3428 (1951)]; P. Charpentier and R. Ducrot, *Compt. rend.*, **232**, 415 (1951); P. Charpentier, P. Gailliot and J. Gaudechon, *ibid.*, **232**, 2232 (1951).

(5) H. Gilman and J. E. Kirby, THIS JOURNAL, **54**, 345 (1932); J. R. Johnson, *ibid.*, **55**, 3029 (1933); H. Gilman and J. F. Nelson, *ibid.*, **61**, 741 (1939); W. G. Young and S. Siegel, *ibid.*, **66**, 354 (1944).

(6) T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, *ibid.*, **56**, 2120 (1934).

(7) Fisher Scientific Co., 80-200 mesh.

(8) F. de Carli, *Gazz. chim. ital.*, **57**, 347 (1927) [*C. A.*, **21**, 3047 (1927)].

(9) H. Gilman, P. R. Van Ess and D. A. Shirley, THIS JOURNAL, **66**, 1214 (1944); H. I. Bernstein and L. R. Rothstein, *ibid.*, **66**, 1886 (1944).

tially solidified. Following evaporation of the ammonia, the mass again became fluid. The mixture was gently refluxed for 3 hours and then a solution of 24.0 g. (0.154 mole) of ethyl iodide in 35 ml. of dry benzene was added dropwise over a period of 2.5 hours. The refluxing with stirring was continued for an additional hour. The hot mixture was then filtered and the residue washed with warm benzene; the total volume of the solution was about 350 ml. The cold solution was chromatographed on a 38 × 180 mm. column of alumina (Alcoa, F-20) giving 16 g. (70%) of crude 10-ethylphenothiazine and some phenothiazine (mixed melting point). Two recrystallizations of the crude product gave 8.1 g. (36%) of yellow needle-like prisms, m.p. 102.5–103°.

(B) Preparation in Liquid Ammonia.—Forty-seven grams (0.236 mole) of phenothiazine was added with stirring to a suspension of 0.26 mole of sodamide[6] in 1600 ml. of liquid ammonia giving a dark red mixture. The stirring was continued for 2.5 hours and then 39 g. (0.354 mole) of ethyl bromide was added dropwise over a period of 45 minutes. During the addition of the ethyl bromide, the color of the mixture gradually became lighter and a gray-brown solid separated. The ammonia was allowed to evaporate and the residue was refluxed with 500 ml. of petroleum ether (b.p. 60–70°) and benzene (1:2). The inorganic material was filtered off and washed with 3 small portions of hot benzene. The golden brown filtrate was concentrated to 150 ml. by distillation. On standing, 19.6 g. of light green, cubic crystals, m.p. 103–104°, separated. The mother liquor was chromatographed on a 38 × 180 mm. column of alumina[7] giving 32.2 g. of light green crystals, m.p. 102–103°. The total yield of pure 10-ethylphenothiazine was 51.8 g. (97%).

In a second preparation of 10-ethylphenothiazine, 19.9 g. (0.1 mole) of phenothiazine was added to a 0.11 mole of sodamide[6] in 650 ml. of liquid ammonia. The resulting mixture was treated with 16.5 g. (0.15 mole) of ethyl bromide in the same manner as in the preceding reaction. After evaporation of the ammonia, the residue was extracted with a solution of benzene and petroleum ether (b.p. 60–70°) (4:1). The solution was chromatographed on a 38 × 200 mm. column of alumina[7] to give 21 g. (92%) of the desired product, m.p. 103–104°, and 0.3 g. (1.5%) of phenothiazine (mixed melting point).

Acknowledgment.—The authors are grateful to Dr. V. A. Fassel and Mr. M. Margoshes for the infrared analyses, the data of which will be published elsewhere.

