TABLE I

HAMMICK REACTIONS WITH PICOLINIC ACID[a] AND VARIOUS CARBONYL COMPOUNDS

Carbonyl compound	Product	Yield Grams	Yield %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Benzaldehyde	Phenylpyridylcarbinol[d]	1.3	17[b]	78	...	...	...	..
		4.1	54[c]					
Benzophenone	Pyridyldiphenylcarbinol[d]	2.1	21[b]	105	...	...	..	.
		4.8	48[c]					
Acetophenone	Phenylpyridylmethylcarbinol[d]	1.9	23[b]	152 (745 mm.)[c]	...	...	..	..
		4.2	50[c]					
p-Methoxybenzaldehyde	*p*-Methoxyphenylpyridylcarbinol	2.3	26[b]	131				
		5.1	59[c]					
m-Nitrobenzaldehyde	*m*-Nitrophenyl pyridyl ketone	1.5	15[b]					
		4.7	48[e]	118	63.22	63.50	3.53	3.32
m-Nitroacetophenone	*m*-Nitrophenylpyridylmethylcarbinol	2.0	20[d]	130	63.91	64.12	4.91	4.86
		4.1	42[c]					
p-Chlorobenzaldehyde	*p*-Chlorophenylpyridylcarbinol	2.0	22[c]	83	65.96	66.32	4.51	4.43
		5.2	58[c]					

[a] 5 g. of acid in 30 g. of carbonyl compound. [b] Refers to reaction without solvent. [c] Refers to reaction with solvent (*p*-cymene). [d] Reference 1 and 2. [e] This is the boiling point.

TABLE II

Acid	Aldehyde	Temp., °C.	Result
Pyrimidine-4-carboxylic	Anisaldehyde	245	Neg.
Thiazole-2-carboxylic	Anisaldehyde	90	Neg.
	Benzaldehyde	90	Neg.
4,5-Dimethylthiazole-2-carboxylic	Anisaldehyde	93	Neg.
	Benzaldehyde	93	Neg.
4-Methylthiazole-5-carboxylic	Benzaldehyde	175	Neg.
	Anisaldehyde	175	Neg.
2-Methylthiazole-4-carboxylic	Benzaldehyde	178	Neg.
	Anisaldehyde	178	Neg.
o-Nitrobenzoic	Benzaldehyde	175	Neg.
	Anisaldehyde	175	Neg.
2,4-Dinitrobenzoic	Benzaldehyde	165	Neg.
	Anisaldehyde	165	Neg.

tained in *p*-cymene. These findings are in agreement with those previously reported by Tilford,[3] Shelton and Van Campen on the effect of solvents on this reaction. The experimental procedure was the same as that employed by Hammick.[1] The yields utilizing *p*-cymene as solvent for the reaction are reported under yield as (b) in Table I.

p-Nitrobenzaldehyde, 2,4-dinitrobenzaldehyde, cinnamaldehyde and *p*-dimethylaminobenzaldehyde gave negative results both with and without the addition of solvents.

In an attempt to extend the reaction to acids other than those successfully employed by Hammick, the reaction was carried out on the thiazole, pyrimidine and nitrobenzoic acids listed in Table II. The reactions were carried out in anisaldehyde and, where the decarboxylation temperature of the acid was low enough, in benzaldehyde. All of the acids gave negative results in that they did not yield the expected carbinol, a coupling product between the decarboxylated acid and the carbonyl compound. Hammick[1] has shown that 2,4,6-trinitrobenzoic acid gives a negative reaction.

The reaction was also carried out on various methyl substituted picolinic acids, utilizing anisaldehyde as the carbonyl reactant and *p*-cymene as the solvent. The results are reported in Table III. All of the methyl substituted picolinic acids gave a positive Hammick reaction and the expected coupling products.

TABLE III

HAMMICK REACTIONS ON METHYL SUBSTITUTED PICOLINIC ACIDS IN 30 GRAMS OF ANISALDEHYDE AND 30 GRAMS OF *p*-CYMENE

Methyl substituted picolinic acid[a]	Product, *p*-methoxyphenylcarbinol	Temp., °C.	Yield, Grams	Yield, %	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
3-Methyl	3-Methylpyridyl-	165	2.8	35	68	73.36	73.23	6.55	6.39
4-Methyl	4-Methylpyridyl-	173	4.9	53	96	73.36	73.10	6.55	6.50
5-Methyl	5-Methylpyridyl-	177	4.3	47	75	73.36	73.21	6.55	6.44
6-Methyl	6-Methylpyridyl-	170	5.2	57	77	73.36	73.53	6.55	6.58
4,6-Dimethyl	4,6-Dimethylpyridyl-	174	5.4	49	95	74.07	74.25	6.76	6.57

[a] 5.5 grams in each case except for 4,6-dimethylpicolinic acid where 6 g. was used.

