4,4-Didodecyl-2,6-dimethylmorpholinium Chloride.—A mixture of didodecylamine (35.3 g., 0.10 mole), bis-(1-chloro-2-propyl) ether (20.6 g., 0.12 mole), sodium carbonate (12.7 g., 0.12 mole) and butyl alcohol (200 ml.) was stirred and refluxed for 72 hours. It was cooled, filtered and evaporated under reduced pressure. The residue was dissolved in hot methanol (400 ml.); this solution was chilled in ice and filtered, giving 16.7 g. of unreacted amine. The filtrate was distilled and its residue was crystallized from ethyl acetate, giving 8.8 g. of waxy, white solid (34% yield, 18% conversion). This was recrystallized from ethyl acetate; m.p. (after drying *in vacuo*), 175–180°.

Anal. Calcd. for $C_{30}H_{62}ClNO$: C, 73.79; H, 12.80; Cl, 7.26. Found: C, 73.85; H, 13.03; Cl, 7.18.

2,6-Dimethyl-4,4-dioctadecylmorpholinium Chloride.—A mixture of dioctadecylamine (84.1 g., 0.16 mole), bis-(1-chloro-2-propyl) ether (33.0 g., 0.19 mole), sodium carbonate (20.5 g., 0.19 mole), and butyl alcohol (400 ml.) was stirred and refluxed for 20 hours. It was diluted to one liter with butyl alcohol and filtered while hot. The filtrate was chilled and filtered again, yielding 64.4 g. of unreacted amine. The filtrate was evaporated, leaving 27.0 g. of residue. This was dissolved in hot methanol (400 ml.), cooled, and filtered to remove a small amount of solid. The filtrate was evaporated to dryness. The residue was recrystallized from ethyl acetate, giving 16.3 g. (65.5% yield, 15.3% conversion) of white solid; m.p., after another recrystallization and drying *in vacuo*, 172–175°.

Anal. Calcd. for $C_{42}H_{86}ClNO$: Cl, 5.38; N, 2.13. Found: Cl, 5.31; N, 2.46.

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Vapor Phase Catalytic Isomerization of *m*-Xylene

BY E. R. BOEDEKER AND W. E. ERNER

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The production of certain of the synthetic fibers requires *p*-xylene as one of the starting materials. The separation of *p*-xylene from a xylene mixture by low temperature crystallization yields a high purity *p*-xylene fraction and a fraction containing a preponderance of *m*-xylene. Additional quantities of *p*-xylene are potentially available from the isomerization of the *m*-xylene-containing fraction to a xylene mixture, the composition of which approximates thermodynamic equilibrium. With this in mind, the vapor phase isomerization of a *m*-xylene-rich fraction over a synthetic silica–alumina cracking catalyst (Houdry Type S-45) was cursorily investigated.

The charge stock used in the present study contained 84% *m*-xylene, 9% *p*-xylene, 5% *o*-xylene and 2% ethylbenzene. The charge stock was obtained from a xylene fraction by freezing out a portion of the material.

The experimental conditions and results are summarized in Table I. The products were distilled to obtain a xylene and lighter overhead fraction; the bottoms from the distillation were C_9-aromatics. The overhead fraction from the distillation was analyzed by infrared absorption spectrometry. In all cases, liquid recoveries were in excess of 98% and were corrected to a no-loss basis.

The effect of operation at reduced pressure is very clearly shown. At atmospheric pressure, the isomerization of *m*-xylene proceeds simultaneously with a disproportionation reaction. In the disproportionation reaction, two molecules of xylene apparently are adsorbed on sites which are located sufficiently close to each other to allow a shift of a methyl group, thereby forming toluene and a C_9-aromatic. If, on the other hand, the operating pressure is reduced so that the catalyst surface is more sparsely covered, the isomerization reaction proceeds to the exclusion of the disproportionation reaction.

TABLE I

Conditions				
Temperature, °C.	515	515	515	
Pressure, mm., Abs.	~760	90	90	Charge
Vol. liq. feed/vol. cat./hr.	0.7	0.6	1.2	Stock
Product analyses, mole %				
Benzene	1.2	..	..	..
Toluene	13.0	1.1	1.0	..
m-Xylene	32.3	59.8	60.3	84.0
p-Xylene	18.9	18.1	20.6	9.0
o-Xylene	13.0	9.2	7.0	5.0
Ethylbenzene	5.1	11.5	11.1	2.0
C_9-Aromatics	16.5	0.3	..	..