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2-β-Aminoethylquinoline

BY REUBEN G. JONES

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Although a number of N-substituted derivatives of 2-β-aminoethylquinoline have been prepared from quinaldine using the Mannich reaction,[1,2] there appears to be some confusion concerning 2-β-aminoethylquinoline itself. Kermak and Muir[1] were unable to obtain the compound by the reaction of β-2-quinolinepropionhydrazide with nitrous acid; however, Hupe and Schramme[3] had previously reported its preparation by hydrogenation of what they believed to be 2-quinolineacetaldehyde oxime. 2-β-Aminoethylquinoline was synthesized in this Laboratory for testing as an analog of histamine.[4] The sample was obtained by the reaction of hypochlorite on β-2-quinolinepropionamide and was isolated as the dihydrochloride. This salt did not melt at 212° as reported by Hupe and Schramme,[3] but decomposed without melting at about 195–200°.

Recently Woodward and Kornfeld[5] have shown that the so-called 2-quinolineacetaldehyde[6] as used by Hupe and Schramme in their synthesis, is, in reality, 3-acetylquinoline. Therefore, it appears that the previously reported 2-β-aminoethylquinoline[3] was in fact 3-α-aminoethylquinoline.

Experimental

2-β-Aminoethylquinoline Dihydrochloride.—A mixture was prepared by absorbing 3.3 g. of chlorine in a solution of 8.7 g. of sodium hydroxide in 25 ml. of water. To this was added 45 g. of chipped ice followed by 8.5 g. of β-2-quinolinepropionamide.[6] After stirring for one hour at room temperature the solution was heated for one-half hour on the steam-bath and then cooled. The mixture was extracted with five 100-ml. portions of ethyl acetate, and the dried extract was treated with ethereal hydrogen chloride. The product was recrystallized by solution in hot methanol followed by the addition of three volumes of ethyl acetate. It did not melt but turned black at 195–200°. The yield was 7.5 g. (71%).

Anal. Calcd. for $C_{11}H_{12}N_2 \cdot 2HCl$: N, 11.42. Found: N, 11.12.

(1) W. O. Kermak and W. Muir, *J. Chem. Soc.*, 3089 (1931).
(2) Tseou Heou-Feo, *Bull. soc. chim.*, **2**, 96 (1935).
(3) R. Hupe and A. Schramme, *Z. physiol. Chem.*, **177**, 315 (1928).
(4) H. M. Lee and R. G. Jones, *J. Pharmacol.*, **95**, 71 (1949).
(5) R. B. Woodward and E. C. Kornfeld, THIS JOURNAL, **70**, 2508 (1948).
(6) A. Einhorn and P. Sherman, *Ann.*, **287**, 26 (1895).

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The Hammett Sigma Value for *m*-Phenyl

BY NORMAN N. LICHTIN AND HARRY P. LEFTIN

RECEIVED MARCH 8, 1952

It has recently been pointed out[1] that the σ-value assigned to the *m*-phenyl group by Hammett[2] is based on unreliable data. A study of the effect of one *m*-phenyl substituent on the ionization equilibrium in liquid sulfur dioxide of triphenylchloromethane[1] has produced data which can be interpreted as resulting from a small fundamental electron attracting influence. Alternative explanations, however, are possible, namely, that the *m*-phenyl group complexed with sulfur dioxide[3] may be responsible rather than the group itself, or that the presence of a positive charge localized in one ring of a biphenyl group decreases the resonance interaction of the two rings. It therefore became of interest to carry out measurements which would provide a more reliable σ-value for the *m*-phenyl group and provide information on its electronic influence subject to less ambiguous interpretation. Berliner and Blommers[4] have recently provided a direct route to these objectives by establishing a ρ-value of $+1.32 \pm 0.06$ for the dissociation of substituted benzoic acids in 50% aqueous butyl cellosolve at 25° and an ionic strength of 0.05. The (non-thermodynamic) pK_A values for benzoic acid and *m*-phenylbenzoic acid have been determined under the conditions employed by these workers and have been employed together with their ρ-value

(1) N. N. Lichtin and H. Glazer, THIS JOURNAL, **73**, 5537 (1951).
(2) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.
(3) L. J. Andrews and R. M. Keefer, THIS JOURNAL, **73**, 4169 (1951).
(4) E. Berliner and E. A. Blommers, *ibid.*, **73**, 2479 (1951).