4.6 g. of the methoxy compound was heated at reflux for one-half hour with 10 g. of anhydrous aluminum chloride in 60 cc. of chlorobenzene. The mixture was then acidified with hydrochloric acid and the chlorobenzene removed by steam distillation; the excess water was distilled off and the residue allowed to cool, whereupon the anthocyanidin separated from solution. It was recrystallized from dilute alcoholic hydrochloric acid.

## Summary

1. The familiar reactions involved in the preparation of 2-phenyl benzopyrylium salts can be extended to include compounds having condensed benzene nuclei.

2. A series of 2-phenylnaphthopyrylium chlorides is described. As might be anticipated the members are very similar to those of the analogous 2-phenylbenzopyrylium series but their colors are much darker.

CHAPEL HILL, N. C. RECEIVED NOVEMBER 18, 1940

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF SWARTHMORE COLLEGE]

# Ethylenediamine. IV.[1] Monoalkyl Derivatives

BY SAMUEL R. ASPINALL

Examples of every type of alkyl ethylenediamine (*viz.*, $RNHCH_2CH_2NH_2$, $RNHCH_2CH_2NHR$, $R_2NCH_2CH_2NH_2$, $R_2NCH_2CH_2NHR$, $R_2NCH_2CH_2NR_2$) are to be found in the literature, but in some cases the syntheses are laborious and give poor yields or ill-defined products. It was thought the amines represented by $RNHCH_2CH_2NH_2$, which are secondary amines having the $\beta$-amino ethyl group in common, might be interesting in themselves or as starting materials for synthetic work. Several representatives of this type are known and have been characterized as derivatives, but the data on the free amines are in many cases lacking or contradictory, presumably because the syntheses yielded very small amounts of impure products.

Since direct alkylation of ethylenediamine is reported[2] to yield only the bis-diquaternary ammonium salt, several indirect methods of controlled monoalkylation have been tried. (1) Johnson and Bailey[3] discuss several reactions which might be expected to yield monoalkylated ethylenediamines, but which in fact fail to do so. They obtained monomethylethylenediamine by the following series of reactions

$$o\text{-}C_6H_4(CO)_2NCH_2CH_2Br \xrightarrow{KNHSO_2CH_2C_6H_5} o\text{-}C_6H_4(CO)_2NCH_2CH_2NHSO_2CH_2C_6H_5 \xrightarrow[CH_3ONa]{CH_3I} o\text{-}C_6H_4(CO)_2NCH_2CH_2N(CH_3)SO_2CH_2C_6H_5 \xrightarrow{HCl} CH_3NHCH_2CH_2NH_2$$

The method is worthless for general synthetic work since only 2 g. of the sulfonamide could be alkylated at one time. (2) Winans and Adkins[4] describe the catalytic hydrogenation of $CH_2{=}NCH_2CN$ to monomethylethylenediamine, but the boiling point reported by them is not the same as that found by others. (3) Von Braun[5] and co-workers produced monomethylethylenediamine by the nitrous acid dephenylation of the acetyl derivative of $C_6H_5(CH_3)NCH_2CH_2NH_2$ (obtained from $C_6H_5(CH_3)NCH_2CH_2Br$ and liquid ammonia), but the yield is only a few per cent. of the theoretical. (4) Schotte[6] and co-workers describe the preparation of monoalkyl ethylenediamines in unspecified yields by the hydrochloric acid fission of $\beta$-guanido ethanols. $NH_2C(NH)N(R)CH_2CH_2OH \xrightarrow{HCl} RNHCH_2CH_2NH_2$. (5) Bleier[7] reports that monobenzylethylenediamine is a by-product from the hydrochloric acid fission of *sym*-dibenzenesulfonyldibenzylethylenediamine together with the expected dibenzylethylenediamine. (6) Van Alphen[8] states that monobenzylethylenediamine is produced in small amounts when the mixture resulting from the interaction of benzaldehyde and excess ethylenediamine is reduced with sodium and alcohol.

