was refluxed and stirred for three hours. The solution was cooled and acidified to congo red with hydrochloric acid and then extracted five times with a total of 1 l. of ethyl ether. After drying over calcium sulfate, the solvent was removed by distillation from the steam-bath, and the residue was recrystallized several times from carbon tetrachloride giving 5 g. (61.5% yield) of product melting at 91–92°.

Anal.[2] Calcd. for $C_6H_6O_3S$: C, 45.56; H, 3.82. Found: C, 45.90; H, 3.77.

(2) Analyses by Oakwold Laboratories, Alexandria, Va.

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2-Acetylfuran Diethyl Mercaptol

In a cooled pressure bottle was placed 5.5 g. (0.05 mole) of 2-acetylfuran, 15 g. (0.234 mole) of ethyl mercaptan and 25 ml. of dry toluene containing 100 mg. of hydrogen chloride. The bottle was stoppered and shaken vigorously, a violet-colored water layer forming immediately. After refrigeration for three hours, the reaction mixture was extracted several times with a saturated solution of sodium bicarbonate, after which the organic layer was dried over potassium carbonate, filtered therefrom and then fractionated to give a yellowish oil boiling at 93–96° (2.5 mm.) in a yield of 4.2 g. (46.7%).

Anal.[1] Calcd. for $C_{10}H_{16}OS_2$: C, 55.51; H. 7.45; S, 29.64. Found: C, 56.11, H, 7.66; S, 29.73.

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(1) Analyses by Oakwold Laboratories, Alexandria, Va.
(2) Present address: Oxford Products, Inc., Cleveland 3, Ohio.

Thiophene-2-methylisothiouronium Chloride and 2-(thiophene-2′-methylthio)-4-methyl-6-oxypyrimidine

Thiophene-2-methylisothiouronium Chloride.—In a 250-ml. three-neck flask fitted with a sealed stirrer and reflux condenser with drying tube, was placed 26.5 g. (0.2 mole) of thiophene-2-methyl chloride,[1] 15.2 g. (0.2 mole) of thiourea and 75 ml. of anhydrous ethanol. The solution was stirred and refluxed gently for five hours. At the end of that time, the volatiles were removed by distillation from the steam-bath under reduced pressure, and the residue washed thoroughly with anhydrous ether, giving 40.8 g. (98% yield) of a white crystalline product melting at 160–161°.[2] The material was of sufficient purity to be used in the subsequent reaction.

2-(Thiophene-2′-methylthio)-4-methyl-6-oxypyrimidine.—The procedure of Johnson and Bailey[3] for the synthesis of thiopyrimidines was used. In a 250-ml. three-neck flask fitted with a sealed stirrer, reflux condenser and drying tube, thermometer and dropping funnel was placed 16.7 g. (0.06 mole) of thiophene-2-methylisothiouronium chloride, 11 g. (0.085 mole) of freshly distilled ethyl acetoacetate and 60 ml. of anhydrous ethanol. The mixture was stirred and chilled to 0 ± 2°, and a solution of 3.7 g. (0.161 mole) of sodium in 100 ml. of anhydrous ethanol was added during one hour. The low temperature was maintained for an additional hour and the mixture was then allowed to stand overnight at room temperature. The solvent was removed by distillation at reduced pressure, the residue suspended in 50 ml. of water and acidified to litmus with glacial acetic acid, causing the formation of a precipitate. This was filtered by suction, washed with a little cold water and ether and recrystallized four times from ethanol to give 9.5 g. (50%) of a product melting at 161°.

Anal.[4] Calcd. for $C_{10}H_{10}N_2OS_2$: C, 50.40; H, 4.23. Found: C, 49.68; H, 4.09.

The technical assistance of Mr. Herbert Landesman is gratefully acknowledged.

