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Memorandum on Organic Chemical Synthesis

Isao YAMAGUCHI

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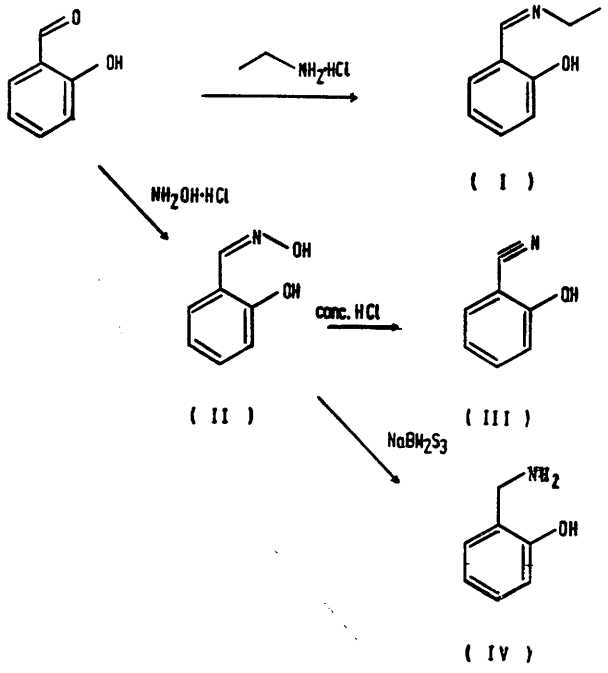
I. Salicylaldehyde derivatives

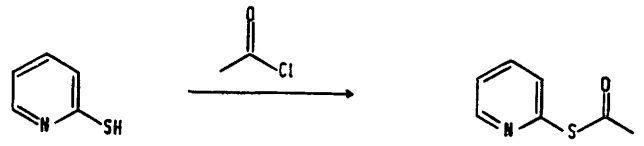
Two Schiff-base compounds, N-salicylideneethylamine (I) and salicylaldoxime (II),[1,2] were synthesized from salicylaldehyde, reacted with ethylamine and hydroxylamine respectively. Salycylaldehydoxime was further derived to 2-cyanophenol (III)[2,3] and salicylamine (IV).[4,5]



The 3rd laboratory of nutrition.

II. 2-Mercaptopyridine derivative

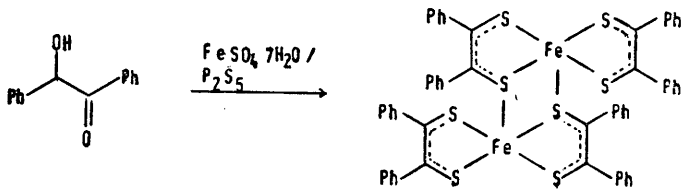
A type of acetyl CoA model compounds, 2-mercaptopyridine acetate (V)[6], was synthesized with 2-mercaptopyridine and acetyl chloride.



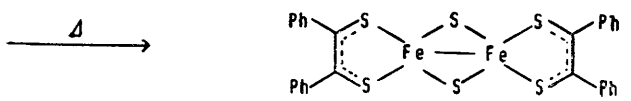
(V)

III. Benzoin-sulfur-iron derivative

From ferrous sulfate, benzoin and phosphorus pentasulfide, that was called, the Schrauzer's complex (VI)[7] was synthesized.



(VI)



(VII)

It has been known the compound (VI) resembled iron-sulfur centers in oxidation-reduction enzymes and the structure of (VI) was converted into that of (VII) by heat.[7]

Experimental

Infrared spectra were measured with a JOEC IRA-1 spectrometer, nuclear magnetic resonance spectra were taken with a Hitachi R-40 90 MHz spectrometer using tetramethylsilane as an internal reference. The elementary analysis was measured by a staff of the laboratory of organic microanalyses, the Institute of Physical and Chemical Research. All chemicals used were of the highest and reagent grade commercially in Japan.

Preparation:

N-Salicylideneethylamine (I) – To 100 ml of benzene in 300 ml of four neck flask connected with a mechanical stirrer, a condenser, a distilling tube receiver with a stopcock and a pressure equalizing funnel, 6.68 g of ethylamine hydrochloride and 10 g of salicylaldehyde were added and stirred. While the mixture was refluxed, 8.3 g of triethylamine was dropped into it. After the calculated amount of water was obtained in the distilling tube receiver with a stopcock, the mixture was kept at room temperature and concentrated with a rotary evaporator, and then the residue was distilled in vacuo, 4.8 g of the fraction of 170°–108°C/13 mmHg was collected (Yield 39.5%), ir(film), 1630 cm^{-1}; nmr ($CDCl_3$), δ 1.30 (t. 3H), 3.58 (q. 2H), 6.70–7.60 (m. 4H). 8.30 (s. 1H), 13.60 (s. 1H) ppm.

Salicylaldoxime (II)–To the mixed solution of 100 ml of ethyl alcohol and 20 ml of water, 44.7 g of salicylaldehyde and 39.7 g of hydroxylamine were added and stirred. After 30 ml of water solution dissolved 72 g of

sodium hydroxide was dropped into the mixture through a dropping funnel, it was refluxed for 2 hr and cooled to room temperature. After it was neutralized with diluted hydrochloric acid with cooling outside with ice, the product was extracted with benzene and the benzene solution was dried over anhydrous sodium sulfate and concentrated with a rotary evaporator. The residue was recrystalized with benzene and petroleum ether three times and 22.3 g of white powdery oxime was obtained (Yield 44.3%), m.p. 55.0°–56.8°C (lit.[1] 59°C), ir (nujol), 1610 cm^{-1}.

