carbon atoms (2.52 kX.) expressed as a fraction of d_{100}. For $h = 80$, the denominator of (1) becomes zero at $\alpha = 18.3°$, and F_{h00} attains its maximum value. The direction of maximum polarizability of the crystal, $''\eta_\gamma$, should lie approximately in the direction of the dimers and thus affords another measure of the angle of tilt. η_γ makes an angle of 17° 23′ with $[d_{100}]$, in good agreement with the value of 18.3° derived from the diffraction data. The conventional "angle of tilt," which is the angle of the dimers with respect to the plane of the carboxyl groups, is $90° - \alpha$, or about 72°.

Acknowledgment.—The authors express their thanks to S. F. Herb for preparing the linoleic acid isomer used.

EASTERN REGIONAL RESEARCH LABORATORY[3]
AND THE DEPARTMENT OF CHEMISTRY
OF TEMPLE UNIVERSITY
PHILADELPHIA, PENNSYLVANIA

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[3] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

NEW COMPOUNDS

Preparation of 2-Bromo-4-nitroethylbenzene and α,α-Dibromo-4-nitroethylbenzene

2-Bromo-4-nitroethylbenzene.—*p*-Nitroethylbenzene,[1] 75.5 g. (0.5 mole) was brominated in the presence of 2.3 g. of iron powder.[2] After the gentle application of heat to start the reaction, a total of 81.6 g. (0.51 mole) of bromine was added at such a rate as to maintain the temperature at 60–70°. After standing over-night the mixture was heated, first on a steam-bath, and finally to 150° until the evolution of hydrogen bromide ceased. The product was washed with dilute sodium bisulfite and water, dissolved in ethyl alcohol, decolorized, dried and concentrated. The residue was distilled under diminished pressure to yield 64 g. (55%), b. p. 155–179° (37 mm.). The distillate partially solidified when cooled to −6°, and the crystalline material was recrystallized repeatedly from ethyl alcohol, and together with some further material from the supernatant liquid, yielded 38.5 g. (34%) of pale yellow prisms, m. p. 31–32°.[3] The material so purified boils at 155–157° (20 mm.).

Anal. Calcd. for $C_8H_8O_2NBr$: C, 41.76; H, 3.50; N, 6.09; Br, 34.73. Found: C, 41.96; H, 3.51; N, 6.2; Br, 34.7.

It was characterized by permanganate oxidation to 2-bromo-4-nitrobenzoic acid, m. p. 170°,[4] which on tin-hydrochloric acid reduction yields *m*-bromoaniline, identified as its acetyl derivative.

α,α-Dibromo-4-nitroethylbenzene.—*p*-Nitroethylbenzene, 83.2 g. (0.55 mole), 2.5 g. of iron powder, 0.2 g. of 20-mesh iron filings, and a crystal of iodine was treated with 175 g. of bromine as above except at 90–100°. After washing the product was steam distilled which removed a much reduced quantity of 2-bromo-4-nitroethylbenzene. The residue, which solidified on cooling, was dissolved in ether, decolorized, dried and the solvent removed, then recrystallized from ethyl alcohol to yield 20.8 g. (12%) of α,α-dibromo-4-nitroethylbenzene as pale yellow needles, m. p. 76–78°.

Anal. Calcd. for $C_8H_7O_2NBr_2$: C, 31.09; H, 2.29; N, 4.53; Br, 51.73. Found: C, 31.35; H, 2.29; N, 4.5; Br, 52.0.

Its identity is tentatively assigned on the bases that permanganate oxidation produces *p*-nitrobenzoic acid which was identified by reduction to *p*-aminobenzoic acid, and while the compound does not produce a precipitate with alcoholic silver nitrate at room temperature, it does on the application of heat.

Attempts to convert 2-bromo-4-nitroethylbenzene into 4-nitro-1,2-diethylbenzene[5] with ethyl bromide and sodium in anhydrous ether were unsuccessful.

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[1] Cline and Reid, THIS JOURNAL, **49**, 3150 (1927).