Doubling the liquid hourly space velocity has no significant effect on the distribution of the xylene isomers.

Data have been published on the equilibrium composition of a xylene mixture.[1] Based on these data, the composition of an equilibrium mixture of xylenes at 515° is as follows: 47% *m*-xylene, 22.5% *o*-xylene, 21.5% *p*-xylene, and 9% ethylbenzene. Comparison of these figures with those obtained experimentally at 90 mm. pressure shows that the products contain approximately equilibrium amounts of *p*-xylene and ethylbenzene; the *m*-xylene content, however, is higher than and the *o*-xylene content lower than the calculated thermodynamic equilibrium.

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HOUDRY PROCESS CORPORATION
MARCUS HOOK, PENNA.

Thiosemicarbazones of Some Vanillin Derivatives

BY R. P. PERRY

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The purpose of the work described in this paper was to prepare a series of substituted vanillin thiosemicarbazones which might be useful as antifungal agents and provide some basis for determining the relation of structure to antimicrobic action. Since the introduction of Tibione (acetylaminobenzaldehyde thiosemicarbazone) by Domagk and his associates,[1-3] many changes have been effected in the structure of the molecule, particularly as regards the subordinate groups *para* to the thiosemicarbazone moiety and in only a few cases have thiosemicarbazones with poly-substituted benzenoid residues been studied.[4,5] Moreover, the thiosemicarbazones thus obtained have been screened generally only for their antitubercular activity.

(1) G. Domagk, R. Behnisch, P. Mietzsch and H. Schmidt, *Naturwissenschaften*, **33**, 315 (1946).

(2) R. Behnisch, P. Mietzsch and H. Schmidt, *Angew. Chem.*, **60**, 113 (1948).

(3) R. Behnisch, P. Mietzsch and H. Schmidt, *Am. Rev. Tuberc.*, **61**, 1 (1950).

(4) J. Bernstein, H. L. Yale, K. Losee, M. Holsing, J. Martins and W. A. Lott, THIS JOURNAL, **73**, 906 (1951).

(5) D. J. Drain, *et al.*, *J. Pharm. Pharmacol.*, **1**, 784 (1949).

TABLE I

SUBSTITUTED VANILLINS

Solvent for crystallization: A, aq. ethanol; B, abs. ethanol

Substituent	Solvent	Yield, %	M.p., °C.	Empirical formula	Halogen, % Calcd.	Found
(2-Hydroxyethyl)-[a]	A	90	55–56	$C_{10}H_{12}O_4$		
5-Bromo-(2-hydroxyethyl)-	A	52	60–61	$C_{10}H_{11}BrO_4$	29.04	29.15
Carboethoxymethyl-[b]	B	80	54–55	$C_{12}H_{14}O_5$		
5-Bromocarboethoxymethyl-	B	45	165–166	$C_{12}H_{13}BrO_5$	25.19	25.06
6-Bromocarboethoxymethyl-	B	40	156–157	$C_{12}H_{13}BrO_5$	25.19	24.93

[a,b] Characterized by conversion into the nitroguanyl hydrazones by the method of Raiford and Perry, *J. Org. Chem.*, **7**, 358 (1942). [a] Obtained as the nitroguanyl hydrazone in 76% yield, m.p. 200–201°. *Anal.* Calcd. for $C_{11}H_{15}N_5O_5$: N, 23.56. Found: N, 23.54. [b] Nitroguanyl hydrazone obtained in 60% yield, m.p. 190–191°. *Anal.* Calcd. for $C_{13}H_{17}N_5O_6$: N, 20.65. Found: N, 20.70.