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(4) Analyses by Oakwold Laboratories, Alexandria, Va.
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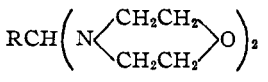
Some Derivatives of Morpholine

The compounds listed in the table were prepared by heating for five minutes on a steam-bath 0.02 mole of the appropriate aldehyde, dissolved in 5 ml. of 95% ethyl alcohol, with 3.5 g. of morpholine. The solution was then cooled in an ice-bath and seeded or scratched to induce crystallization; the crude product was removed by filtration and recrystallized from a small volume of ethyl alcohol, acetone or diethyl ether. The yields were essentially quantitative if additional crops were recovered by evaporating the mother liquors. These compounds are soluble in all the common organic solvents; they are readily hydrolyzed.



R	Formula	M. p., °C. (cor.)	N Analyses, %[a] Calcd.	Found
2-$NO_2C_6H_4$–	$C_{15}H_{21}O_4N_3$	130.5–131.5	13.68	13.48
3-$NO_2C_6H_4$–	$C_{15}H_{21}O_4N_3$	132–133	13.68	13.46
2-ClC_6H_4–	$C_{15}H_{21}O_2N_2Cl$	98–99	9.44	9.43
4-ClC_6H_4–	$C_{15}H_{21}O_2N_2Cl$	135–136	9.44	9.25
2-HOC_6H_4–	$C_{15}H_{22}O_3N_2$	123–124	10.07	10.09
4-$CH_3OC_6H_4$–	$C_{16}H_{24}O_3N_2$	114.5–115.5	9.58	9.58
4-$(CH_3)_2NC_6H_4$–	$C_{17}H_{27}O_2N_3$	130.5	13.76	13.68
3,4-$CH_2O_2C_6H_3$–	$C_{16}H_{22}O_4N_2$	109–110	9.15	9.14
	$C_{13}H_{20}O_3N_2$	120–120.5	11.10	11.17

[a] Micro-Dumas method.

Non-crystallizable sirups were formed under these conditions with 3- and 4-methylbenzaldehyde, 3-hydroxybenzaldehyde and 2-methoxybenzaldehyde.

A 1:1-addition product was isolated when 0.04 mole of morpholine was added slowly with agitation to 0.04 mole of furfural at 0°. The solid product, after extraction with small quantities of cold absolute diethyl ether, melted at 49–50° with decomposition.

Anal. Calcd. for $C_9H_{13}O_3N$: N, 7.64. Found: N, 7.92.

On standing, this addition product decomposed to furfural and 4,4′-furfurylidenedimorpholine, m. p. 120–120.5°. 2-Chlorobenzaldehyde and salicylaldehyde also yielded very unstable 1:1-addition products with morpholine.

4,4′-Benzylidenedimorpholine–Sulfur Dioxide Addition Product.—A solution of 5 g. of benzylidenedimorpholine[1] in 60 ml. of diethyl ether was cooled in a salt–ice mixture and saturated with dry sulfur dioxide. A white solid precipitated almost immediately; it was recovered by filtration and washed with three 10-ml. portions of ether; m. p. 131–133°. This material was water soluble

(1) Blicke and Leonard, THIS JOURNAL, **68**, 1934 (1946).
(2) All melting points were taken with a Fisher–Johns apparatus.
(3) Johnson and Bailey, THIS JOURNAL, **35**, 1007 (1913).

(1) Zief and Mason, *J. Org. Chem.*, **8**, 5 (1943); Herlocker, Kleinholz and Watkins (to Sinclair Refining Co.), U. S. Patent 2,388,058 (1945).

and was decomposed by acid with the evolution of sulfur dioxide.

Anal. Calcd. for $C_{15}H_{22}O_2N_2.SO_2$: N, 8.58. Found: N, 8.50.

