natural *l*-sparteine. *Anal.* Calcd. for $C_{19}H_{30}O_7N_2$ (Oxosparteine tartrate) : N, 7.03. Found : N, 6.85.

ii) Dioxosparteine, m.p. 160°, was reduced in 5% HCl solution at a room temperature over PtO_2 as in the foregoing. The product was derived to the dipicrate, m.p. 219° (from EtOH-dioxane). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot 2C_6H_3O_7N_3$ (α-Isosparteine dipicrate) : C, 46.82; H, 4.66; N, 16.28. Found : C, 46.58; H, 4.74; N, 15.85.

iii) Dioxosparteine, m.p. 184°, was reduced in 5% HCl solution at 80~90° over PtO_2 as before. The product formed a dipicrate, m.p. 244~246° (from EtOH). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot 2C_6H_3O_7N_3$: C, 46.82; H, 4.66; N, 16.28. Found : C, 46.52; H, 5.26; N, 15.87.

Summary

Dioxosparteine, obtained from 1-ethoxycarbonyl-3-(α-pyridyl)-4-oxoquinolizine, was chromatographically separated into three isomers : (A) m.p. 135~137°, (B) m.p. 159~160°, and (C) m.p. 182~184°. They were respectively reduced to oxosparteine, α-isosparteine, and a new isomer of sparteine.

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44. Shigehiko Sugasawa and Takashi Tatsuno : Oxidation of N-(β-3′,4′-Methylenedioxyphenethyl)-3-ethylpyridinium Salt and the Constitution of the Resultant Pyridone.

(*Pharmaceutical Institute, Medical Faculty, University of Tokyo**)

The course of the oxidation of 3-substituted pyridinium salts (I) is governed only by the nature of R′, whereas R seems to have hardly any influence. The results hitherto obtained in our laboratories are as follows :

When R′ is carboxyl¹⁾, N-methylpyrrolidyl-2²⁾, phenyl³⁾, or α-ethylenedioxyethyl³⁾, pyridone-6 (III) type of derivatives are the main, if not the sole, products, while N-methyl-3-ethylpyridinium salt gave only N-methyl-3-ethylpyridone-2 in a good yield⁴⁾. In these cases, the constitution of pyridones were proved by chemical method, but in some cases this method of confirmation is not always an easy task to do.

One of us (T. T.) proposed to make use of the dipole moment data in such cases to deduce the constitution and his attempts along this line have achieved substantial results. The present paper adds another successful example of his method of deduction.

When N-β-3′,4′-methylenedioxyphenethyl-3-ethylpyridinium bromide was subjected to alkaline ferricyanide oxidation, there was obtained a single pyridone derivative in a good yield. By measuring the dipole moment of this pyridone Tatsuno attributed N-(β-3′,4′-methylenedioxyphenethyl)-3-ethylpyridone-2 (IIb) to this substance, which was proved to be correct by an independent synthesis.

Ethyl α-carbethoxy-γ-cyanobutyrate (IV)⁵⁾ was prepared from acrylonitrile and diethyl malonate and this was then reduced to furnish ethyl 2-ketonipecotate (V), followed by ethylation (VI). After hydrolysis the latter was subjected to decarboxylation, yielding (VII), N-potassio derivative of which was then condensed with β-3,4-methylenedioxyphe-

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* Hongo, Tokyo (菅沢重彦, 辰野 高).

1) Sugasawa, Sakurai, Okayama : Ber., **74**, 537 (1941).

2) Sugasawa, Tatsuno : J. Pharm. Soc. Japan, **72**, 248 (1952).

3) Sugasawa, Kirisawa : Unpublished.

4) Sugasawa, Ban : J. Pharm. Soc. Japan, **72**, 1336 (1952).

5) Koelsch : J. Am. Chem. Soc., **65**, 2460 (1943).