The present investigation has resulted in a synthesis for molecules of the type $RNHCH_2CH_2NH_2$ in pure condition and reasonable yields using well known reactions with cheap reagents.

$$NH_2CH_2CH_2NH_2 \xrightarrow{CH_3COOC_2H_5}$$

(1) For the third paper of this series see THIS JOURNAL, **62**, 1202 (1940).

(2) Schneider, *Ber.*, **28**, 3073 (1895).

(3) Johnson and Bailey, THIS JOURNAL, **38**, 2135 (1916).

(4) Winans and Adkins, *ibid.*, **55**, 4167 (1933).

(5) Von Braun, *Ber.*, **70**, 979 (1937).

(6) Schotte, *Z. physiol. Chem.*, **174**, 119 (1928); German Patent 446,547.

(7) Bleier, *Ber.*, **32**, 1829 (1899).

(8) Van Alphen, *Rec. trav. chim.*, **54**, 594 (1935).

$$NH_2CH_2CH_2NHCOCH_3 \xrightarrow[NaOH]{C_6H_5SO_2Cl} C_6H_5SO_2NHCH_2CH_2NHCOCH_3 \xrightarrow[NaOH]{RX} C_6H_5SO_2N(R)CH_2CH_2NHCOCH_3 \xrightarrow{HCl} RNHCH_2CH_2NH_2$$

The previously described[9] monoacetylation of ethylenediamine was modified by carrying out the reaction at room temperature. This procedure gives slightly lower yields than heretofore reported but enables one to prepare large quantities of material at once. The benzenesulfonation was conducted in the usual Schotten–Baumann manner and the alkylation was according to Hinsberg, but fission of the mixed acetyl-sulfonyl amide was accomplished by refluxing with 25% hydrochloric acid according to Schreiber and Shriner.[10] This modification of the original Hinsberg fission permits hydrolysis of large amounts of material without resort to pressure apparatus. The free base is liberated from its hydrochloride by one of the standard methods, and after drying successively over solid sodium hydroxide and metallic sodium the water-white amine is fractionated. The high degree of purity of the products is indicated by the narrow boiling ranges and the fact that they may be quantitatively converted to solid derivatives.

## Experimental

**Monoacetylethylenediamine.**—Five hundred twenty-eight grams (6 moles) of ethyl acetate and 1550 g. (18 moles) of commercial 70% aqueous ethylenediamine are allowed to stand together several days after the mixture has become homogeneous. The fraction boiling about 115–130° (5 mm.) is collected and redistilled at 125–130° (5 mm.). The monoacetylethylenediamine weighs 365 g. (60% theoretical) and contains only traces of ethylenediamine, lysidine and diacetylethylenediamine.

**N - Benzenesulfonyl - $N^1$ - acetylethylenediamine.**—Five hundred thirty grams (3 moles) of benzenesulfonyl chloride and 1200 g. (3 moles) of 10% aqueous sodium hydroxide are slowly and simultaneously added with stirring to 306 g. (3 moles) of monoacetylethylenediamine dissolved in an equal weight of water. After standing for several hours the solution is faintly acidulated with mineral acid and the amide filtered. The N-benzenesulfonyl-$N^1$-acetylethylenediamine is recrystallized from dilute ethanol, enough of the organic solvent being used to prevent oiling out of the amide. Dibenzenesulfonylethylenediamine, arising from the traces of ethylenediamine present in the monoacetylethylenediamine, is not soluble in the dilute ethanol and is filtered from the hot solution, while the diacetylethylenediamine also present as an impurity stays in solution in the cool mother liquor. The pure N-benzenesulfonyl-$N^1$-acetylethylenediamine melts at 103° (cor.)[11] and weighs 500 g. (about 70% theoretical).

The following description of the preparation of monomethylethylenediamine applies also for the preparation of monoethylethylenediamine and, with modifications, for the preparation of monobenzylethylenediamine.

