was carried out with molecular hydrogen under 40 pounds of pressure, and was stopped as soon as the theoretical amount of hydrogen had been absorbed (approximately 24 hr.). The catalyst was filtered off, and the dioxane removed by distillation under reduced pressure at about 40–50°. The residue was treated with 10% hydrochloric acid, charcoal added and filtered. The filtrate was made definitely alkaline with 15% ammonia and cooled. The free *p*-aminophenyl-2-amino-5-pyrimidyl sulfone (VIII), upon standing, separated as a white solid; yield crude powder, 2.2 g. or 88%. After recrystallization from water, the product melted at 207–208°; white, microscopic needles.

*Anal.* Calcd. for $C_{10}H_{10}O_2N_4S$: C, 47.99; H, 4.03; N, 22.39. Found: C, 48.37; H, 4.09; N, 22.41.

**2-Sulfanilamido-5-phenylmercaptopyrimidine (X).**—2-*p*-Nitrophenylsulfonamido-5-iodopyrimidine was prepared from 2-*p*-nitrophenylsulfonamidopyrimidine with a yield of 65–70% according to the method given by Shepherd and Fellows[9] for direct iodination of phenylsulfonamido heterocycles.

Eight and twelve-hundredths grams (0.02 mole) of pure and dry 2-*p*-nitrophenylsulfonamido-5-iodopyrimidine (m.p. 288–290°) was mixed with 50 ml. of quinoline (Eastman Kodak Company, practical grade). To this 4.22 g. (0.015 mole) of cupric thiophenolate was added and the mixture was then heated in an oil-bath at 180–190° for 30 minutes. Upon pouring the resulting dark solution into 200 ml. of 70–80% acetic acid and cooling, a precipitate separated which was filtered and washed with water. The precipitate was treated with 10% ammonia (10 ml./g.), charcoal added, filtered and to the filtrate an equal volume of 5 *N* sodium hydroxide solution was added. The sodium salt of 2-*p*-nitrophenylsulfonamido-5-phenylmercaptopyrimidine (IX) separated upon cooling. It was filtered off and washed with aqueous alkali. After solution in warm 20% alcohol, the free IX was precipitated by acidification with 30% acetic acid; yield 4.5 g. or 58%. The product after recrystallization from 95% ethanol melted at 223–224°; light yellow, fine crystals.

Three and eighty-eight hundredths grams (0.01 mole) of IX was boiled with 80 ml. of commercial ammonium sulfide solution for 5 minutes. The resulting red-brown mixture was added to a large amount of 60% acetic acid, and the solid formed was purified by solution in 50 ml. of 10% ammonia solution, heating with charcoal and filtering. The filtrate was poured into 50 ml. of 5 *N* sodium hydroxide solution and cooled. This caused separation of the sodium salt of X as a white solid, which was filtered and washed with aqueous alkali. The precipitate was dissolved in warm 20% alcohol and X was reprecipitated by acidification with 30% acetic acid. The yield was 2.8 g. or 78%. The product after recrystallization from 95% ethanol melted at 217–218°; white brilliant crystals.

*Anal.* Calcd. for $C_{16}H_{14}O_2N_4S_2$: N, 15.63. Found: N, 15.11.

PHILADELPHIA, PENNA.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

# Derivatives of 2,2-Dimethylethylenimine

BY HENRY M. KISSMAN[1] AND D. S. TARBELL

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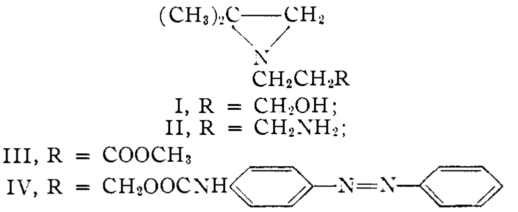
The urethan (XVI) derived from 2,2-dimethyl-1-(γ-hydroxypropyl)-ethylenimine and 4-(*p*-*d*-camphorsulfonylamino)-phenylazonaphthyl isocyanate was synthesized in an attempt to prepare optically active intermediates for the resolution of ethylenimine derivatives. The syntheses of two other optically active isocyanates are discussed.

