

The analogous triterpene ketones are found rarely in nature. Cycloartenone has been isolated from *Artocarpus integrifolia*<sup>5)</sup> and *Tillandsia usneoides*,<sup>6)</sup> and recently, the isolation of 31-norcyclolaudenone from *Musa sapientum*<sup>7)</sup> was reported by F.F. Knapp, *et al.* And the corresponding ketones of the other triterpenes have not been found. The cycloneolitsin was the first example having geminal dimethyl group at C-24 from *Neolitsea dealbata*<sup>8)</sup> and this substance was synthesized by Rafael Labriola, *et al.*<sup>8)</sup> But the other derivatives of this substance have not been found from natural sources.

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### Novel Synthesis of Thiophene Derivatives from 1,3-Oxathiol-2-ylideneimmonium Salt

In a continuation of our previous studies of the chemistry of sulfur-containing heterocyclic  $\pi$ -electron systems, we have synthesized a novel trihetero cation system, the 1,3-oxathiol-2-ylideneimmonium ion (I),<sup>1)</sup> which has a resonance contribution from 2-dialkylamino-1,3-oxathiolium ion (I'). We also demonstrated that reaction with some active methylene compounds give 1,4-oxathiafulvenes (II) and ketene S,N-acetals (III). We now wish to report a novel and ready synthesis of thiophene derivatives<sup>2)</sup> from I.

Reaction of 4-phenyl-1,3-oxathiol-2-ylidene-piperidinium hydrogensulfate (I: X=HSO<sub>4</sub>)<sup>1)</sup> with acetylacetone in the presence of triethylamine in CH<sub>2</sub>Cl<sub>2</sub> gave yellow crystals of mp 121—123°, the physical data of which suggest the thiophene structure IVa (yield 41.5%): C<sub>19</sub>H<sub>21</sub>O<sub>2</sub>NS (M<sup>+</sup> 327); UV  $\lambda_{\max}^{\text{EtOH}}$  m $\mu$  (log  $\epsilon$ ): 250 (4.14), 360 (4.15); IR  $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 1683 (COCH<sub>3</sub>), 1616 (COC<sub>6</sub>H<sub>5</sub>); NMR (CDCl<sub>3</sub>)  $\tau$ : 7.78 (CH<sub>3</sub>), 7.56 (COC<sub>6</sub>H<sub>5</sub>).

On the other hand, reaction of I-HSO<sub>4</sub><sup>-</sup> with three molar equivalents of the sodium salt of the anion prepared from NaH and acetylacetone in abs. tetrahydrofuran, gave 29.8%.

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yield of IVa accompanied by Va, mp 101–103°, in 32.6% yield. On standing in ether at room temperature, compound Va readily converted to IVa. The analysis,  $C_{19}H_{23}O_3NS$ , and infrared (IR) spectrum, 3460 (OH), 1684 ( $C_6H_5COCH<$ ), 1615  $cm^{-1}$  ( $CH_3CO-C=C-N<$ ), suggest a ketol structure for Va. Isolation of the intermediate Va was not necessary and when the reaction of  $I \cdot BF_4^-$  with 1.2 molar equivalents of the Na salt of the anion was carried out in tetrahydrofuran, thiophene IVa was obtained in 71% yield.

In an analogous reaction with benzoylacetone ( $I \cdot BF_4^-$  and the Na salt of the anion in tetrahydrofuran) ketol Vb, mp 112–114°, and thiophene IVb, mp 132–133°, were obtained in 71 and 11% yield, respectively. The possibility of the compounds having the alternative structure,  $R_1=C_6H_5$  and  $R_2=COCH_3$ , arising from condensation in another direction, was eliminated by spectral data considerations: IVb IR  $\nu_{max}^{KBr}$   $cm^{-1}$ . 1648 (4-COC<sub>6</sub>H<sub>5</sub>), 1615 (2-

