Oxidation of 2-Methyl 5-Ethyl Pyridine to Isocinchomeronic Acid

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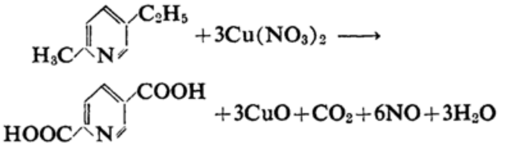
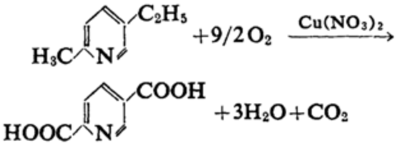
In the preparation of isocinchomeronic acid (ICA) from 2-methyl 5-ethyl pyridine (MEP), several kinds of oxidizing reagents, such as sulfuric acid[1], selenium peroxide[2], nitric acid[3] and cupric nitrate[4] have been used. Cupric nitrate (with or without nitric acid) is said to give the highest yield of ICA among them, where this process consumes a large quantity of nitrate or nitric acid (more than 10 mol. as NO_3 to 1 mol. MEP oxidized).



MEP can not be oxidized with molecular oxygen as in the case of *p*-xylene with catalysts such as cobalt or manganese acetates. But the combined use of oxygen (a little more than theoretical moles for the oxidation of MEP) with cupric nitrate was found to be effective to obtain ICA (through its cupric salt) with a yield higher than 85 ml. % to MEP consumed, where the used cupric nitrate was easily recovered and reused.



Experimental

Materials.—MEP of more than 98% purity was purchased from Carbide and Carbon Chem. Co. Ltd., and used without purification. Its specifications are as following; specific gravity (20°/20°), 0.918~0.922; b. p., 171~181°C (760 mmHg); water content, less than 0.2% by weight. Reaction vessel was 1 l. auto-clave (18 : 8 stainless steel) with magnetic stirrer.

Oxidation. — MEP, cupric nitrate (as 200 cc. aqueous solution) and oxygen were charged in the

TABLE I. REACTION VARIABLE IN THE OXIDATION OF MEP.

Exp. No.	MEP mol.	$Cu(NO_3)_2$[a] mol.	Charged mol. ratio $Cu(NO_3)_2$/MEP	N_2[d]$+O_2$ atm.	O_2% by vol.	Duration min.[b] 180~200°C	200~230°C
1	0.149	0.79	5.30	Not charged		10	200
2	〃	0.476	3.20	〃		〃	〃
3	〃	0.155	1.04				
4	0.197	0.203	〃	〃		〃	〃
5	0.149	0.103	0.69	50	54	〃	130
6	〃	0.155	1.04	〃	55	3	100
7	〃	0.103[c5]	0.69	〃	53	10	180
8	0.198	0.155	0.77	58	56	5	85
9	〃	〃 [c8]	〃	〃	48	3	90
10	〃	〃 [c9]	〃	〃	42	〃	120
11	0.197	0.203	1.04	〃	45	5	130
12	〃	〃	〃	〃	40	5	120
13	〃	〃	〃	50	44	〃	160
14	〃	〃	〃	53	50	30	95
15	〃	〃	〃	60	54	240	0
16	0.296	〃	0.69	90	48	30	180
17	〃	〃 [c16]	〃	80	53	20	150

a) Used as 200 cc. aqueous solution in each experiments.
b) See Figs. 1, 2 and 3.
c) Recovered $Cu(NO_3)_2$ charged c5), c8), c9) and c16) mean recovered ones in Exps. No. 5, 8, 9 and 16 respectively.
d) Measured at 20°C before heating the vessel.

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[1] T. E. Jordan, *Ind. Eng. Chem.*, **44**, 332 (1952).
[2] D. Jercher, *Chem. Ber.*, **88**, 156 (1955).
[3] U. S. Pat. 2524957 (1950).
[4] U. S. Pat. 2552268 (1951).