[2] Ferrum reductum or "iron by hydrogen" was used.

[3] Thermometers calibrated against U. S. P. Melting Point Standards.

[4] Scheufelen, *Ann.*, **231**, 172 (1885).

[5] Lambooy, THIS JOURNAL, **71**, 3756 (1949).

DEPARTMENT OF PHYSIOLOGY AND VITAL ECONOMICS
UNIVERSITY OF ROCHESTER
ROCHESTER 20, N. Y. JOHN P. LAMBOOY

Substituted α-(4-Morpholinyl)-acetonitriles and Related Compounds

The nitriles listed in the table were prepared by one or more of the following methods, adapted from reported procedures: (1) from morpholine and the cyanohydrin in the presence of potassium cyanide,[1] (2) from morpholine, the aldehyde or ketone–sodium bisulfite complex, and potassium cyanide,[1,2] or (3) from morpholine hydrochloride, the carbonyl compound, and potassium cyanide.[3] The recovery and purification of the product was essentially the same for each method: If the product was solid, it was removed by filtration, washed with cold water, and recrystallized from aqueous ethyl alcohol. If the product was an oil, it was extracted with ethyl ether, dried over anhydrous sodium sulfate, and vacuum distilled. Mandelonitrile gave a 55% yield of α-phenyl-α-(4-morpholinyl)-acetonitrile by method 1, whereas 85 and 82% yields, respectively, of the same compound were obtained when benzaldehyde was used in methods 2 and 3. With acetone the yields of nitrile were only 20% by either methods 2 or 3; with formaldehyde the yield was 78% by method 3.

α-Phenyl-α-(4-morpholinyl)-acetamide. A.—A mixture of 3.3 g. of potassium cyanide and 8.1 g. of benzylidene dimorpholine[4] in 20 ml. of water was refluxed on the water-bath until homogeneous (about eleven hours); some ammonia was evolved. The solution was filtered hot after dilution with 20 ml. more of water. Rosettes of needles, m. p. 153.5–154.5,[5] crystallized on cooling; recrystallization from water raised the melting point to 157.5–158.5°. The yield was 4.8 g. or 70%.

Anal. Calcd. for $C_{12}H_{16}O_2N_2$: N, 12.73. Found: N, 12.82.

The compound was readily soluble in alcohol, hot water, and cold concentrated hydrochloric acid, but only slightly soluble in diethyl ether.

B.—Hydrolysis of α-phenyl-α-(4-morpholinyl)-acetonitrile in cold concentrated sulfuric acid gave a product melting at 156° after one recrystallization from water. A mixed melting point with a sample prepared by A was the same. The yield was 4.3 g. or 79% of theory.

α-Phenyl-α-(4-morpholinyl)-thioacetamide.—The crude product as obtained from phenyl morpholinylacetonitrile and hydrogen sulfide by the method of Gabriel and

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[1] Knoevenagel, *Ber.*, **37**, 4082 (1904).

[2] v. Braun, *ibid.*, **41**, 2118 (1908); Bucherer and Schwalbe, *ibid.*, **39**, 2796 (1906).

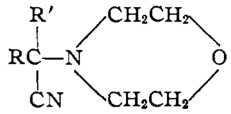
[3] Strecker, *Ann.*, **75**, 28 (1850); Zelinsky and Stadnikoff, *Ber.*, **39**, 1726 (1906); Marvel and Noyes, THIS JOURNAL, **42**, 2264 (1920).

[4] Zief and Mason, *J. Org. Chem.*, **8**, 5 (1943).

[5] All melting points are corrected.