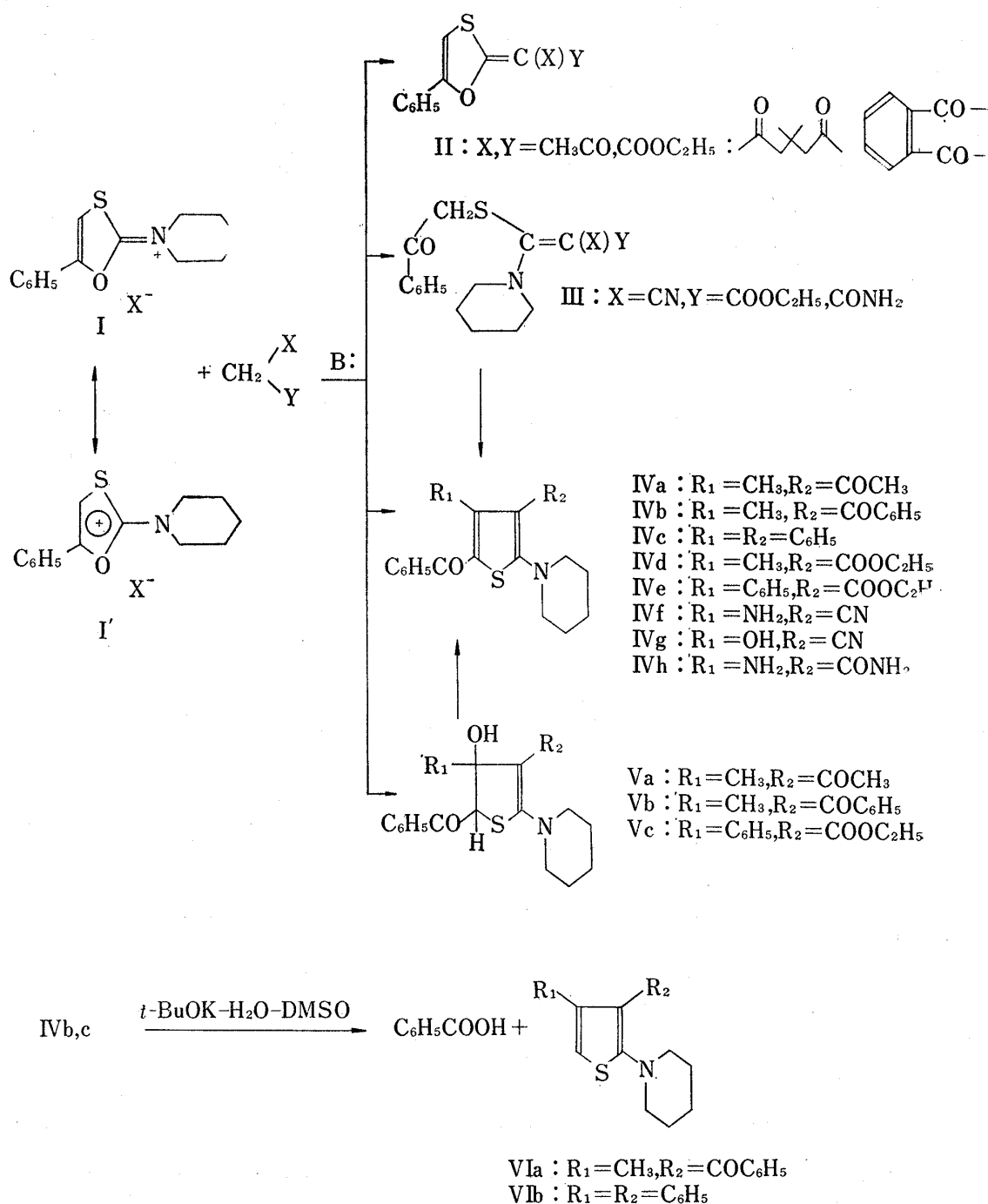


Chart 1

$\text{COC}_6\text{H}_5$ ),<sup>3)</sup> NMR ( $\text{CDCl}_3$ )  $\tau$ : 7.78 (3- $\text{CH}_3$ ); UV  $\lambda_{\text{max}}^{\text{EtOH}}$   $m\mu$  ( $\log \epsilon$ ): 256 (4.37), 278 (sh), (4.06), 375 (4.27); Vb IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3373<sup>b</sup> (OH), 1690 (2- $\text{COC}_6\text{H}_5$ ), 1605 (4- $\text{COC}_6\text{H}_5$ ); NMR ( $\text{CDCl}_3$ )  $\tau$ : 8.12 ( $\text{CH}_3\text{-C}$ ), 6.67<sup>b</sup> (OH), 5.07 (CO- $\text{CH-S}$ ). Treatment of IVb by Gassman's procedure<sup>4)</sup> for the cleavage of non-enolizable ketones using *tert*-BuOK- $\text{H}_2\text{O}$ -DMSO gave benzoic acid and oily VIa whose nuclear magnetic resonance (NMR) spectrum showed a quartet due to the thiophene ring proton at  $\tau$  3.64 ( $J=1.2$  Hz), and a doublet due to the  $\text{CH}_3$  group at  $\tau$  7.81 ( $J=1.2$  Hz), and whose ultraviolet (UV) spectrum showed a strong absorption at 253  $m\mu$  ( $\log \epsilon$  4.22) and a weak one at 379  $m\mu$  ( $\log \epsilon$  3.24).