DEPARTMENT OF CHEMISTRY
FORDHAM UNIVERSITY
NEW YORK 58, N. Y.

---

[3] C. H. Tilford, R. S. Shelton and M. S. Van Campen, THIS JOURNAL, **70**, 4001 (1948).

Reactions of Ethylenimines. IV. With Carbon Disulfide

BY LEALLYN B. CLAPP AND JOHN W. WATJEN[1]

RECEIVED JULY 24, 1952

In repeating Gabriel's[2,3] synthesis of a 2-thiothiazolidone from an ethylenimine and carbon disulfide in ether, a 27% yield (Gabriel reported no yields) of 4,4-dimethyl-2-thiothiazolidone was ob-

---

[1] Taken in part from the Senior Thesis of John W. Watjen, Brown University, June, 1952.

[2] S. Gabriel and R. Stelzner, *Ber.*, **28**, 2929 (1895).

[3] S. Gabriel and C. F. von Hirsch, *ibid.*, **29**, 2747 (1896).

TABLE I

2-THIOTHIAZOLIDONES

Substituents	M.p., °C.	Yields From ethylenimine	Yields From amino alcohol	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
....	104.8–105.1		58[a]						
4-Methyl	99.0–99.5[b]	64	76						
5-Methyl	91.0–91.5[c]		70						
4,4-Dimethyl[d]	93.4–93.8	83.5		40.78	41.06	6.16	6.37	9.51	9.34
4,4-Dimethyl[d]	117.8–118.3		71.5		41.13		6.18		9.42, 9.28
4-Ethyl[e]	48.8–49.4	71.5	97	40.78	41.11	6.16	6.35	9.51	9.84
[f]	84.6–85.2		79	45.77	45.37	6.92	7.03	10.68	10.65

[a] Stevenson, ref. 4, reported a 95% yield. [b] Ref. 5, m.p. 98.5–99°. [c] C. Y. Hopkins. *Can. J. Research.* **20B**, 268 (1942), reported the m.p. 93–94°, yield "poor"; ref. 5, m.p. 88–89°. [d] Two crystalline forms. See Experimental part. [e] See ref. 6b. Analysis not published previously. [f] 5-Ethyl-2-thioöxazolidone.

TABLE II

3-*p*-NITROBENZOYL-2-THIOTHIAZOLIDONES

Substituent	M.p., °C.	Mol. formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
......	162.6–163.2	$C_{10}H_8N_2S_2O_3$	44.76	44.89	3.01	3.31
4-Methyl	159.0–160.0	$C_{11}H_{10}N_2S_2O_3$	46.79	46.83	3.57	3.82
5-Methyl	139.0–139.2	$C_{11}H_{10}N_2S_2O_3$	46.79	47.04	3.57	3.89
4,4-Dimethyl[a]	168.0–168.5	$C_{12}H_{12}N_2S_2O_3$	48.63	48.55	4.08	4.30
[b]	172.4–173.6	$C_{12}H_{13}NS_2O$	57.34	57.52	5.21	5.34
4-Ethyl	121.6–122.4	$C_{12}H_{12}N_2S_2O_3$	48.63	48.41	4.08	4.34
[c]	92.2–93.6	$C_{12}H_{12}N_2SO_4$	51.42	50.83	4.32	4.52

[a] *Anal.* Calcd.: N, 9.45. Found: N, 9.51. [b] 3-Benzoyl derivative. *Anal.* Calcd.: N, 5.57. Found: N, 5.52. [c] 3-*p*-Nitrobenzoyl-5-ethyl-2-thioöxazolidone. *Anal.* Calcd.: N, 10.00 Found: N, 10.36.

tained from 2,2-dimethylethylenimine. The low yield left in doubt the fate of the remainder of the ethylenimine. However, without solvent and under pressure following the work of Stevenson[4] the yield of 4,4-dimethyl-2-thiothiazolidone was increased to 83.5%; two other unsymmetrical ethylenimines gave the corresponding 4-alkyl-2-thiothiazolidones in somewhat lower yields (Table I). One may conclude that the three-membered ethylenimine ring opens predominantly at the primary carbon with carbon disulfide under favorable conditions.