This paper describes experiments carried out in continuation of work designed to test the resolvability of the trivalent nitrogen atom in 2,2-dimethylethylenimine.[2]

2,2-Dimethyl-1-(γ-hydroxypropyl)-ethylenimine (I), the amino analog (II) of which was reported previously,[2b] has been prepared by two methods. The first was the addition of 2,2-dimethylethylenimine to allyl alcohol in the presence of sodium allyloxide[3]; the second, and more satisfactory, method was the lithium aluminum hydride reduction of 2,2-dimethyl-1-(β-carbomethoxymethyl)-ethylenimine (III), which was prepared by the addition of 2,2-dimethylethylenimine to methyl acrylate.

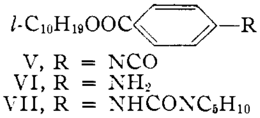


$(CH_3)_2C$—$CH_2$, N, $CH_2CH_2R$

I, R = $CH_2OH$;
II, R = $CH_2NH_2$;
III, R = $COOCH_3$
IV, R = $CH_2OOCNH-C_6H_4-N{=}N-C_6H_5$

A colored urethan IV was prepared from the alcohol (I) and *p*-phenylazophenyl isocyanate,[4] with the object of resolving it by adsorption on lactose following Prelog's elegant method for resolving Troeger's Base[5]; this was unsuccessful, due probably to lack of proper surface activity of the lactose.

The other derivatives of I and II were prepared from optically active reagents with the object of separating the resulting diastereoisomers by crystallization or chromatography,[6] and thus demonstrating the existence of asymmetry due to the trivalent nitrogen atom. The urethan and urea derivatives prepared from I and II and *l*-α-phenylethyl isocyanate[2a] were non-crystalline, as were also those from the isocyanate (V) derived from *l*-menthyl *p*-aminobenzoate (VI). This isocyanate was prepared from the ester V with phosgene and was characterized as the crystalline piperidine derivative VII.



*l*-$C_{10}H_{19}OOC-C_6H_4-R$

V, R = NCO
VI, R = $NH_2$
VII, R = $NHCONC_5H_{10}$

The synthesis of a colored optically active isocyanate was undertaken, using the *l*-menthoxyacetyl derivative of 4-amino-2-methyl-4′-nitroazobenzene (VIII) as starting material. However,

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[1] Beaunit Mills Fellow, 1949–1950.

[2] Previous papers: (a) T. L. Cairns, THIS JOURNAL, **63**, 871 (1941); (b) D. S. Tarbell and D. K. Fukushima, *ibid.*, **68**, 2499 (1946).

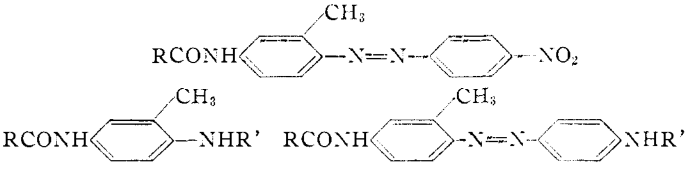
[3] *Cf.* O. Hromatka, *Ber.*, **75**, 131, 379 (1942); A. W. Weston, U. S. Patent 2,437,984 (*C. A.*, **42**, 4605 (1948)).

[4] L. C. Raiford and H. B. Freyermuth, *J. Org. Chem.*, **8**, 230 (1943).

[5] V. Prelog and P. Wieland, *Helv. Chim. Acta*, **27**, 1127 (1944).

