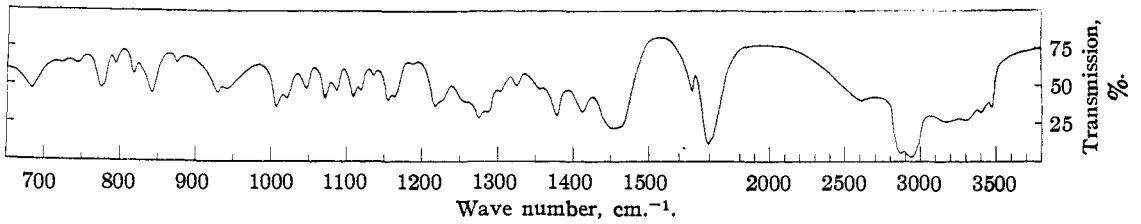

Fig. 1.—Infrared spectrum of β-longinecic acid (isatinecic acid) determined in Nujol mull.

and β-longinecic acid (isatinecic acid). Barger, *et al.*,[6] gave a similar description of the reduction and reduction product of retrorsine, but they hydrolyzed with sodium hydroxide and obtained retronecanol and retronecic acid which is the stable geometrical form.

We have now determined the infrared spectra of specimens of retrorsine and isatinecic acid and found them to be identical with those of β-longilobine and β-longinecic acid (*cf.* Adams and Govindachari[1]). Furthermore, a mixture of isatinecic acid, m. p. 148–148.5° (cor.) and β-longinecic acid, m. p. 148–149° (cor.) gave no depression. These results establish unequivocally the identity of the two alkaloids.

The sample of β-longinecic acid used for the infrared absorption reported in a previous paper[1] was found to contain small amounts of impurity, probably retronecic acid lactone. The infrared spectrum of a perfectly pure sample of β-longinecic acid which is identical with that of isatinecic acid is given in Fig. 1.

The melting points of the various *Senecio* alkaloids and the acid moieties from them deserve comment. Rather marked differences in values are reported in the literature for the same products even in those cases where the products can be assumed to be essentially pure. The values recorded above for the acids were obtained by starting in a cold bath and heating at about 2° a minute. Using a preheated bath at 136° and heating 1° a minute lowers the m. p. by about 5°. The alkaloids themselves decompose gradually upon heating so that the only satisfactory procedure is to use a preheated bath (180°).

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The Use of N-Methylformanilide in the Preparation of Thiophenecarboxaldehydes

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The formation of 2-thiophenecarboxaldehydes by the direct formylation of the thiophene nucleus, employing N-methylformanilide and phosphorus oxychloride, has recently been disclosed.[1] This note presents some of our observations regarding this thiophenecarboxaldehyde preparation which we had also investigated[2] in connection with an alternate synthesis of N,N-dimethyl-N′-(2-pyridyl)-N′-(2-thenyl)-ethylenediamine (Thenylene.)[3]

With thiophene, we found that N-ethylformanilide gave yields of 2-thiophenecarboxaldehyde comparable to those obtained with N-methylformanilide. On the other hand, substitution of formamide for N-methylformanilide proved detrimental as only a trace of aldehyde was formed. Phosphorus oxychloride was the preferred condensing agent because of its solvent properties. Although phosphorus oxybromide gave similar results, a solvent such as chlorobenzene was usually necessary to ensure a homogeneous reaction mixture.

In contrast to the reported conditions,[1] in which the reaction mixture is heated on the steam-bath and then quickly removed as the exothermic reaction progresses, we found that the reaction proceeded equally well at room temperature, thereby increasing its utility. Under our conditions, an appreciable increase in the reaction temperature usually resulted in a decrease in the amount of aldehyde formed. This depended somewhat upon the nature of the group attached to the thiophene nucleus, the halogenated thiophenes being less affected than the alkylthiophenes or thiophene itself. Equimolar amounts of the reactants or a slight excess of the thiophene gave the best results.

With 2-bromothiophene, an impure 5-bromo-2-thiophenecarboxaldehyde was formed, due apparently to halogen interchange with the phosphorus oxychloride. The material obtained, however, could be purified by careful fractionation. King and Nord[1] obtained only the 5-chloro derivative from this reaction. This difficulty can be overcome by employing phosphorus oxybromide.[4] 2-Nitro- and 2,5-dichlorothiophene gave no isolable amounts of aldehyde. An attempt to formylate 2-thiophenecarboxaldehyde further resulted in tar formation.