Evidence for the structure of the 4-alkyl-2-thiothiazolidones as given by Gabriel and Ohle[5] has been corroborated in an independent way by synthesis from the appropriate aminoalcohol.[4] Application of Stevenson's method again gave good yields of 2-thiothiazolidones in all but one case. While 1-amino-2-propanol gave 70% 5-methyl-2-thiothiazolidone, the corresponding thioöxazolidone was obtained in 79% yield from 1-amino-2-butanol. Ettlinger[6] has suggested a mechanism in which the proportion of thiothiazolidone formed from an amino alcohol should diminish with increasing hindrance of the hydroxyl group.[7] Comparison of these results with those of Rosen[8] on the reaction of amino alcohols (including 1-amino-2-propanol and 2-methyl-2-amino-1-propanol) with carbon disulfide in alcoholic alkali shows that formation of thiothiazolidones is favored by absence of the alkaline solvent.

The properties of the *p*-nitrobenzoyl derivatives of these 2-thiothiazolidones are recorded in Table II. That these derivatives should be called N-acyl[9] rather than S-acyl compounds seems very probable from the infrared spectra. In agreement with Ettlinger,[10] the infrared spectra of 4,4-dimethyl-2-thiothiazolidone indicate the presence of an N–H stretching band at 3.24 μ and the absence of a band due to C=N in the region 6–6.3 μ. This normally strong C=N absorption band is also missing in the benzoyl derivative of 4,4-dimethyl-2-thiothiazolidone and the three *p*-nitrobenzoyl derivatives of 5-ethyl-2-thioöxazolidone, 2-thiothiazolidone and 4,4-dimethyl-2-thiothiazolidone. Strong absorption bands do occur in these four compounds at 5.87, 5.88, 5.92 and 5.91 μ, respectively, which in the absence of a C=N bond may be interpreted[11a] as due to carbonyl groups on nitrogen.[11b]

Experimental[12]

4,4-Dimethyl-2-thiothiazolidone.—All the compounds reported in Table I were prepared in a stainless steel cylinder 15 inches long, one inch in diameter, and closed by a screw-cap carrying a lead washer. Ten grams of carbon disulfide was placed in the cylinder and cooled by a Dry Ice–isopropyl alcohol-bath while 5.0 g. of 2,2-dimethylethylenimine was added dropwise. After allowing the mixture to cool 15 minutes longer, the cylinder was sealed and transferred to the autoclave at 100° for 6 hours heating. Hydrogen sulfide was allowed to escape from the cylinder at the end of the heating period after cooling it to room temperature.

---

[4] H. B. Stevenson, U. S. Patents 2,364,398–9 (1944).

[5] S. Gabriel and H. Ohle, *Ber.*, **50**, 840 (1917).

[6] M. G. Ettlinger, THIS JOURNAL, **72**, 4792 (1950).

[7] Compare J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 3094 (1952).

[8] A. A. Rosen, THIS JOURNAL, **74**, 2994 (1952).

[9] Suggested by Dr. Martin G. Ettlinger who cited the following references to support the conclusion that acylation of thioamides derived from carbonic acid yields N-acyl amides: H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **24**, 189 (1900); M. Delepine, *Bull. soc. chim.*, [3] **29**, 48 (1903); A. E. Dixon and J. Hawthorne, *J. Chem. Soc.*, **91**, 122 (1907); A. E. Dixon and J. Taylor, *ibid.*, **117**, 720 (1920).

[10] M. G. Ettlinger, THIS JOURNAL, **72**, 4699 (1950).

[11] (a) The authors are indebted to Mr. Charles E. Grabiel, Brown University, for taking and interpreting the infrared spectra. (b) H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 24 ff.

[12] All melting points are corrected. Analyses by S. M. Nagy, Microchemical Laboratory, Massachusetts Institute of Technology.