[6] Examples of chromatographic separation of diastereoisomers are cited by L. Zechmeister, "Progress in Chromatography," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 10.

it was found that ammonium sulfide reduction of the nitro group[7] was accompanied by some cleavage of the azo linkage, with the formation of the diamine IX, as well as the desired product X; these substances were identified as their phenylurea derivatives XI and XII. Compound X could not be obtained in sufficient yield to make the method feasible.



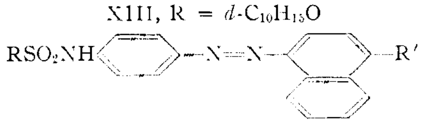
IX, R′ = H
XI, R′ = CONHC$_6$H$_5$

X, R′ = H
XII, R′ = CONHC$_6$H$_5$

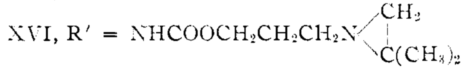
R = *l*-C$_{10}$H$_{19}$OCH$_2$

Another approach to a colored optically active isocyanate involved the coupling of the diazoimine from the *d*-camphorsulfonyl-*p*-phenylenediamine[8] (XIII) with α-naphthylamine to yield XIV. This was converted into the isocyanate XV and the latter was condensed with the ethylenimine derivative I to yield a deeply colored amorphous solid which had the composition required by structure XVI.

XIII, R = *d*-C$_{10}$H$_{15}$O



XIV, R′ = NH$_2$
XV, R′ = NCO



$$\text{XVI, R}' = \text{NHCOOCH}_2\text{CH}_2\text{CH}_2\text{N}\left<\begin{array}{l}\text{CH}_2\\ |\\ \text{C(CH}_3)_2\end{array}\right.$$

It is of interest to compare the difficulty of obtaining crystalline urethans or ureas from the ethylenimine derivatives I and II when optically active isocyanates are used with the ease with which such crystalline adducts are formed with inactive compounds such as phenyl, α-naphthyl and *p*-phenylazophenyl isocyanate. This seems to support the formation of diastereoisomers in the reaction with optically active compounds.

The infrared spectra of the ethylenimine derivatives I, II, III and several other compounds previously described[2b,9] will be discussed in detail in a future publication[10]; it may be mentioned, however, that all the compounds have a strong band near 1089 cm.$^{-1}$, which is provisionally regarded as characteristic of the ethylenimine ring.[11]

## Experimental[12]

**2,2-Dimethyl-1-(γ-hydroxypropyl)-ethylenimine** (I) (**A**).—To a stirred solution of 11.2 g. (0.071 mole) of 2,2-dimethyl-1-(β-carbomethoxyethyl)-ethylenimine[13] in 100 ml. of ether was added dropwise 55 ml. (0.41 mole) of a 0.761 molar solution of lithium aluminum hydride in ether over a period of 40 minutes. The mixture was refluxed for 30 minutes after completed addition and was then decomposed with wet ether. After separation from precipitated inorganic salts, the ether solution was dried over potassium carbonate; the inorganic salts were allowed to dry in air and were then extracted with chloroform for 24 hours in a Soxhlet apparatus. The chloroform extract was combined with the ether solution and the resulting mixture was freed from solvents and distilled under reduced pressure to yield 6.87 g. (76%) of a colorless liquid; b.p. 110° (24 mm.); $n^{20}\mathrm{D}$ 1.4535.

*Anal.* Calcd. for C$_7$H$_{15}$NO: C, 65.07; H, 11.70. Found: C, 64.88; H, 11.61.

A **phenylurethan** was prepared in hexane and after three recrystallizations from that solvent melted at 96.5–97°.

*Anal.* Calcd. for C$_{14}$H$_{20}$N$_2$O$_2$: C, 67.71; H, 8.12. Found: C, 67.53; H, 7.90.

An α-**naphthylurethan** was prepared and crystallized in the same solvent; m.p. 102.5–103°.

*Anal.* Calcd. for C$_{18}$H$_{22}$N$_2$O$_2$: C, 72.45; H, 7.43. Found: C, 72.87; H, 7.53.