TABLE II. RESULTS OF EXPERIMENTS IN TABLE I

Exp. No.	O_2 Consumed moles	mol. ratio O_2/MEP	CO_2 Produced moles	mol. ratio CO_2/MEP	Cupric Isocinchomronate moles×2[a]	yield[b] %	ICA Yield[b] %
1	Not charged		0.18	1.2	Not charged		87
2	〃		0.17	1.1	〃		40
3	〃		0.19	1.3	〃		7
4	〃		0.20	1.0	〃		0
5	0.70	4.7	0.13	0.9	0.133	89	84
6	0.76	5.1	0.12	0.8	0.127	85	80
7	0·68	4.6	0.20	1.3	0.138	92	87
8	0.83	4.2	0.18	0·9	0.179	90	85
9	0.75	3.8	0.22	1.1	0.174	88	83
10	0.76	〃	0.24	1.2	0.179	90	85
11	0.87	4.4	0.20	1.0	0.180	91	86
12	0.80	3.9	0.16	0.8	〃	〃	〃
13	0.74	3.8	0.25	1.3	0.177	90	85
14	0.82	4.2	0.24	1.2	0.182	92	87
15	0.84	4.3	0.23	〃	0.181	〃	〃
16	1.27	〃	0.36	〃	0.278	94	88
17	1.25	4.2	0.33	1.1	0.279	〃	〃

a) 1 mol. of cupric salt is prepared from 2 mol. of MEP
b) Based upon consumed moles of MEP

TABLE III. FORMATION OF ICA FROM ITS CUPRIC SALT

Exp. No.	Aqueous soln. of NaOH Concn. of NaOH % by wt.	gr.	Mol. ratio NaOH/ICA	Conditions Temp. °C	Duration hr.	ICA Moles	Yield[a] % by wt.
1	10	300	4.9	95	1.0	0.141	93
2	〃	200	3.3	〃	〃	0.143	94
3	〃	100	1.6	〃	〃	0.064	42
4	〃	〃	〃	〃	3.0	0.053	35
5	5	400	3.3	〃	1.0	0.145	95
6	〃	300	2.5	〃	〃	0.143	94
7	〃	〃	〃	75	〃	0.144	95

a) Based upon the cupric salt consumed, and in each Exp. 0.076 mol. (30.0 g.) of the cupric salt was used.

autoclave, where oxygen was diluted to less than 60% by volume with nitrogen. In some experiment, oxygen was not charged, in order to compare their results with that of other experiments, in which oxygen was used. The vessel was heated and its temperature was kept at 180~230°C, until oxygen was sufficiently absorbed to the oxidate and its pressure stopped dropping.

After the vessel was cooled to room temperature, the content of oxygen and carbon dioxide in the blowing gas was measured. The reaction product was filtered, where the deposit obtained was submitted to elementary analysis after being washed with water and dried in an air oven.

A certain quantity of the deposit was mixed and stirred with hot alkali aqueous solution, and copper was filtered off as cupric oxide from the solution.

Sodium salt of ICA (very soluble in water) formed in the filtrate was neutralized with concentrated aqueous hydrochloric acid, and white deposit liberated at pH 1.8~2.0, was also submitted to elementary analysis after being washed with water and dried in the air oven.

Results and Discussion

Reaction variables in the oxidation of MEP and their results were shown in Tables I and II respectively.

With no oxygen charged as in Exps. 1—4, the cupric salt of I. C. A. in the reaction product was not pure, being mixed with other cupric salts such cupric oxide, cupric hydroxide, and cupric nitrite.

Furthermore the yield of ICA fell markedly with decrease of cupric nitrate charged.

In Exps. 5—17 with oxygen used, the deposits obtained were uniformly found to be pure cupric isocinchomeronate (2 mol. of isocinchomeronate combined with 1 mol. of Cu^{2+}).

Found: C, 42.09; H, 2.22; N, 7.02; Cu, 16.25. Calcd. for $(C_7H_4O_4N)_2Cu$: C, 42.49; H, 2.04; N, 7.08; Cu 16.05%.

With decrease of cupric nitrate charged, the yield was not lowerd (always not less than

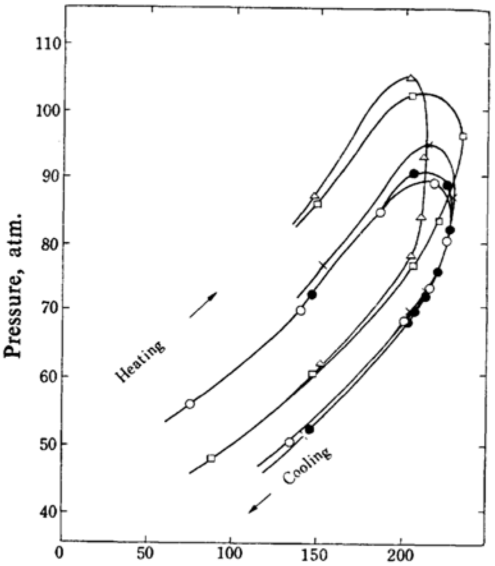

Fig. 1. Absorption of oxygen in the oxidation of MEP.
(Exp. Nos. 5—9) plotted per 30 min.