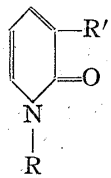
nethyl bromide in boiling xylene in the presence of copper powder, giving N-(β-3′,4′-methylenedioxyphenethyl)-3-ethylpiperidone-2 (VIII). Since this compound was not induced to crystallize, it was ring-closed by boiling with phosphoryl chloride and the resultant quaternary compound (IX) was reduced catalytically over Adams' Pt, yielding hexahydrobenzoquinolizine derivative (X), again an oil; but this gave crystalline picrate, which melted over a range of 154~166°. When this picrate was purified from alcohol about two-thirds of the original substance was recovered as hexagonal plates of m.p. 168~171°.

On the other hand, the pyridone supposed to be (IIb), obtained by the oxidation method, was ring-closed to furnish (XI), which was then reduced catalytically over Adams' Pt to an oily hydrobenzoquinolizine derivative. The picrate of the latter separated as needles of m.p. 159~161°, which on admixture with the one of m.p. 168~171°, mentioned above, melted over a range of 156~166°. Therefore, the lower melting picrate was inoculated to the mother liquor of the higher melting one and there separated a picrate of m.p. 159~161° in an yield of about one-third of the higher melting one.

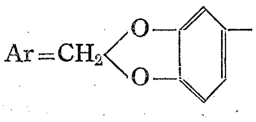
When, however, the pyridone (IIb) first reduced in a neutral solution over Raney Ni, the resultant piperidone (XII) ring-closed (XIII), and was reduced catalytically over Adams' Pt, there was obtained an oily hydrobenzoquinolizine derivative from which only a higher melting picrate (m.p. 169~171°) was isolated, the melting point not being depressed on admixture with the higher melting one obtained by synthesis.

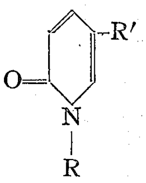
Thus, it was proved beyond doubt that the pyridone obtained by oxidation is N-(β-3′,4′-methylenedioxyphenethyl)-3-ethylpyridone-2 (IIb), as was deduced by Tatsuno from its dipole moment measurement.

(I)

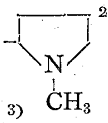


(II) { (a) $R=CH_3$, $R'=C_2H_5$
(b) $R=Ar\text{-}CH_2\text{-}CH_2\text{-}$, $R'=C_2H_5$