TABLE II

SUBSTITUTED VANILLIN THIOSEMICARBAZONES

Substituent	Yield, %	M.p., °C.	Empirical formula	Analyses, % Calcd. N	Calcd. Halogen	Found N	Found Halogen
Unsubstituted[a]	96	191–192	$C_9H_{11}N_3O_2S$				
5-Bromo-[b]	90	222–223	$C_9H_{10}BrN_3O_2S$	13.81	26.27	13.84	26.20
6-Bromo-	70	235–236 d.	$C_9H_{10}BrN_3O_2S$	13.81	26.27	13.78	26.34
5-Chloro-	90	219–220	$C_9H_{10}ClN_3O_2S$	16.56	13.64	16.49	13.60
6-Chloro-	70	234–235 d.	$C_9H_{10}ClN_3O_2S$	16.56	13.64	16.51	13.67
5-Iodo-	69	212–214 d.	$C_9H_{10}IN_3O_2S$	11.96	36.14	11.90	36.10
Acetyl-	73	216–217	$C_{11}H_{13}N_3O_3S$	15.72		15.70	
5-Bromoacetyl-	70	208–209	$C_{11}H_{12}BrN_3O_3S$	12.14	23.08	12.10	23.14
2-Amino-5-bromo-	55	206–207	$C_9H_{11}BrN_4O_2S$	17.55	25.03	17.62	25.04
5-Bromomethyl-	70	184–185	$C_{10}H_{12}BrN_3O_2S$	13.20	25.14	13.15	25.19
(2-Hydroxyethyl)-	65	187–188	$C_{11}H_{15}N_3O_3S$	15.60		15.40	
5-Bromo-(2-hydroxyethyl)-	70	151–152	$C_{11}H_{14}BrN_3O_3S$	12.06	22.94	12.00	22.90
Carboethoxymethyl-	65	166–167	$C_{13}H_{17}N_3O_4S$	13.49		13.40	
5-Bromocarboethoxymethyl-	72	211–212	$C_{13}H_{16}BrN_3O_4S$	10.76	20.47	10.78	20.40
6-Bromocarboethoxymethyl-	61	203–204	$C_{13}H_{16}BrN_3O_4S$	10.76	20.47	10.70	20.58
Benzyl-	80	147–148	$C_{16}H_{17}N_3O_2S$	13.32		13.20	

[a] Prepared previously by Bernstein and co-workers.[4] [a,b] Referred to as Vanithiozone and Bromothiozone, respectively, in the earlier report.[6]

Recently, however, it was shown that Vanithiozone (vanillin thiosemicarbazone) and Bromothiozone (5-bromovanillin thiosemicarbazone)[6] are highly effective against *Cryptococcus neoformans* and several times more active as antifungal agents than Tibione. In view of the promising behavior of these two compounds, the synthesis of additional vanillin thiosemicarbazones seemed important for screening as potential polysubstituted antifungal agents.

Most of the vanillins used in this work are known and were prepared by methods already described in the literature. Five, however, are new and are given in Table I. They were obtained by introducing the (2-hydroxyethyl)- and the carboethoxymethyl- groups into the phenolic hydroxyl of the appropriate vanillin to give the corresponding O-substituted vanillins. The general methods of preparation are described in the Experimental part.

The thiosemicarbazones, their yields, melting points and analyses are given in Table II. The microbiological data will be reported elsewhere.

Experimental Part

(2-Hydroxyethyl)-vanillin.—To a solution of 76 g. (0.5 mole) of vanillin and 20 g. (0.5 mole) of sodium hydroxide in 200 ml. of water was added 40 g. (0.5 mole) of ethylene chlorohydrin. The mixture was stirred and refluxed on the steam-bath for 10 hours. It was then made strongly alkaline and allowed to stand and cool to room temperature, whereupon a heavy, brown oil separated. Further stirring produced a mass of crystals. The aldehyde was then filtered, washed with water and allowed to dry. Recrystallization from 50% ethanol gave a 90% yield of soft, feathery needles which melted at 55–56°.

5-Bromocarboethoxymethylvanillin.—To a solution of 5.75 g. (0.25 mole) of sodium in 600 ml. of absolute ethanol was added 57.5 g. (0.25 mole) of 5-bromovanillin. The mixture was stirred and shortly thereafter the vanillin salt separated. Ethyl chloroacetate, 30.5 g. (0.25 mole), was added and the stirring and refluxing continued for 25 hours. The hot mixture was filtered rapidly and from the residue 15 g. of unchanged 5-bromovanillin was extracted. The filtrate was concentrated on the steam-bath to one-tenth its volume, and on cooling gave 37 g. of the desired vanillin in the form of small, colorless crystals. Upon recrystallization from ethanol the product weighed 35 g. (45% yield) and melted at 165–166°.

Vanillin Thiosemicarbazones.—The general method used in the preparation of the vanillin thiosemicarbazones is illustrated as follows:

5-Bromovanillin Thiosemicarbazone.—To a boiling solution of 23.1 g. (0.1 mole) of 5-bromovanillin in 200 ml. of absolute ethanol was added a hot solution of 9.1 g. (0.1 mole) of thiosemicarbazide in 100 ml. of water. The mixture was refluxed for one hour and allowed to cool to room temperature. The solid was filtered, allowed to dry and recrystallized from aqueous ethanol to give 21.6 g. (90% yield) of slightly yellow needles melting at 222–223°.

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