Analogous treatment of I with ketone,  $\beta$ -ketoesters, and cyano compounds gave products as shown in Chart 1. Thiophene IVc, obtained from the reaction of  $\text{I}\cdot\text{BF}_4^-$  and the Na salt of the anion of deoxybenzoin, showed C=O stretching absorption at 1610  $\text{cm}^{-1}$  due to the 2- $\text{COC}_6\text{H}_5$  group. Treatment of IVc with *tert*-BuOK- $\text{H}_2\text{O}$ -DMSO gave benzoic acid and thiophene VIb, mp 156–158°, in 92% yield. Reaction of  $\text{I}\cdot\text{BF}_4^-$  with the Na salt of the anion of ethyl benzoylacetate in tetrahydrofuran gave thiophene IVe, mp 84–86°, and dihydrothiophene Vc, mp 117–118°, in 43 and 17% yield, respectively. The IR spectrum of IVe showed IR absorption bands at 1690, 1245 ( $\text{COOC}_2\text{H}_5$ ), 1608  $\text{cm}^{-1}$  (2- $\text{COC}_6\text{H}_5$ ), but Vc showed bands at 3400<sup>b</sup> (OH), 1699 ( $\text{COC}_6\text{H}_5$ ), 1615, 1315  $\text{cm}^{-1}$  ( $\text{COOC}_2\text{H}_5$ ). When  $\text{I}\cdot\text{HSO}_4^-$  was allowed to react with malononitrile in the presence of triethylamine in  $\text{CH}_2\text{Cl}_2$ , thiophene IVf was obtained in 86% yield. Ketene S,N-acetals (III) obtained in the previous report<sup>1)</sup> were treated with  $\text{CH}_3\text{ONa}$  to give the aromatized products IVg,h in good yield.