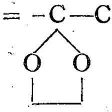


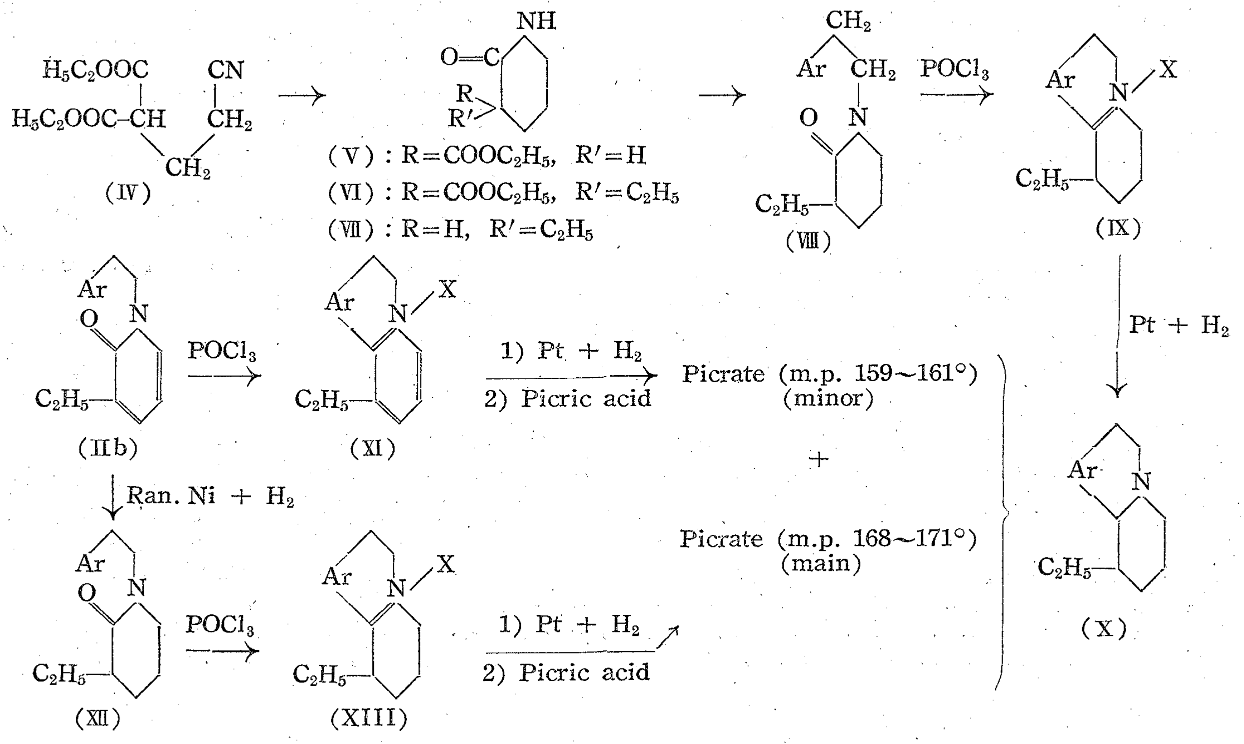


(III) { $R=Ar\text{-}CH_2\text{-}CH_2\text{-}$ [1)]
$R'=\text{-}COOH$
$R=Ar\text{-}CH_2\text{-}CH_2$, $R'=$ [2)]



$R=CH_3$, $R'=C_6H_5$ [3)]
$R=CH_3$, $R'=\text{-}C\text{—}CH_3$ [3)]





The authors are grateful to Messrs. Saito and Muneyuki for microanalytical data.

Experimental

N-(β-3′,4′-Methylenedioxyphenethyl)-3-ethylpyridone-2 (IIb)—3-Ethylpyridine (2 g., b.p. 163~165°) and 3,4-methylenedioxyphenethyl bromide (4.3 g.) were condensed in boiling benzene, yielding the corresponding pyridinium bromide of m.p. 190~191° in nearly quantitative yield. This (5 g.) in conc. aq. solution was mixed with a cold saturated solution of $K_3Fe(CN)_6$ (15 g.), precipitating the double salt as a faint orange solid. To this a large excess of KOH pellet (35 g.) was added at 25° with vigorous stirring. The mixture was covered with benzene (50 cc.) and the whole was stirred for 4 hrs. at 20~25°. The supernatant benzene layer was then separated and the remaining aq. solution was repeatedly extracted with benzene. The combined benzene solution was washed with water, dried and evaporated, and the residue was distilled *iu vacuo*, yielding an oily distillate of b.p$_{0.05}$ 175~182°, which solidified on standing. Yield, 3.3 g. Purified from hexane, forming colorless scales of m.p. 82~83°. *Anal.* Calcd. for $C_{16}H_{17}O_3N$: C, 70.6; H, 6.3; N, 5.2. Found : C, 70.2; H, 6.1; N, 5.6.

N-(β-3′,4′-Methylenedioxyphenethyl)-3-ethylpiperidone-2 (VIII)—(a) By synthetic method : 3-Ethylpiperidone-2 (2 g., prepared according to Koelsch) in pure xylene (10 cc.) was heated for 1 hr. with K (0.6 g.) to give N-potassio derivative. 3,4-Methylenedioxyphenethyl bromide (4 g., 0.4 g. in excess) and Cu powder (0.1 g.) were added and the whole was refluxed for about 20 hrs. until neutral to litmus. The filtrate from KBr and Cu powder was washed with water, dried, and evaporated. The residue obtained was dissolved in pure benzene and was purified through an alumina column and fractionated, giving a faint yellow viscous syrup of b.p$_{0.2}$ 189~195° (this piperidone will be referred to as piperidone-(*a*) (VIII)). Yield, 1.1 g. This is devoid of basicity and gives no hydrochloride, picrate, or picrolonate.