The *p*-**phenylazophenylurethan** (IV) was prepared by refluxing I for a few minutes with an equivalent amount of *p*-phenylazophenyl isocyanate[4] in dry benzene. The orange substance melted sharply at 124° after several recrystallizations from benzene–hexane.

*Anal.* Calcd. for C$_{20}$H$_{24}$N$_4$O$_2$: C, 68.16; H, 6.86. Found: C, 68.57; H, 6.58.

(B).—To a hot solution of 2.3 g. of sodium (0.1 mole) in 17.4 g. (0.3 mole) of allyl alcohol was added 7.1 g. (0.1 mole) of 2,2-dimethylethylenimine. The mixture was kept at an internal temperature of 105° for 30 hours and, after having been cooled, was then poured into 125 ml. of water. The resulting solution was saturated with potassium carbonate, the colored upper layer which formed due to this treatment was combined with the chloroform extracts of the lower layer, and the mixture was distilled under reduced pressure. There was obtained 5.6 g. (42%) of a colorless liquid, b.p. 85–98° (12 mm.), which on redistillation yielded 3.3 g., b.p. 93–95° (6 mm.), $n^{23}\mathrm{D}$ 1.4536. No identifiable substance could be isolated from the colored odoriferous distillation residue (6.3 g.).

A **phenylurethan** (m.p. 97–97.5°) and α-**naphthylurethan** (m.p. 102–102.5°) prepared from the reaction product did not depress the melting points of the corresponding derivatives obtained from I prepared by method A.

*l*-*p*-**Carbomenthoxyphenyl Isocyanate** (**V**).—A solution of 5.24 g. (0.019 mole) of *l*-menthyl *p*-aminobenzoate (VI)[14] in 200 ml. of benzene was saturated with hydrogen chloride in the cold. Phosgene was then passed into the mixture for 4 hours while the latter was slowly brought to the reflux point. The solution was cooled, and solvent and excess phosgene were removed under reduced pressure without the use of external heat. The residue (5.80 g.) crystallized spontaneously when the last traces of solvent had been removed. Part of the material was distilled with great loss; b.p. 183° (2 mm.). The distillate solidified and was purified once more by evaporative distillation; m.p. 58–61°, $[\alpha]^{26}\mathrm{D}$ −74.25° (*c* 0.4943 in benzene). A few drops of dry piperidine was added to a small portion of the compound in hexane and the resulting **piperidine urea** (VII) after having been washed with pentane was recrystallized three times from hexane; m.p. 147–147.5°.

*Anal.* Calcd. for C$_{23}$H$_{34}$N$_2$O$_3$: C, 71.47; H, 8.86. Found: C, 71.23; H, 8.69.

**2-Methyl-4-(N-*l*-menthoxyacetyl)-amino-4′-nitroazobenzene (VIII).**—A solution of 9.30 g. (0.04 mole) of freshly distilled *l*-menthoxyacetyl chloride in benzene was added to 12.24 g. of 2-methyl-4-amino-4-nitroazobenzene[15] in

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[7] R. Meldola, *J. Chem. Soc.*, **43**, 432 (1883).

[8] G. T. Morgan and F. M. G. Mickelthwait, *ibid.*, **87**, 78 (1905); **91**, 1512 (1907). The more modern dipolar structure for the diazoimines is used; *cf.* K. H. Saunders, "The Aromatic Diazo Compounds," Edward Arnold Co., London, 1949, p. 36.

[9] D. S. Tarbell and P. Noble, THIS JOURNAL, **72**, 2657 (1950).

[10] K. N. Tanner, H. M. Kissman and P. Noble, in preparation.

[11] The infrared spectrum of ethylenimine itself has been studied by H. W. Thompson and W. T. Cave, *Trans. Faraday Soc.*, **47**, 95 (1951), and by H. F. Hofman, THIS JOURNAL, **73**, 3028 (1951).