—○— No. 5 —△— No. 8
—×— 〃 6 —□— 〃 9
—●— 〃 7

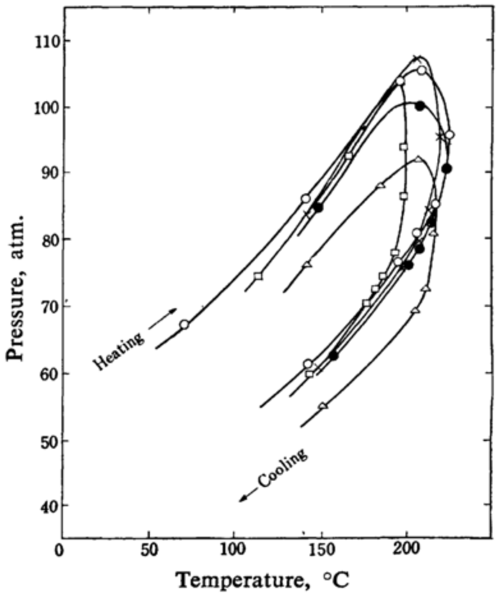

Fig. 2. Absorption of oxygen in the oxidation of MEP.
(Exp. Nos. 10—15) plotted per 30 min.

—○— No. 10 —△— No. 14
—×— 〃 11, 12 —□— 〃 15
—●— 〃 13

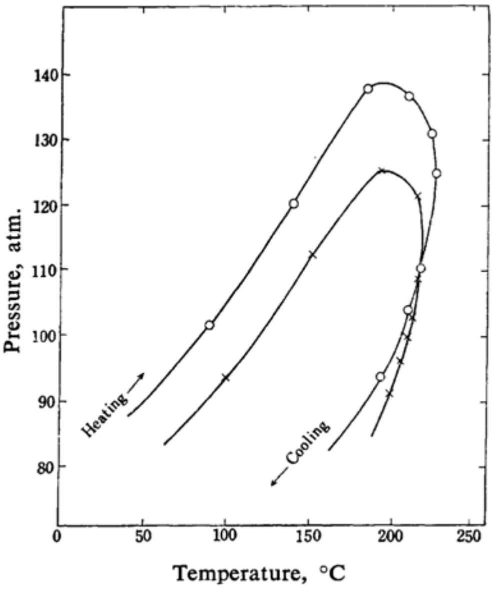

Fig. 3. Absorption of oxygen in the oxidation of MEP.
(Exp. 16 and 17) plotted per 30 min.

—○— No. 16 —×— No. 17

85 mol. % to MEP consumed), and any trace of nitrogen oxide or nitrogen dioxide was not detected in the reaction product and blowing gas. Cupric nitrate used was easily recovered by cupric oxide or cupric hydroxide being dissolved in the recovered filtrate and it was reused as in Exps. 7, 9, 10 and 17.

As shown in Figs. 1, 2 and 3, oxygen was absorbed at 180∼230°C, where overheating was found to cause violent explosion. Molar ratio of oxygen consumed and carbon dioxide formed to that of MEP oxidized were approximately consistent to the theoretical values, 4.5 and 1.0 respectively. Based upon the results in Tables I, II and Figs. 1—3, the oxidation of MEP to cupric isocinchomeronate is considered to proceed as following;

$$C_2H_5(C_5NH_3)CH_3+9/2\,O_2+1/2\,Cu(NO_3)_2 \rightarrow$$

$$1/2(HOOC_5NH_3COO)_2Cu+3H_2O+CO_2+HNO_3$$

and oxygen only is consumed to oxidize MEP.

ICA prepared from its cupric salt, as shown in Table III, and its dimethyl ester melted at 237 and 164°C respectively, both of which agree with the values in the literature[5].

Isocinchomeronic acid in Table II.

Found: C, 49.98; H, 2.96; N, 8.34. Calcd. for $C_7H_5O_4N$: C, 50.34; H, 3.01; N, 8.38%.

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5) Beilstein, Band 12, p. 154, 155.