(b) By reduction of the pyridone (IIb) : The pyridone (2 g.) in EtOH (20 cc.) was reduced over Raney Ni (prepared from 3 g. of the alloy), prompt absorption of H_2 being observed. The catalyst was filtered off and EtOH was removed from the filtrate. The residue was distilled *in vacuo*, furnishing a fraction of b.p$_{0.04}$ 188~197° (referred to as piperidone-(*b*) (XII)) as a viscous oil, which does not give a hydrochloride, picrate, nor picrolonate. Yield, 1.7 g.

4′,5′-Methylenedioxy-3,4,5,6,7,8-hexahydro-8-ethyl-(1,2 : 2′,1′-benzoquinolizine)(X)—i) From piperidone-(*a*) (VIII) : Piperidone-(*a*) (1 g.) and $POCl_3$ (5 cc.) were boiled for 1 hr. Excess of $POCl_3$ was removed *in vacuo* and the residue was treated with ice-water to give about 20 cc. of a solution which was shaken with benzene to remove some resinous substance that remained undissolved. The aq. layer was filtered through a wet filter, neutralized with $NaHCO_3$, and added with KI, separating an oily iodide. The latter was taken up in $CHCl_3$, washed with saturated NaCl solution, dried, and evaporated, leaving a yellowish residue (0.6 g.). This was then converted to the corresponding chloride as usual in EtOH, purified with a little decolorizing carbon, and reduced catalytically over Adams' Pt. The reduction product was obtained as a yellowish syrup (0.3 g.) from which a picrate with a melting range of 154~166° was obtained. This was purified from EtOH, giving yellow hexagonal plates of m.p. 168~171°, difficultly soluble in EtOH, in a yield of 0.28 g., corresponding to about two-thirds of the original crude picrate. By inoculating the mother liquor with a picrate of m.p. 159~161°, mentioned below, the same picrate of m.p. 159~161° was obtained in 0.08 g. yield. *Anal.* Calcd. for $C_{22}H_{24}O_9N_4$ (for the picrate of m.p. 168~171°) : C, 54.1; H, 5.0; N, 11.5. Found : C, 53.7 ; H, 4.7 ; N, 11.3.

ii) From the pyridone (IIb) : The pyidone (IIb, 2 g.) was ring-closed by boiling with $POCl_3$ (10 cc.) and the product was worked up as above. The quaternary iodide (XI) precipitated as a yellow solid, the supernatant liquid was poured off, and washed with cold water. The corresponding chloride in EtOH, prepared from the iodide as usual, was reduced catalytically over Adams' Pt and the reduction product was obtained as a yellowish viscous syrup. Yield, 0.9 g. The crude picrate (m.p. 154~158°), once crystallized from EtOH, gave fine yellow needles of m.p. 159~161°. *Anal.* Calcd. for $C_{22}H_{24}O_9N_4$: C, 54.1; H, 5.0; N, 11.5. Found : C, 54.0; H, 5.2; N, 11.1. No trace of the sparingly soluble picrate of m.p. 168~171° was detected.

iii) From piperidone-(*b*) (XII) : The piperidone-(*b*) (1.7 g.) was ring-closed with $POCl_3$ (10 cc.) and the product was worked up us above. The oily iodide (XIII), which was collected in $CHCl_3$, amounted to 1.1 g. This was dissolved in EtOH, treated with decolorizing carbon, and the filtrate was hydrogenated over Adams' Pt, yielding a faint yellow solution after absorbing 84 cc. of H_2. The picrate was prepared from the oily reduction product as yellow solid melting at 163~167°, which was purified from EtOH. The picrate was obtained as yellow hexagonal plates of m.p. 167~170°, which was not depressed on admixture with the one obtained under (i) from piperidone-(*a*) (VIII).

Though the mother liquor was inoculated with the lower melting picrate, nothing but a small amount of higher-melting, sparingly-soluble picrate separated on prolonged cooling and standing.