**Monomethylethylenediamine.**—One hundred twenty-one grams (0.5 mole) N-benzenesulfonyl-$N^1$-acetylethylenediamine is dissolved in one equivalent of boiling alcoholic potassium hydroxide (35 g. of 85% potassium hydroxide dissolved in 200 cc. absolute ethanol) and 142 g. (1 mole) of methyl iodide added dropwise during fifteen minutes. The mixture is refluxed for two hours and the precipitated potassium iodide (about 60 g.) filtered from the cool reaction mixture. The filtrate is steam distilled until excess methyl iodide and ethanol are completely removed and the remaining alkylated sulfonamide[12] refluxed for twelve hours with 500 cc. of concentrated hydrochloric acid to which is added additional amounts of concentrated acid from time to time. The hydrolyzate is distilled nearly to dryness under diminished pressure and after addition of excess solid sodium hydroxide a concentrated water solution of the amine is distilled over. Solid sodium hydroxide is added to the distillate until the amine appears as a separate phase which is then drawn off and successively dried over fresh sodium hydroxide and finally by refluxing over metallic sodium. The sodium hydroxide is filtered and the amine is obtained as a water-white liquid by fractionation through a Vigreux column from a fresh piece of sodium metal. The yield is 28 g. (80% theoretical).

**Monobenzylethylenediamine.**—The isolation of monobenzylethylenediamine is accomplished by freeing the amine from the crude hydrochloride with excess sodium hydroxide, extracting with chloroform, drying over anhydrous magnesium sulfate and distilling at reduced pressure. The monobenzylethylenediamine is finally refluxed over metallic sodium and fractionated through a Vigreux column. The yield is 15 g. (20% theoretical). The low yield of the benzyl derivative is in part a reflection of two observed facts. (1) A significant amount of benzyl chloride is liberated during the hydrochloric acid fission of the benzylated amide[13] and (2) a considerable residue containing nitrogen and sulfur remains after distillation of the product.[14]

Complete identification of the amines was accomplished by converting them to dipicrates, dibenzamides and disulfonamides. The picrates were prepared in the usual way

(9) A. J. Hill and Aspinall, THIS JOURNAL, **61**, 822 (1939).

(10) Schreiber and Shriner, *ibid.*, **56**, 1618 (1934).

(11) Amundsen and Longley report 105° (cor.), *ibid.*, **62**, 2811 (1940).

(12) The alkylated sulfonamide may be triturated with 10% alkali to remove traces of unalkylated amide, but in some cases this is not necessary. No purpose is served by isolating the alkyl amides and they are rather difficult to crystallize, but the benzyl derivative may be obtained in good crystalline form from dilute ethanol; m. p. 92° (cor.) N calcd. 8.43; found 8.37.

(13) This "de-benzylation" is consistent with Bleier's observation that *sym.*-dibenzenesulfonyldibenzylethylenediamine yields some monobenzylethylenediamine during hydrochloric acid fission. *Ber.*, **32**, 1829 (1899).

(14) This residue represented some by-products rather than unreacted material, because repeated treatment with boiling hydrochloric acid for twenty-four hours failed to yield more of the monobenzyl amine.

TABLE I

MONOALKYL ETHYLENEDIAMINES AND SOLID DERIVATIVES

| Base | B. p., °C. | Mm. | Yield,[a] % | Dipicrate M. p., °C., cor. | Dipicrate N, % Calcd. | Dipicrate N, % Kjeld.[b] | Dibenzamide M. p., °C., cor. | Dibenzamide N, % Calcd. | Dibenzamide N, % Kjeld.[b] | Disulfonamide M. p., °C. cor. | Disulfonamide N, % Calcd. | Disulfonamide N, % Kjeld.[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CH_3$—$C_2H_7N_2$ | 115–116[c] | 757 | 33 | 220[d] | 21.05 | 20.98 | 112 | 9.93 | 9.92 | 94[e] | 7.91 | 7.82 |
| $C_2H_5$—$C_2H_7N_2$ | 129–131[f] | 759 | 20 | 195[g] | 20.51 | 20.36 | 120 | 9.46 | 9.47 | 126[h] | 5.32 | 5.32 |
| $C_6H_5CH_2$—$C_2H_7N_2$ | 100[i] | 4 | 10 | 222[j] | 18.42 | 18.36 | 188[k] | 7.82 | 7.86 | 198[l] | 4.76 | 4.75 |