Then the contents of the cylinder were dissolved in warm 5% sodium hydroxide, charcoal was added to the warm yellow solution, and the mixture was allowed to stand 15 minutes. The filtered solution was cooled to 5° in ice and cold dilute hydrochloric acid was added dropwise with stirring until the solution was neutral to litmus. (Ammonium chloride solution was preferred for an acid near the end-point.) The 4,4-dimethyl-2-thiothiazolidone, collected on a buchner funnel, weighed 8.0 g. after drying. By extracting the water solution with ether, 0.66 g. more was obtained; total yield 8.66 g., 83.5%, m.p. 87–91°. An analytical sample was obtained by recrystallization from 95% ethanol and sublimation at 60–75° (0.4 mm.), m.p. 93.4–93.8°.

By the procedure just described 9.5 g. of 2-methyl-2-amino-1-propanol was sealed with 20 g. of carbon disulfide in the stainless steel cylinder. After working up the resulting product in the same way, 11.25 g. of 4,4-dimethyl-2-thiothiazolidone, m.p. 112–116°, was obtained. An analytical sample obtained in the same way as that just described gave a m.p. 117.8–118.3°.[8,13]

The anomaly in the melting points of the two samples of 4,4-dimethyl-2-thiothiazolidone appears to be a case of dimorphism in which the two crystalline forms have nearly the same stability. The mixed melting point was 93–116°. Upon recrystallizing 1 g. of a 1:1 mixture of the two forms from 95% ethanol, 0.80 g. was obtained of m.p. 94–115° and a second crop by adding a few drops of water, of 0.12 g., m.p. 91–93°. The higher melting, less soluble crystals were almost spheroidal in shape, bounded by numerous surfaces while the lower melting form may be described as elongated plates. Seeding the melt of the lower melting crystals with the higher gave only a partial conversion to the second form, with a new m.p. 93–110°. The two samples gave the same 3-benzoyl derivative, the same 3-*p*-nitrobenzoyl derivative, and identical infrared spectra in carbon tetrachloride solution.

The acyl derivatives described in Table II were prepared by the standard Schotten–Baumann procedure and recrystallized from 95% ethanol in which they were all sparingly soluble. The thiothiazolidones except 4-ethyl-2-thiothiazolidone were easily sublimed at low pressure for analytical samples. The thioöxazolidone decomposed upon sublimation.

---

(13) J. P. English, American Cyanamid Co., reports m.p. 115–116°; private communication.

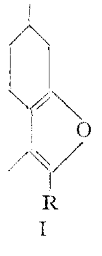
DEPARTMENT OF CHEMISTRY
BROWN UNIVERSITY
PROVIDENCE 12, R. I.

Substituted Menthofurans

BY RICHARD H. EASTMAN AND ROSS P. WITHER

RECEIVED SEPTEMBER 26, 1952

In continuing the study of the autoxidation of menthofuran[1] (I, R = H) we have prepared piperidinomethylmenthofuran (I, R = CH$_2$NC$_5$H$_{10}$), menthofuroic acid (I, R = COOH) and its anilide (I, R = CONHC$_6$H$_5$), and menthofurfuryl alcohol (I, R = CH$_2$OH) to determine whether the presence of the α-hydrogen atom on the furan nucleus is requisite for the production of the remarkable deep blue color that develops in solutions of menthofuran undergoing autoxidation. The piperidinomethyl compound and menthofurfuryl alcohol are readily autoxidized but do not show the blue color phenomenon. Menthofuroic acid and its anilide are stable towards autoxidation.



I

Experimental

Piperidinomethylmenthofuran (I, R = CH$_2$NC$_5$H$_{10}$).—A solution of 5.1 g. of menthofuran,[2] 1.5 g. of piperidine hydrochloride and 1.5 g. of paraformaldehyde in 50 ml. of absolute alcohol was heated under reflux for 1 hour. Removal of most of the solvent under reduced pressure caused the separation of 4.4 g. of white solid of m.p.[3] 202–204° (dec.). Crystallization from an alcohol–hexane–ethyl acetate mixture gave 4.1 g. of piperidinomethylmenthofuran hydrochloride of m.p. 208.5–209° (dec.). An additional 3.0 g. of pure material was isolated from the reaction liquor by concentration, bringing the yield to 84% of the theory.

Anal.[4] Calcd. for C$_{16}$H$_{26}$ClNO: C, 67.70; H, 9.23; Cl, 12.50. Found: C, 67.45; H, 9.13; Cl, 12.17.

The presence of nitrogen was established by sodium fusion; and the ultraviolet absorption spectrum showed $\lambda_{\max}^{\text{alc.}}$ 233 mμ (4.01) which is expected on the basis that menthofuran shows $\lambda_{\max}^{\text{alc.}}$ 219.5 mμ (3.78).