Summary

Oxidation of N-(β-3′,4′-methylenedioxyphenethyl)-3-ethylpyridinium bromide by alkaline potassium ferricyanide furnished a single pyridone in a good yield. One of the writers (Tatsuno) attributed N-substituted 3-ethylpyridone-2 to this compound by measuring the dipole moment of this substance. The correctness of his deduction is now supported by an independent synthesis of the compound which was also derived from this pyridone.

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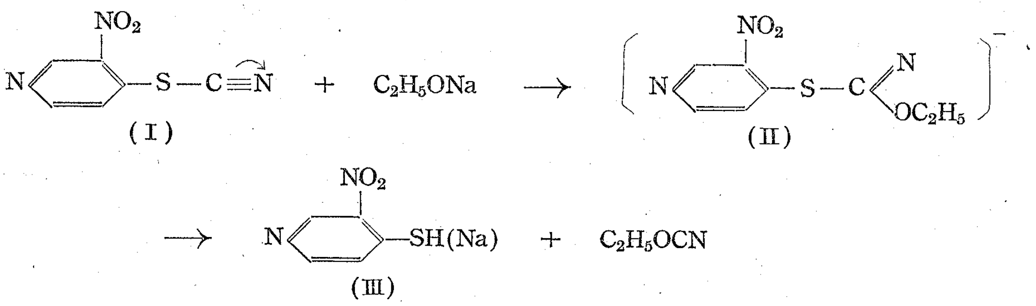
45. **Torizo Takahashi, Kan-ichi Ueda, and Toshiro Ichimoto**: Sulfur-containing Pyridine Derivatives. XLI*. Synthesis of 3-Nitro-4-mercaptopyridine Derivatives and Pyrido[3,4:4′,5′]thiazoles.

*(Pharmaceutical Institute, Medical Faculty, University of Kyoto**)*

A few investigations have been made by Ross1), and Davies and Sexton2) about the reaction of organic thiocyano compounds with sodium ethoxide. In one of them Ross has shown that thiocyanobenzene reacted with sodium ethoxide in ethanol to give diphenyl disulfide, ethyl phenyl sulfide, and sodium thiophenate. Furthermore, in the case of 2-thiocyanobenzothiazole, Davies and Sexton reported that they obtained 2-mercaptobenzothiazole and 2-ethylthiobenzothiazole by the reaction analogous to the foregoing. In this paper, the result of the reaction of 3-nitro-4-thiocyanopyridine3) with sodium ethoxide is described.

3-Nitro-4-thiocyanopyridine (I) was reacted with sodium ethoxide in ethanol under the same conditions as had been employed by Davies and Sexton and formed 3-nitro-4-mercaptopyridine (III)4) in a good yield, which was ascertained by the formation of 3-nitro-4-ethylthiopyridine4) by the reaction between (III) and C_2H_5I. In addition, formation of by-products of 3,3′-dinitrodipyridyl-(4,4′) mono- and disulfides4) in very small amounts was observed. However, ethylthio compound corresponding to ethylthiobenzene or 2-ethylthiobenzothiazole which Ross and Davies had mentioned in their respective cases, was not obtained. This reaction mechanism can be assumed as follows:



C_2H_5OCN would isomerize to isocyanate and by combining with ethanol or sodium ethoxide, form ethyl ethylcarbamate, EtNHCOOEt, or its sodium enolate, but the latter was not detected.

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* Part XL: This Bulletin, **2**, 78 (1954).

** Yoshida-konoe-cho, Sakyo-ku, Kyoto (高橋酉蔵, 上田寛一, 櫟本敏郎).

1) Ross: J. Am. Chem. Soc., **56**, 727 (1934).

2) Davies, Sexton: J. Chem. Soc., **1944**, 11.

3) Takahashi, Ueda: This Bulletin, **2**, 34 (1954).

4) Takahashi, Ueda: *Ibid.*, **2**, 78 (1954).