[12] Melting points are uncorrected. Analyses by Micro-Tech Laboratories and Mrs. G. L. Sauvage.

[13] This compound was prepared by Mr. A. C. Boucher, from 2,2-dimethylethylenimine and methyl acrylate in 78% yield; b.p. 73–75° (8 mm.), $n^{23}\mathrm{D}$ 14380. *Anal.* Calcd. for C$_8$H$_{15}$NO$_2$: C, 61.12; H, 9.62. Found: C, 61.23; H, 9.42.

[14] K. L. McCluskey and B. C. Sher, THIS JOURNAL, **49**, 452 (1927).

[15] H. Mehner, *J. prakt. Chem.*, [2] **65**, 456 (1902).

70 ml. of anhydrous pyridine. The mixture was allowed to reflux for 3 hours, and was then cooled and poured slowly into 80 ml. of *N* hydrochloric acid and 40 ml. of benzene. A dark solid which remained undissolved was filtered off; it was identified as the hydrochloride of the starting amine and corresponded to 1.8 g. of that substance. The organic and aqueous layers of the filtrate were separated and the latter was extracted with another 50 ml. of benzene. The combined organic extracts were washed twice with dilute sodium bicarbonate solution and then with water. Partial evaporation of benzene and the addition of 20 ml. of hexane caused the precipitation of 14.24 g. (79%) of a red substance which after three recrystallizations from chloroform–ethanol melted at 144.5–145°. The substance was too highly colored to allow rotation measurements.

*Anal.* Calcd. for $C_{25}H_{32}N_4O_4$: C, 66.35; H, 7.13. Found: C, 66.20; H, 7.26.

**Reduction of 2-Methyl-4-(N-*l*-menthoxyacetyl)-amino-4′-nitroazobenzene.**—A suspension of 2.26 g. (0.005 mole) of VIII in 50 ml. of ethanol and 2 ml. of concentrated ammonium hydroxide was cooled to 5° and saturated with hydrogen sulfide.[7] Another 2 ml. of ammonium hydroxide was added and the mixture was stirred and warmed (55–60°) for 20 minutes, after which it was filtered free from sulfur and unreacted starting material, and poured into 150 ml. of water. The aqueous mixture was thoroughly extracted with ether; the ether was replaced by benzene and, after partial evaporation of that solvent there was obtained 15 ml. of a highly colored solution. This was chromatographed on a column of alumina (25 × 2 cm.). Elution with benzene yielded free sulfur and 0.4 g. of a colored substance which was identified as starting material by a mixed melting point. Elution with 10% ethyl acetate in benzene brought down 1 g. of a reddish gum which could not be obtained crystalline.

**3-(N-*l*-Menthoxyacetyl)-amino-6-(N-phenylcarbamyl)-aminotoluene (XI).**—A portion of this red gum was dissolved in benzene and the solution was saturated with hydrogen chloride. A white hydrochloride which crystallized from the dark green solution on standing, melted at 146–148° after recrystallization from benzene–methanol; $[\alpha]^{25}D$ −108° (*c* 0.01008 in methanol). The free base corresponding to this salt was obtained by dissolving 1 g. of the salt (prepared in another run) in 20 ml. of 3 *N* hydrochloric acid and neutralizing the solution with sodium bicarbonate. The mixture was extracted with ether and the combined ethereal extracts were dried over potassium carbonate and the solvent was removed under reduced pressure. This left a gummy substance which was boiled with benzene to remove traces of water, and was then allowed to react with 1 ml. of phenyl isocyanate in boiling benzene. Addition of pentane to the cooled mixture caused the precipitation of a white substance (0.6 g.), which was recrystallized three times from benzene–hexane and twice from methanol; m.p. 171–172°; $[\alpha]^{27}D$ −52.5° (*c* 0.0103 in chloroform).

*Anal.* Calcd. for $C_{26}H_{35}N_3O_3$: C, 71.36; H, 8.06. Found: C, 71.40; H, 8.10.