The free base was generated by treating the hydrochloride with an excess of 20% sodium carbonate solution. It was obtained as a colorless, water-insoluble oil of b.p. 189.5–191.5° at 20 mm.

Anal. Calcd. for C$_{16}$H$_{25}$NO: C, 77.68; H, 10.19; N, 5.66; neut. equiv., 247. Found: C, 77.72; H, 10.20; N, 5.68; neut. equiv., 236.

The ultraviolet absorption showed $\lambda_{\max}^{\text{alc.}}$ 228 mμ (4.10) and 294 mμ (1.28). The weak absorption at 294 mμ is ascribed to an autoxidation product of the base since the intensity of absorption at this wave length increased to log ϵ 2.30 on exposure of the free base to air during 14 days.

The picrate of the base constituted bright-yellow crystals of m.p. 139.5–140° after crystallization from aqueous alcohol.

Anal. Calcd. for C$_{22}$H$_{28}$N$_4$O$_8$: C, 55.45; H, 5.92. Found: C, 55.48; H, 5.85.

Menthofuroylanilide (I, R = CONHC$_6$H$_5$).—Menthofuran (28 g.) and phenyl isocyanate (45 g.) were heated with protection from moisture at 160° for 24 hours. Upon cooling the reaction mixture 25 g. of yellowish crystals separated which were crystallized from aqueous alcohol to give 24 g. of white needles of m.p. 156–156.5°.

Anal. Calcd. for C$_{17}$H$_{19}$NO$_2$: C, 75.84; H, 7.11. Found: C, 75.56; H, 6.89.

This substance is assigned the structure of menthofuroyl anilide on the basis of its analysis, insolubility in acid and base, and its ultraviolet absorption which showed $\lambda_{\max}^{\text{alc.}}$ 292 mμ (4.40) and great similarity to that of furoyl anilide, $\lambda_{\max}^{\text{alc.}}$ 276 mμ (4.27).

In subsequent experiments, using carefully purified phenyl isocyanate, it was discovered that the Friedel-Crafts reaction did not proceed well unless a trace of hydrogen chloride was added to the reaction mixture. The quantity of hydrogen chloride in ordinary samples of phenyl isocyanate was sufficient to catalyze the reaction.

Menthofuroic Acid (I, R = COCH).—Attempts to hydrolyze menthofuroyl anilide using 6 *N* hydrochloric acid, 10% aqueous or alcoholic potassium hydroxide, and the methods of Baum[5] and of Marquis[6] for furoyl anilide returned the anilide unchanged. Hydrolysis of the anilide (1.0 g.) with barium hydroxide octahydrate (4.7 g.) in 25 ml. of ethylene glycol at 140° for 4 hours gave a 76% yield (0.55 g.) of a white acidic solid of m.p. 179–179.5° (dec.) which is assigned the structure of menthofuroic acid on the basis of its analysis, decomposition into menthofuran by heat, and ultraviolet absorption spectrum which showed $\lambda_{\max}^{\text{alc.}}$ 270 mμ (4.24) to be compared with that for furoic acid $\lambda_{\max}^{\text{alc.}}$ 246 mμ (4.05).

Anal. Calcd. for C$_{11}$H$_{14}$O$_3$: C, 68.02; H, 7.27. Found: C, 67.98; H, 7.44.

Menthofurfuryl Alcohol (I, R = CH$_2$OH).—Ten grams of menthofuroic acid in 150 ml. of dry ether was added dropwise to 130 ml. of ether containing 2.42 g. of lithium aluminum hydride. Following the addition, stirring was continued for 15 minutes. The unreacted hydride was decomposed by the addition of water and then 80 ml. of 10% sulfuric acid was added. The ether layer was separated, washed with dilute sodium bicarbonate solution and dried

---

(1) R. B. Woodward and R. H. Eastman, THIS JOURNAL, **72**, 399 (1950).

(2) R. H. Eastman, *ibid.*, **72**, 5313 (1950).

(3) Melting points are corrected.

(4) Analyses by Microchemical Specialties Co., Berkeley, California.

(5) F. Baum, *Ber.*, **37**, 2949 (1904).

(6) R. Marquis, *Ann. chim. phys.*, [8] **4**, 279 (1905).