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Preparation of N-Substituted Aminoacetals[1]

In the course of an extensive investigation involving the syntheses of compounds possessing anti-histaminic or spasmolytic properties, the need arose for some N-substituted aminoacetals of the general formula $R'-N(R'')-CH_2-CH(OR)_2$, where R may be methyl or ethyl and R′ and R″ may be hydrogen, alkyl, N-substituted aminoalkyl, -arylalkyl or heterocyclic groups. The products were all prepared by refluxing ethyl chloroacetal or methyl chloroacetal[2] with two or more equivalents of the amine[3] for a period of time which varied with the nature of the amine. In the case of di-*n*-butylaminoacetal best yields were obtained after a reflux period of five days. Most of the products were refluxed for three to five days. The time of reflux was decreased in the preparations of dimethyl benzylaminoacetal to two and one-half hours, of dimethyl cyclohexylaminoacetal to sixteen hours, of dimethyl piperidinoacetal to twenty hours and of dimethyl morpholinoacetal and of dimethyl methyl benzylacetal to six and one-half hours because the yields of these products were not improved, and in many cases were actually decreased, by a longer reaction time. Dimethyl diethylaminoacetal was prepared by refluxing the reaction mixture for twenty-four days because of the low boiling point of diethylamine. After cooling, ether was added until precipitation of the amine hydrochloride seemed complete. This mixture was filtered and the precipitate washed well with ether. After removal of the ether, the residue was fractionated *in vacuo*, using a short Vigreux column.

The hydrochlorides were prepared by treating an anhydrous ether solution of the free base with ethereal hydrogen chloride. The salt was separated by filtration, washed well with dry ether and recrystallized from an appropriate solvent. Oxalates were similarly prepared. Methiodides were prepared by treating the free base with excess methyl iodide at room temperature until the mass solidified. This was suspended in dry ether, filtered, washed well with ether and recrystallized.

When condensation with di-isopropyl- or dicyclohexylamines was attempted, no precipitate of amine hydrochloride of any significant amount appeared even after a week's refluxing, and the starting materials were recovered unaltered. This has been experienced similarly by others. Smith and Burn[4] were unable to esterify dicyclohexylacetic acid with ethyl alcohol while Braun and Fischer[5] experienced the same difficulty with di-isopropylacetic acid. Burnet, *et al.*,[6] reported a very low yield of product

TABLE I

N-SUBSTITUTED AMINOACETALS OF FORMULA $\begin{matrix} R' \\ R'' \end{matrix}\!\!>\!N-CH_2-CH(OR)_2$