[a] Over-all yield from ethylenediamine. [b] Reported analytical results are the averages of two or more determinations none of which differs from the theoretical by more than 0.15%. [c] 115–117°, *Ber.*, **70**, 979 (1937). [d] 220–222° decomp., THIS JOURNAL, **38**, 2135 (1916); 225° decomp., *Z. physiol. Chem.*, **174**, 119 (1928). [e] Dibenzenesulfonamide. [f] "About 130°," German Patent 446,547. [g] Precipitates as a solvate. After drying at 100° over phosphorus pentoxide for several hours, the picrate is distinctly lighter in color, melts higher and gives the correct analysis. [h] Di-*p*-bromobenzenesulfonamide. Recrystallized from absolute ethanol. [i] 162–165° at 20 mm., *Ber.*, **32**, 1829 (1899); 165° at 18 mm., *Rec. trav. chim.*, **54**, 594 (1935). [j] 222° decomp., *Ber.*, **32**, 1829 (1899). [k] 187°, *Rec. trav. chim.*, **54**, 594 (1935). [l] Di-*p*-bromobenzenesulfonamide. Recrystallized from glacial acetic acid.

in dilute ethanol and recrystallized from the same solvent. The amides were made from the appropriate acid chlorides by the Schotten–Baumann technique and were recrystallized from dilute ethanol except when otherwise stated.

The author is indebted to Mr. Samuel M. Raymond for some of the analytical data in this publication. The production of N-alkylated ethylenediamines by the reductive alkylation of monoacetylethylenediamine will be described in a forthcoming paper.

## Summary

1. A practical synthesis for pure monoalkyl ethylenediamines has been developed.

2. The amines produced have been thoroughly characterized as solid derivatives.

SWARTHMORE, PA. RECEIVED NOVEMBER 26, 1940

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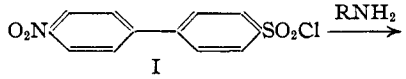
[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY, MEDICAL SCHOOL OF BUENOS AIRES]

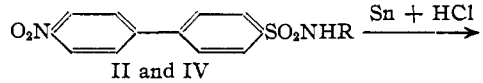
# Sulfonamide. II.[1] Diphenyl Derivatives

BY ARMANDO NOVELLI AND J. C. SOMAGLINO[2]

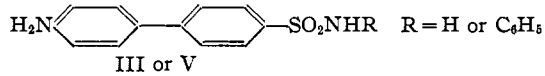
The appearance of a report by Van Meter and co-workers[3] prompts us to advance the publication of our results in the same field. By a method similar to that described by the above authors, we have prepared some derivatives, part of which we report here; we are not publishing details because they coincide along general lines. As we have prepared these compounds by another procedure as well, which also corroborates their structure, this experimental part is reported in detail. The reactions are summarized in the chart; we start from *p*-(*p*-nitrophenyl)-benzenesulfonyl chloride (I) and *p*-(*p*-nitrophenyl)-benzenesulfonamide (II) prepared according to Gabriel and Dambergis.[4]




I




II and IV




III or V

The aim of this work has been to determine whether, when amino and sulfonamide groups, fundamental in the action of sulfonamide as demonstrated by Fourneau and co-workers,[5] are found in different nuclei, they are still capable of maintaining their bactericidal effect. This is also interesting from a chemical point of view, because Le Fèvre and Turner[6] accept that in the molecule of diphenyl both of the nuclei are independent.

Besides the compounds described in this work, the derivatives 2-aminopyridine and 3-methyl-2-aminothiazole are being prepared (patent).

(1) First paper, *Ciencia*, **1**, 260 (1940).

(2) With a grant from the Asociacion Argentina para el Adelanto de las Ciencias.

(3) Van Meter, Bianculli and Lowy, THIS JOURNAL, **62**, 3146 (1940).

(4) Gabriel and Dambergis, *Ber.*, **13**, 1408 (1880).

(5) Fourneau, Tréfouel, Tréfouel, Nitti and Bovet, *Compt. rend. soc. biol.*, **122**, 652 (1936).

(6) Le Fèvre and Turner, *J. Chem. Soc.*, 246 (1928).