TABLE I

SUBSTITUTED α-(4-MORPHOLINYL)-ACETONITRILES



R	R'	B. p., °C.	Mm.	M. p. (cor.), °C.	·HCl m. p., °C.	Formula	N Analyses, % Calcd.	N Analyses, % Found
H—	H—			60–61	171.5–172.5	$C_6H_{10}ON_2$	22.21	22.19
CH_3—	H—	127	26			$C_7H_{12}ON_2$	19.19	
C_2H_5—	H—	136–137	27			$C_8H_{14}ON_2$	18.17	18.06
$CH_3CH_2CH_2$—	H—	151–152	30			$C_9H_{16}ON_2$	16.65	16.73
$CH_3CH{=}CH$—	H—	169–171	26			$C_9H_{14}ON_2$	16.86	16.89
$(CH_3)_2CH$—	H—	132	19	54.5		$C_9H_{16}ON_2$	16.65	16.54
CH_3—	CH_3—	123–125	21			$C_8H_{14}ON_2$	18.17	18.00
C_2H_5—	CH_3—	130–132	20			$C_9H_{16}ON_2$	16.65	16.70
C_6H_5—	H—			67–68	199–200	$C_{12}H_{14}ON_2$	13.85	13.97
4-$CH_3OC_6H_4$—	H—			79–80	189.5–190.5	$C_{13}H_{16}O_2N_2$	12.06	11.97
2-ClC_6H_4—	H—	195–196	21	51–52	171–172	$C_{12}H_{13}ON_2Cl$	11.84	11.85
3-$CH_3C_6H_4$—	H—	197–198	20		183–184	$C_{13}H_{16}ON_2$	12.96	12.86
$OCH{=}CHCH{=}CH$—	H—	168–169	23		129–131	$C_{10}H_{12}ON_2$	14.58	14.42

Heymann[6] crystallized from water as plates; m. p. 168.6–170° (dec.). *Anal.* Calcd. for $C_{12}H_{16}ON_2S$: N, 11.86. Found: N, 11.89.

α-(4-Morpholinyl)-acetamide.—Five grams of chloroacetamide and 9.3 g. of morpholine in 35 ml. of benzene refluxed for three and one-half hours gave 6.1 g. of the amide (79%); shining plates from benzene, m. p. 122–122.5°. *Anal.* Calcd. for $C_6H_{12}O_2N_2$: N, 19.35. Found: N, 19.43.

α-(4-Morpholinyl)-thioacetamide.—One gram of material melting at 174–176° was obtained from 5.9 g. of morpholinylacetonitrile by the method of Olin and Johnson.[7] Recrystallization from benzene gave rectangular plates; m. p. 178–179°. From the mother liquors 3.1 g. of the starting nitrile were recovered. *Anal.* Calcd. for $C_6H_{12}ON_2S$: N, 17.49. Found: N, 17.38.

2-(4-Morpholinyl)-4-methylthiazole Hydrochloride.—A solution of 0.7 g. of α-(4-morpholinyl)-thioacetamide and 0.4 g. of chloroacetone in 5 g. of absolute ethyl alcohol was refluxed for one and a half hours on the water-bath. The resulting brown solution was filtered while hot and the filtrate evaporated to dryness. The solid residue was extracted with two 10-ml. portions of hot benzene to remove unchanged reactants, and the insoluble material was recrystallized by dissolving in a minimum amount of boiling 95% ethyl alcohol and adding two to three volumes of benzene. On cooling in an ice-bath, small plates separated which darkened and sintered at 193–195° and melted at 203–204°. *Anal.* Calcd. for $C_9H_{15}ON_2SCl$: N, 11.93. Found: N, 11.89.

2-(4-Morpholinyl)-4-methyloxazole Hydrochloride.—The same procedure as above was employed, except that 1.4 g. of morpholinylacetamide and 0.9 g. of chloroacetone were used; colorless needles, m. p. 172–173°. *Anal.* Calcd. for $C_9H_{15}O_2N_2Cl$: N, 12.81. Found: N, 13.00.

β-Phenyl-β-(4-morpholinyl)-ethylamine.—Five grams of α-phenyl-α-(4-morpholinyl)-acetonitrile in 70 ml. of absolute ethyl alcohol was reduced with 8 g. of sodium according to the procedure of Ladenburg.[8] The product was a colorless, mobile liquid with a strong ammoniacal odor; b. p. 143–145° at 23 mm.

The α-naphthyl isocyanate derivative melted at 212–213°. *Anal.* Calcd. for $C_{23}H_{25}O_2N_2$: N, 11.19. Found: N, 11.16.