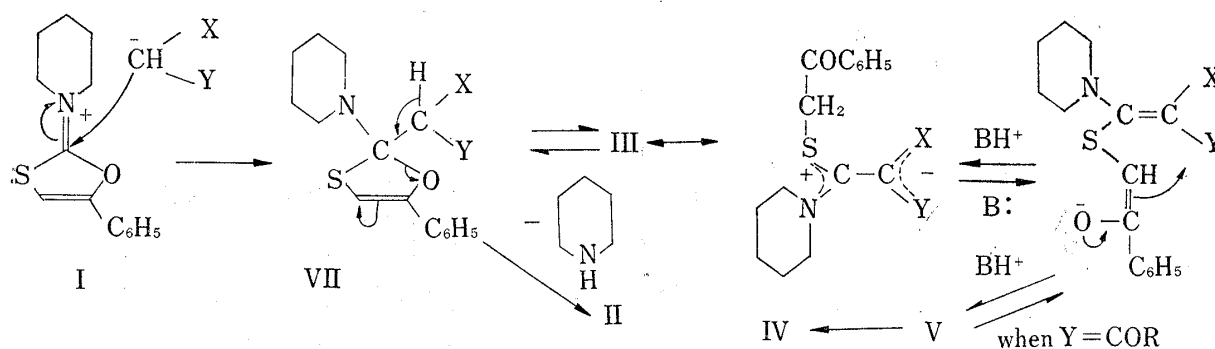


Chart 2

A possible mechanism for the reaction is outlined in Chart 2. The anion from the active methylene compound attacks the C-2 position of the 1,3-oxathiole ring giving the intermediate VII. With dimedone or indandione, strain arising from thiophene formation causes preferential elimination of piperidine to give 1,4-oxathiafulvene II. With other active methylene compounds, however, the 1,2-elimination occurs in the direction of C-O bond fission giving ketene S,N-acetal III. Isomerization easily occurs due to the low barrier for rotation around the C=C bond.<sup>5)</sup> When  $\text{Y}=\text{COR}$  and  $\text{X}=\text{COR}$ ,  $\text{COOR}$  or  $\text{CN}$ , Aldol type condensation occurs giving ketol V, subsequent dehydration affording thiophene IV. When  $\text{Y}=\text{CN}$  and  $\text{X}=\text{CN}$  or  $\text{CONH}_2$ , Thorpe-Ziegler type condensation occurs to give IVf,h, and when  $\text{Y}=\text{COOC}_2\text{H}_5$  and  $\text{X}=\text{CN}$ , Dieckmann type condensation occurs giving IVg.

Work is currently in progress with other nucleophiles.

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### The Absolute Configuration of Cularine: A Chemical Correlation to L(S)-Laudanosine

Alkaloids of the cularine group<sup>1)</sup> isolated from the genera *Dicentra* and *Corydalis* (Papaveraceae) have the unique structural feature of the diphenyl ether linkage forming a seven-membered heterocycle in their molecules.

The absolute stereochemistry of cularine (I) has been assigned by optical rotatory dispersion (ORD) measurement of its sodium-liquid ammonia reduction product (II) that it has D(R)-configuration.<sup>2)</sup> We describe here our results on the determination of the absolute configuration of this group of alkaloids by chemical correlation to L(S)-romneine (III),<sup>3,4)</sup> of which configuration has previously been correlated to L(S)-laudanosine (IV).<sup>5)</sup>

Bromination of L(S)-romneine (III)<sup>4b)</sup> gave a monobromo derivative (V), mp 101.5—102°,  $[\alpha]_D + 49.0^\circ$  (EtOH). This was characterized as L(S)-6'-bromoromneine (V) by nuclear magnetic resonance (NMR) measurement and by spectral (infrared (IR), NMR, ultraviolet (UV)) and thin-layer chromatography (TLC) comparisons with dl-6'-bromoromneine<sup>6)</sup> obtained *via* standard Bischler-Napieralski synthesis starting from 6-bromohomoveratric acid and homo piperonylamine. V and guaiacol were submitted to Ullmann condensation in pyridine in presence of cupric oxide<sup>7)</sup> and potassium carbonate to afford L(S)-6'-(2-methoxyphenoxy)-romneine (VI) as an oily product,  $[\alpha]_D + 70.0^\circ$  (EtOH). Sodium-liquid ammonia reduction of VI resulted in concomitant fission of both methylenedioxy group and diphenyl ether linkage to afford a mixture of two species of diphenolic bases (VII) and (VIII) in agreement with the prediction<sup>8)</sup> of the direction of ether fission. Without separation this mixture was treated with ethereal diazomethane for 24 hours, and a monomethylated derivative (IX) was isolated from the reaction mixture as an alkali-insoluble fraction, colorless oil,  $[\alpha]_D - 26.8^\circ$  (EtOH), NMR (CDCl<sub>3</sub>)  $\tau$ : 7.41 (3H, s, NCH<sub>3</sub>), 6.29, 6.24, 6.20 (3×3H, s, 3×OCH<sub>3</sub>), 3.65—2.83 (5H, arom. H). Being soluble in Claisen's alkali,<sup>9)</sup> this base (IX) was found to

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