**2-Methyl-4-(N-*l*-menthoxyacetyl)-amino-4′-(N-phenylcarbamyl)-aminoazobenzene (XII).**—Another 1-g. portion of the red material obtained from the chromatogram was dissolved in 50 cc. of benzene and was saturated first with hydrogen chloride and then, at the boiling point, with phosgene (30 minutes). The color changed from deep green to red during this reaction. Most of the solvent and the excess phosgene was removed *in vacuo* and the residue was dissolved in hot hexane and decanted from tarry material. A solution of 2 ml. of aniline in 15 ml. of ether was added and the resulting yellow precipitate (0.8 g.) was filtered off and recrystallized three times from chloroform–methanol. It melted sharply at 229–230°, resolidified at 233° and melted finally with decomposition at 255–257°. This behavior did not change when the substance was recrystallized from benzene–hexane; $[\alpha]^{25}D$ −49.8° (*c* 0.00623 in acetone).

*Anal.* Calcd. for $C_{32}H_{39}N_5O_3$: C, 70.95; H, 7.26. Found: C, 70.95; H, 7.16.

The solution from which XII had been obtained yielded 0.4 g. of another substance upon further dilution with hexane. This material, which was white, melted at 168–170° after two recrystallizations from methanol; it did not depress the melting point of the phenylurea XI which had been obtained by the addition of phenyl isocyanate to the free base isolated from the chromatogram of the crude reduction mixture.

**4-(*p*-*d*-Camphorsulfonylamino)-phenylazonaphthylamine (XIV).**—An intimate mixture of the diazoimine XIII, prepared from *d*-camphorsulfonyl-*p*-phenylenediamine[16] according to the method of Morgan and Micklethwait,[8] (0.6 g., 0.018 mole), and 0.28 g. of α-naphthylamine was warmed on the steam-bath until it turned into a deep red gum. It was then taken up in 30 ml. of benzene and chromatographed on an alumina column (15 × 1.5 cm.). Ethyl acetate eluted 0.73 g. (85%) of a red substance which melted at 172–175° after one crystallization from 40% aqueous methanol. The substance slowly decomposed on standing and further recrystallization. A pure sample for analysis could not be obtained.

**4-(*p*-*d*-Camphorsulfonylamino)-phenylazonaphthyl Isocyanate (XV).**—A solution of 0.73 g. (0.0015 mole) of XIV in 60 ml. of dry benzene was saturated with hydrogen chloride, which caused the precipitation of a violet compound. Phosgene was then passed into the stirred, refluxing suspension for 30 minutes, and refluxing was continued for an additional 30 minutes. After this time, all the precipitate had gone into solution and the color had changed to red. Excess phosgene and most of the solvent was removed under reduced pressure and 30 ml. of dry hexane was added to the residue. This caused the precipitation of an orange substance which was filtered off and washed with hexane containing 10% benzene. The substance was not purified but used immediately in the following step.

**Reaction of 2,2-Dimethyl-1-(γ-hydroxypropyl)-ethylenimine with XV.**—A solution of 0.05 g. (0.00038 mole) of I in 5 ml. of dry benzene was added to 0.1737 g. (0.00035 mole) of the isocyanate XV in 20 ml. of the same solvent. The solution was refluxed for five minutes and then chromatographed on a column of alumina (15 × 1 cm.). The main reaction product, which was eluted with 20% ethyl acetate in benzene, was an orange material which melted at 118–120°; 0.12 g. (53%). The substance was amorphous and could only be purified by precipitating it with cyclohexane out of hot ethyl acetate solution. The compound was too highly colored to permit rotation measurements.

*Anal.* Calcd. for $C_{34}H_{51}N_5O_5S$: C, 63.62; N, 8.01. Found: C, 63.32; N, 7.98.

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(16) A. S. Galloway and J. Read, *J. Chem. Soc.*, 1219 (1936).