The derivative with phenyl mustard oil melted at 187.5–188.5°. *Anal.* Calcd. for $C_{19}H_{23}OSN_3$: N, 12.31. Found: N, 12.23.

α-Phenyl-α-(4-morpholinyl)-acetic Acid.—Two grams of phenylmorpholinylacetamide in 25 g. of a 10% solution of sodium hydroxide was refluxed for five hours. The solution was neutralized with concentrated hydrochloric acid and any insoluble material removed by filtration and discarded. The filtrate was evaporated to dryness on the water-bath and the residue dried in a vacuum desiccator. The acid was recovered by repeatedly extracting the powdered residue with boiling absolute ethyl alcohol and evaporating the alcoholic extract. Recrystallization from benzene gave a product melting at 202° (dec.). The yield was 1.8 g. or 90%. *Anal.* Calcd. for $C_{12}H_{15}O_3N$: N, 6.36. Found: N, 6.27.

This acid is readily soluble in cold water, alcohol, or ethyl acetate, only moderately soluble in benzene, and difficultly soluble in diethyl ether or carbon tetrachloride. It gives a deep blue colored precipitate with copper sulfate solution. Attempts to hydrolyze α-phenyl-α-(4-morpholinyl)-acetonitrile to this acid with either a 6 *N* solution of hydrochloric acid or with a 2 *N* solution of potassium hydroxide were not successful.

α-(4-Methoxyphenyl)-α-(4-morpholinyl)-acetic Acid.—Four grams of the corresponding nitrile was refluxed for twelve hours with 3.0 g. of potassium hydroxide in 10 ml. of ethyl alcohol and 15 ml. of water. After adding 10 ml. of water, the solution was acidified with hydrochloric acid and allowed to stand overnight so that the precipitation was complete. The crude product was removed by filtration and recrystallized from 95% ethyl alcohol; needles, decomposing at 233–234° after some preliminary shrinking. *Anal.* Calcd. for $C_{13}H_{17}O_4N$: N, 5.58. Found: N, 5.65.

α-(4-Morpholinyl)-acetic Acid.—A solution of 6.1 g. of di-(4-morpholinyl)-methane and 2.2 g. of potassium cyanide in 10 ml. of water was refluxed until ammonia was no longer evolved. The solution was filtered and evaporated in a current of air to about 3 ml. The pasty mass was dried on a porous plate and then repeatedly extracted with hot benzene to remove any morpholinylacetamide. The residue was dissolved in a small volume of hot 95% ethyl alcohol, filtered, and treated with two volumes of hot benzene. On cooling, beautiful plates of the potassium salt separated; these crystals melted in their water of hydration at 76–78°. The yield was 2.3 g. *Anal.* Calcd. for $C_6H_{10}O_3NK{\cdot}2.5H_2O$: N, 7.65; H_2O, 19.7; K (anhydrous basis), 21.3. Found: N, 7.66; H_2O, 19.2; K, 20.7.

Ethyl α-(4-Morpholinyl)-acetate Hydrochloride.—A solution of 4.0 g. of morpholinyl acetonitrile in 30 g. of absolute ethyl alcohol, saturated with dry hydrogen chloride, was heated for six hours. The precipitated ammonium chloride was filtered from the hot solution and washed with 5 ml. of absolute alcohol. The filtrate on cooling deposited crystals melting at 173°; recrystallization from alcohol yielded plates, m. p. 174–174.5° (dec.).

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[6] Gabriel and Heymann, *Ber.*, **23**, 158 (1890).

[7] Olin and Johnson, *Rec. trav. chim.*, **50**, 72 (1931).

[8] Ladenburg, *Ber.*, **18**, 2956 (1885); **19**, 780 (1886).

A mixed melting point with the hydrochloride of morpholinylacetonitrile was 135–140°; a mixed melting point with the hydrochloride of the following compound was 173°. The yield was quantitative. *Anal.* Calcd. for $C_8H_{16}O_3NCl$: N, 6.68. Found: N, 6.69.