2-Cyanophenol (III)–The synthetic direction and procedure were similar to that described in the compound (II) except neutralization. 2-Cyanophenol was obtained from the reacted mixture neutralized and acidified with concentrated hydrochloric acid to pH.2, m.p. 91.0°C (lit.[3] 92°C), ir (nujol), 2250 cm^{-1}.

Salicylamine (IV)–To 500 ml of tetrahydrofurane, 51.0 g of sulfur powder was added and stirred at 0°C in an ice bath, and 15.1 g of sodium borohydride was added, then the hydrogen sulfide gas was generated and the color of the solution became red-brown. After the generation of the gas was finished, 22.7 g of salicylaldoxime in 50 ml of tetrahydrofurane was dropped into the solution through a dropping funnel and it was continued to stir after dropping for one hr at room temperature.[4]

And 200 ml of water was added to the mixture solution then, tetrahydrofurane was removed with a rotary evaporator. The product was extracted with benzene and diethyl ether and these were combined, concentrated to dryness and the residue was recrystalized with carbon tetrachloride, 15.9 g of pale orange powdery amine was obtained (Yield 78.0%); m.p. 122°C (lit.[4] 125°C); ir (nujol), 1600, 1570, 1490, 1450, 1380, 1315, 1260, 1200, 1160, 1135, 1080, 1040, 980, 930, 860, 750, 730 cm^{-1}; nmr ($CDCl_3$), δ 1.50 (s. 2H), 3.73 (d. 2H), 6.65–7.30 (m. 4H) ppm.

2-Mercaptopyridine acetate (V)–To 100 ml of tetrahydrofurane, 10.0 g of 2-mercaptopyridine and 9.1 g of triethylamine were added and stirred, then 8.5 g of acetyl chloride was dropped into the mixture solution and it was continued to stir for 2 hr at room temperature, then the precipitate was filtered and the filtrate was concentrated with a rotary evaporator, the residue was dissolved in 100 ml of ehtyl acetate and 30 ml of water, after the pH of water layer was adjusted to pH 7.2 with 10% of sodium hydroxide solution, the product was extracted with ethyl acetate and the solution was concentrated with a rotary evaporator, the residue was distilled in vacuo, then 3.0 g of the yellow fraction of 106.5°–117.0°C/12 mmHg was obtained (Yield 22.0%); ir (film), 3055, 2980, 2900, 1720, 1620, 1580, 1500, 1460, 1430, 1380 (sh), 1365, 1292, 1265, 1250, 1230, 1190, 1140, 1110, 1090, 1050, 990, 950, 765, 740, 720 cm^{-1}; nmr ($CDCl_3$), δ 2.45 (s. 3H), 7.15–7.35 (m. 1H), 7.45–7.95 (m. 2H), 8.58 (d. 1H) ppm.

Schrauzer's complex (VI)–To 250 ml of xylene, 25 g of benzoin and 25 g of phosphorus pentasulfide were added and refluxed for 3 hrs, then 25 g of ferrous sulfate heptahydrate, dissolved in 25 ml of methyl alcohol and 50 ml of water, was dropped into the refluxing mixed solution through a dropping funnel and more 25 ml of methyl alcohol was added to it, the color of the solution became dark green. It was continued to stir and reflux for more 2 hrs, after it was cooled to room temperature and filtered, and the residue on the filter paper was washed with methyl alcohol, 5.2 g of black powder was obtained (Yield 16.3%); m.p. > 300°C (lit.[4] 295°C); ir (nujol), 1580, 1520, 1270, 1180, 1160, 1080, 1030, 850, 775, 755, 740, 690 cm^{-1}; *Anal.* Calcd for $C_{28}H_{20}S_4Fe$: C, 62.2; H, 3.73. Found: C, 62.4; H, 3.89.

Discussion

Salicylamine (IV) was tried to make to react further with acetaldehyde for the purpose of obtaining acetylidene o-hydroxybenzylamine, but the desired compound could not been obtained,[8,9,10] in spite of that it was though first that acetylidene o-hydroxybenzylamine would be made to react with carbon dioxide to get the amino acid after hydrolysis.

If the active acetyl group was produced from 2-mercaptopyridine acetate, carbon dioxide would be allowed to react with it, and the Schrauzer's complex (VI) was used already for the catalyst for the reaction of carbon dioxide fixation with an acylthioalkyl compound to oftain α-keto acids.[11]

Finally these works were taken from the graduation

thesis by Misses Mitsuko Mochizuki and Yoshiko Nakagawa in my laboraotry.

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有機化学合成についての覚え書

山　口　　功

（昭和58年8月31日受理）

合成された化合物の多くは，炭酸ガス固定反応に役立つ物質であると考えている。その中でシュラウザー錯体に関しては，すでに田伏らによって試みられ成功している。2—メルカプトピリジンアセテートは今後共興味ある化合物として研究を続けて行くつもりである。サリチルアミンの誘導体は文献からも目的物を得るのは困難であり断念せざるを得なかった。