Aminoacetals						Derivatives			N Analyses, %	
R	R′	R″	B. p. °C.	B. p. Mm.	Yield, %	Formula	Solvent	M. p., °C.	Calcd.	Found
Me	Et	Et	155–163	764	24.4[a]	$C_8H_{19}NO_2\cdot CH_3I$	Acetone–ether	75–76	4.62	4.64
Me	*n*-Pr	*n*-Pr	96–97	22	53.2[b]	$C_{10}H_{23}O_2N\cdot CH_3I$	[c]	53–55	4.23	4.12
Me	Allyl	Allyl	77–83	10	44.8	$(C_{10}H_{19}NO_2)_2H_2C_2O_4$	Ethyl acetate–ether	61–62	6.08	5.73
Me	*n*-Bu	H	86–90	19	76.6[d]	$C_8H_{19}NO_2\cdot HCl$	Methanol–ether	158.5 (dec.)	7.09	7.08
Me	*n*-Bu	*n*-Bu	119–120	18	68.3	$(C_{12}H_{27}NO_2)_2H_2C_2O_4$	Acetone	98–99	5.34	5.16
Et	*n*-Bu	*n*-Bu	115.5–117.5	12	81	$C_{14}H_{31}NO_2\cdot CH_3I$	Ethyl acetate–ether[e]	72–73	3.61	3.76
Me	Methallyl	H	75	25	57.8	$(C_8H_{17}NO_2)_2H_2C_2O_4$	Ethanol	185–186.5	6.86	7.19
Me	Methallyl	Methallyl	102–104	13	35	$(C_{12}H_{23}NO_2)\cdot HCl$	Methanol–ether	116–117	5.60	5.42
Me	$(Et)_2N(CH_2)_4-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}$	H	137.5–139	10	38.2	$C_{18}H_{30}N_2O_2\cdot 2HCl$	Isopropyl alc.–ether	131–132 (dec.)	8.77	8.77
Me	Cyclohexyl	H	118–119	17	77.8	$C_{10}H_{21}NO_2\cdot HCl$	Methanol–ether	139–140	6.26	6.59
Et	Cyclohexyl	H	141–145	23	80	$C_{12}H_{25}NO_2\cdot HCl$	Methanol–ether	120.5–121 (dec.)	5.56	5.65
Me	Piperidino[f]		94–96	19	91.7	$C_9H_{19}NO_2\cdot CH_3I$	Acetone[g]	134.5–134.8	4.44	4.35
Et	Piperidino[f]		110	18	80.5[h]	$C_{11}H_{23}NO_2\cdot CH_3I$	Acetone–ether	118–119	4.08	4.12
Me	Morpholino[f]		107–108	19	76.3	$C_8H_{17}NO_3\cdot HCl$	Acetone[i]	136–138 (dec.)	6.62	6.71
Et	Morpholino[f]		123	25	70.8	$C_{10}H_{21}NO_3\cdot HCl$	Acetone[j]	146–147 (dec.)	5.84	5.57
Me	Benzyl	H	147–149	18	72.7	$C_{11}H_{17}NO_2\cdot HCl$	Methanol–ether	110–111 (dec.)	6.05	5.87
Me	Benzyl	Me	130–132	13	60.1	$C_{12}H_{17}NO_2\cdot HCl$	[c]	107–108 (dec.)	5.70	5.96
Me	Benzyl	Benzyl	96	0.03	73.9	$C_{18}H_{23}NO_2\cdot HCl$	Methanol–ether	154 (dec.)	4.35	4.33
Me	Phenylethyl	H	149–153	12	43	$C_{13}H_{21}O_2N\cdot HCl$	Ethyl acetate	109–111 (dec.)	13.65[k]	13.75

[a] The corresponding diethyl acetal has been described by Stoermer and Prall, *Ber.*, **30**, 1505 (1897) and Guha, Rao and Verghese, *Current Sci.*, **12**, 82–83 (1938). [b] Refluxing for nineteen and one-half hours gave only a 27.4% yield. [c] The salt was not recrystallized. [d] The corresponding diethyl acetal has been prepared by Paal and Van Gember, *Arch. Pharm.*, **246**, 307–311 (1908). [e] The oxalate, recrystallized from the same mixture, melted at 118–119°. Analysis of the free base, $C_{14}H_{31}O_2N$; Calcd.: N, 5.71. Found: N, 5.70. [f] The radical replaces R′R″N–. [g] The hydrochloride, recrystallized from the same solvent, melted at 130–131°. [h] Prepared by Stoermer and Burkert, *Ber.*, **28**, 1248 (1895). [i] The methiodide, recrystallized from methanol–ether, melted at 194–196°. [j] The methiodide, recrystallized from acetone–ether, melted at 131.5–132.5°. [k] Chloride analysis.

(1) The authors gratefully acknowledge the financial assistance in this project of Endo Products, Inc.

(2) When this project was initiated, ethyl chloroacetal was available from the Niacet Chemicals Corp. and this compound was used in the preparation of several of the compounds described in this paper. When the company discontinued production of this compound, it was replaced by methyl chloroacetyl, presently available from the General Aniline and Film Corp.

(3) The amines were all commercial products and were used without further purification. Diallylamine, methallylamine and dimethallylamine were generously contributed by the Shell Chemical Co., Emeryville, Calif.

(4) Smith and Burn, THIS JOURNAL, **66**, 1494 (1944).

(5) Braun and Fischer, *Ber.*, **66B**, 101 (1933).

(6) Burnett, Jenkins, Peet, Drager and Adams, THIS JOURNAL, **59**, 2349 (1937).