Ethyl α-(4-Morpholinyl)-acetate.—A solution of 5.5 g. of ethyl bromoacetate and 5.5 g. of morpholine in 20 ml. of benzene was refluxed for thirty minutes. After the solution was cold, 5.4 g. of morpholine hydrobromide (representing a 98% conversion) was removed by filtration, and the filtrate fractionated. The boiling point of the colorless ester was 227–228° at 767 mm. *Anal.* Calcd. for $C_8H_{15}O_3N$: N, 8.09. Found: N, 8.00.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WASHINGTON
SEATTLE 5, WASHINGTON
RONALD A. HENRY
WILLIAM M. DEHN

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Miscellaneous Derivatives of Morpholine

Diphenylcarbamyl Morpholide.—One-hundredth molar quantities of diphenylcarbamyl chloride and morpholine were mixed without benefit of dilution. When the mixture was cold, 20 ml. of water and 1.0 g. of sodium bicarbonate were added and the solution heated to boiling. The precipitated morpholide was removed by filtration and recrystallized twice from ethyl alcohol; large monoclinic prisms, m. p. 110–111°.[1] *Anal.* Calcd. for $C_{17}H_{13}O_2N_2$: N, 9.92. Found: N, 9.82.

Morpholine with Isothiocyanates.—The following thioureas were prepared by heating equivalent quantities of morpholine and the indicated isothiocyanate, and recrystallizing the product from aqueous ethyl alcohol or acetone.

TABLE I

RNCS (R =)	Formula of derivative	M. p. of derivative, °C.	N Analyses, % Calcd.	Found
Phenyl	$C_{11}H_{14}ON_2S$	130.5	12.60	12.62
o-Tolyl	$C_{12}H_{16}ON_2S$	144.5–145.5	11.86	11.79
p-Tolyl	$C_{12}H_{16}ON_2S$	151–151.5	11.86	11.84
Allyl	$C_8H_{14}ON_2S$	56–57	15.04	15.03

4-(Picryl)-morpholine.—To a hot solution of 5.0 g. of picryl chloride in 20 ml. of ethyl alcohol was added 3.4 g. of morpholine in 10 ml. of alcohol. The solution was refluxed for thirty minutes, then poured into 50 ml. of water. The precipitate was removed by filtration and washed carefully with water. The yield was 5.4 g., or 90%; m. p. 160–161°. Recrystallization from ethyl alcohol gave orange-yellow needles exhibiting two melting points. If heated rapidly, the compound melted at 147.5–148.5°, then resolidified and melted a second time at 166–166.5°. If heated slowly only the second melting point was observed. *Anal.* Calcd. for $C_{10}H_{10}O_7N_4$: N, 18.79. Found: N, 18.45.

4-(Picramyl)-morpholine.—This compound was prepared by the reduction of 4-(picryl)-morpholine with hydrogen sulfide in ammoniacal ethyl alcohol; dark red, fern-like crystals from 95% ethyl alcohol, decomposing at 256°. *Anal.* Calcd. for $C_{10}H_{12}O_5N_3$: N, 20.89. Found: N, 20.80.

(4-Morpholinyl)-thiocarbonic Acid Amide.—A solution of 2.1 g. of morpholine hydrochloride, 1.6 g. of potassium thiocyanate, and 10 ml. of water was evaporated to dryness on the water-bath. The amide was separated from the potassium chloride by extraction with absolute ethyl alcohol; partial evaporation of the alcohol and cooling gave needles, which melted at 111.5–112.5° after a second crystallization from absolute alcohol.

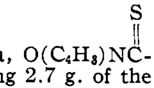
Anal. Calcd. for $C_5H_{10}ON_2S$: N, 19.2. Found: N, 19.3.