It has been found possible to introduce a 3-formyl group into a thiophene derivative by this reaction. 2,5-Dimethylthiophene gave the corresponding 3-carboxaldehyde although the yield was much lower than in the other cases. With

(1) King and Nord, *J. Org. Chem.*, **14**, 635 (1948).

(2) British Patent Specification No. 27,882 (1947).

(3) Weston, THIS JOURNAL, **69**, 980 (1947).

(4) After this manuscript was submitted, King and Nord, *J. Org. Chem.*, **14**, 405 (1949), reported a similar preparation of the 5-bromo-2-thiophenecarboxaldehyde.

TABLE I

THIOPHENECARBOXALDEHYDES AND DERIVATIVES X—  —CHO

Ring substituent X	B. p., °C.	Mm.	Ref. index $n^{25}D$	Yield, %	Acid m. p., °C.	Phenylhydrazones M. p.,[l,m] °C.	Nitrogen, % Calcd.	Found	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
H[a]	91–92[g]	25	1.5888	77	129–130[j]	137–139[n,o]	13.85	14.08	65.31	65.59	4.98	4.93
5-Br[a,c,f]	114–115[h]	14	1.6328	70	141–142[j]	112–113[p]	9.97	9.83	46.98	47.18	3.23	3.23
5-Cl[a]	91–92[g]	13	1.6017	59	154–154.5[j]	109–110	11.84	11.87	55.81	55.90	3.83	3.64
5-*t*-C_4H_9[a,d,f]	135–136	25	1.5428	76	128–128.5[j]	153–155	10.85	10.88	69.73	69.97	7.02	7.06
5-CH_3[a]	113–114[g]	25	1.5782[i]	81	137–138[j]	125–126[q]	12.96	12.99	66.63	66.72	5.59	5.89
3-CH_3[a]	113–114[g]	25	1.5833	83	147–148[j]	148–149	12.96	13.07	66.63	66.77	5.59	5.65
2,5-Di-CH_3[b,e,f]	116–117	25	1.5599	20	116–117[k]	95–96	12.17	12.14	67.79	67.79	6.13	6.27

[a] 2-Carboxaldehyde. [b] 3-Carboxaldehyde. [c] Calcd. for C_5H_3OSBr: C, 31.43; H, 1.58. Found: C, 31.77; H, 1.85. [d] Calcd. for $C_9H_{12}OS$: C, 64.24; H, 7.19. Found: C, 64.41; H, 7.11. [e] Calcd. for C_7H_8OS: C, 59.97; H, 5.75. Found: C, 59.74; H, 5.77. [f] Carried out on material obtained from $NaHSO_3$ complex. [g] See ref. (1) for other b. p. values. [h] Ref. (4) gives b. p. 80–83° (2 mm.). [i] Taken at 29°. Grishkevich-Trokhimovskii, *J. Russ. Phys.-Chem. Soc.*, **43**, 803 (1911) [*C. A.*, **6**, 477 (1912)] reports $n^{21}D$ 1.58166. [j] These values agree with those given by Hartough and Conley, THIS JOURNAL, 69, 3096 (1947). [k] Steinkopf, Poulsson and Herdey, *Ann.*, **536**, 128 (1938), report m. p. 115°; Kitt, *Ber.*, **28**, 1810 (1895), gives m. p. 117–118°. [l] All melting points are uncorrected. [m] All the phenylhydrazones were crystallized from 95% alcohol. [n] Hantzsch, *Ber.*, **22**, 2839 (1889), reports m. p. 134.5°. [o] Biedermann, *ibid.*, 19, 636 (1886), gives m. p. 119°. [p] Gattermann, *Ann.*, **393**, 215 (1912), records m. p. 105°. [q] Grishkevich-Trokhimovskii (see footnote *i*) gives m. p. 116–117°.

thianaphthene, the 3-carboxaldehyde was also formed in a small yield. King and Nord[1] report that the latter compound failed to react with N-methylformanilide.

The aldehydes obtained after distillation of the extracts from the hydrolyzed reaction mixtures were satisfactory for most purposes, although they gave slightly high analytical values for carbon. However, purer material[5] was readily obtained *via* the bisulfite addition complex but some loss was entailed in this operation. For comparative purposes the aldehydes were converted to the corresponding acids by silver oxide and sodium hydroxide.

Experimental[6]

2-Thiophenecarboxaldehyde.—A mixture of 67.5 g. (0.5 mole) of N-methylformanilide[7] and 76.5 g. (0.5 mole) of phosphorus oxychloride was placed in a 500-cc. flask equipped with a calcium chloride drying tube, and then allowed to stand for one-half hour. While the temperature was maintained at 25–30°, 46.2 g. (0.55 mole) of thiophene was added. After the initial exothermic reaction had subsided, the resulting solution was allowed to stand sixteen hours at room temperature. The reaction mixture was poured into ice-water accompanied by vigorous stirring. The oily layer was separated and combined with the subsequent ether extracts. This ether solution was then washed with dilute sodium bicarbonate solution until the washings were neutral, dried over sodium sulfate and concentrated. Distillation of the residual oil gave 42.6 g. (76%) of product, b. p. 91–92° at 25 mm., $n^{25}D$ 1.5888.

The addition of alkali to the original acidic solution gave an oil which was extracted with ether. The ether solution was dried, concentrated and the residue distilled. There was thus recovered 43 g. (81%) of N-methylaniline, b. p. 96° at 25 mm., $n^{26.5}D$ 1.5689.

5-Bromo-2-thiophenecarboxaldehyde.—Phosphorus oxybromide, 86.1 g. (0.3 mole), was dissolved in 100 cc. of chlorobenzene followed by the addition of 40.5 g. (0.3 mole) of N-methylformanilide. To the resulting solution maintained at 50°, there was added dropwise 58.7 g. (0.36 mole) of 2-bromothiophene. This reaction mixture was stirred at room temperature for eighteen hours then hydrolyzed and the aldehyde isolated in the foregoing manner. Distillation of the ether residue gave 40 g. (70%) of product, b. p. 118–121° at 15 mm. The aldehydic material was converted to the sodium bisulfite derivative, regenerated and fractionated. The pure aldehyde boiled at 114–115° at 14 mm., $n^{25}D$ 1.6328.

By replacing the phosphorus oxybromide with an equivalent amount of phosphorus oxychloride and following the procedure of the first example, there was obtained an impure product, b. p. 125–130°. However, two fractionations gave 24.9 g. (44%) of fairly pure aldehyde, b. p. 129–131° at 25 mm., $n^{25}D$ 1.6295. The acid and phenylhydrazone derivatives prepared from this material proved to be identical with those obtained from the aldehyde described above.

Additional data regarding these and the other aldehydes prepared in this manner are recorded in Table I.

Thianaphthene-3-carboxaldehyde.—A mixture of 40.2 g. (0.3 mole) of thianaphthene,[8] 40.5 g. (0.3 mole) of N-methylformanilide and 45.9 g. (0.3 mole) of phosphorus oxychloride was allowed to react in the manner described for 2-thiophenecarboxaldehyde. The crude product from the ether extracts was shaken with an equal volume of saturated sodium bisulfite solution whereupon the solid addition complex separated. The complex (15 g.) was decomposed with alkali and the resulting aldehyde was extracted with ether. Concentration of the dried ether extracts gave 4.3 g. (9%) of aldehyde, m. p. 52–54°. After crystallization from alcohol, the material melted at 58°. The phenylhydrazone prepared in the usual manner melted at 204–205° after crystallization from alcohol.

Anal.[9] Calcd. $C_{15}H_{12}N_2S$: C, 71.39; H, 4.80; N, 11.10. Found: C, 71.52; H, 4.90; N, 10.86.

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(5) King and Nord reported high carbon values (0.4–0.7%) for all their aldehydes.

(6) The 2-methyl-, 3-methyl- and 2-*t*-butylthiophenes were obtained through the courtesy of Dr. George A. Harrington of the Socony-Vacuum Oil Company.

(7) "Organic Syntheses," Vol. 20, John Wiley and Sons, New York, N. Y., 1940, p. 66.

(8) This material was furnished through the courtesy of the Jefferson Chemical Company.

(9) We are indebted to Mr. Shelberg and members of the Microanalytical Department for the microanalyses reported in this note.