N,N,N',N'-Bis-(oxydiethylene)-thiuram Sulfide, O(C4-

$O(C_4H_8(N\underset{\|}{\overset{}{C}}SCN(C_4H_8)O$ $\left(\text{with } =S \text{ on each C}\right)$

oxydiethylene thiuram disulfide,[2] 0.7 g. of potassium cyanide, 40 ml. of 95% ethyl alcohol, and 10 ml. of water was refluxed for thirty minutes. The precipitate that formed when 50 ml. of water was added was removed by filtration and washed with water. One recrystallization from alcohol gave bright yellow prismatic needles; m. p. 126–126.5°. *Anal.* Calcd. for $C_{10}H_{16}O_2N_2S_3$: N, 9.21. Found: N, 9.21.

N,N,N',N'-Bis-(oxydiethylene)-thiourea,



$O(C_4H_8)N\overset{\overset{S}{\|}}{C}N(C_4H_8)O$.—The melt obtained by heating 2.7 g. of the thiuram disulfide[2] with 1.5 g. of morpholine for four hours at 120° was extracted with 10 ml. of water. The residue consisted of sulfur. The filtrate upon partial evaporation yielded a compound melting at 85 to 90°; two recrystallizations from water gave colorless, hexagonal plates of the monohydrate; m. p. 89.5–90°. *Anal.* Calcd. for $C_9H_{18}O_3N_2S$: N, 11.93. Found: N, 11.92, 11.94.

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[1] All melting points are corrected.

[2] Prepared by Schupe, *J. Assoc. Off. Agr. Chem.*, **23**, 824 (1940), by the action of potassium ferricyanide on morpholinium (4-morpholinyl)-dithiocarbamate.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WASHINGTON
SEATTLE 5, WASHINGTON
RONALD A. HENRY
WILLIAM M. DEHN

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Some Derivatives of the 3- and 5-Nitro-2-aminopicolines[1]

In connection with our work on the cyclization of 2-aminopyridine derivatives it became of interest to prepare the following compounds derived from the 3- and 5-nitro-2-aminopicolines.

3- and 5-Nitro-2-aminopicolines.—These were prepared by the nitration of the 2-aminopicolines. All except 3-nitro-2-amino-5-methylpyridine have been previously reported.[2,3,4] This compound was prepared by the nitration of 10 g. (0.093 mole) of 2-amino-5-methylpyridine at 0° in sulfuric acid following the method of Seide.[3] The yield of pale yellow crystals was 8.5 g. (60%), m. p. after recrystallization from water, 190–191°. *Anal.*[5] Calcd. for $C_6H_7O_2N_3$: N, 27.45. Found: N, 27.38.

2,3-Diaminopicolines.—These were prepared by low pressure catalytic hydrogenation of the corresponding 3-nitro-2-aminopicolines in ethanol solution using a palladium-on-charcoal catalyst. In each case the reaction required twenty-four hours for completion when 7.7 g. (0.05 mole) of the starting material was used. The products were purified by recrystallization from benzene-hexane mixture. The purified diaminopicolines darkened rapidly on exposure to air and eventually became tars. When this procedure was applied to the 5-nitro-2-aminopicolines only tars could be isolated from the hydrogenation.

2,3-Diamino-4-methylpyridine.—Yield 4.3 g. (70%), m. p. 115–116°. *Anal.*[5] Calcd. for $C_6H_9N_3$: N, 34.15. Found: N, 34.06.

2,3-Diamino-5-methylpyridine.—Yield 2.0 g. (32%), m. p. 85–86°. *Anal.*[5] Calcd. for $C_6H_9N_3$: N, 34.15. Found: N, 34.24.

2,3-Diamino-6-methylpyridine.—Yield 3.6 g. (54%), m. p. 69–70°. *Anal.*[5] Calcd. for $C_6H_9N_3$: N, 34.15. Found: N, 34.00.

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[1] The work described in this paper was carried out under a Frederick Gardner Cottrell Special Grant-in-Aid from the Research Corporation.

[2] Seide, *Ber.*, **57**, 791 (1924).

[3] Seide, *ibid.*, **57**, 1802 (1924).

[4] Seide, *J. Russ. Phys.-Chem. Soc.*, **50**, 534 (1924).

[5] Microanalysis by the Clark Microanalytical Laboratory, Urbana, Ill.