

SYNTHESIS UTILIZING  $\beta$ -CARBONYL SYSTEM. IV

A NOVEL CYCLIZATION OF 1,9-DIIMINO-3,7-DICARBONYL AND -3,5,7-  
TRICARBONYL COMPOUNDS

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Bis-(3-methyl-5-isoxazolylmethyl) ketone

(1) was converted into 1,9-diimino-3,7-dicarbonyl compounds (3 and 7), which were cyclized to 8-isoquinolinols (5 and 10) by hydrochloric acid in high yields. The compound (12) containing a sterically crowded 1,9-diimino-3,5,7-tricarbonyl system was prepared from the methyl analogue (11) of the ketone (1). The cyclization of 12 afforded the 4-pyridone (13) exclusively.

In continuation of our studies on the preparation of bis-isoxazole-ketones<sup>1)</sup>, we now wish to report the behavior of these ketones toward hydrogenolysis and subsequent recyclization under acidic media.

Partial hydrogenation of the ketone (1)<sup>2)</sup> using platinum

oxide gave the carbinol (2a) [bp 140~145° (0.15 mm); IR(liquid): 3350  $\text{cm}^{-1}$ ] first, whereas uptake of 3 mol equiv of hydrogen led it to the diimino-diketo-alcohol (3a) in 96.4% yield. This produced the 8-isoquinolinol (5a) hydrochloride [mp >270°; IR(nujol): 1660 and 1610  $\text{cm}^{-1}$ ; NMR( $\text{d}_6$ -DMSO-TFA)  $\tau$ : 2.08~2.82 (4H), 6.74 (3H, s) and 7.34 (3H, s); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm( $\epsilon$ ): 376 (5600), 308 (3200), 247 (sh) (16800), 235 (sh) (21200) and 226 (26400);  $\lambda_{\text{max}}^{\text{EtOH-0.1N NaOH}}$  nm( $\epsilon$ ): 370 (5900), 328 (4300) and 250 (12500)<sup>3)</sup>; m/e 173 ( $\text{M}^+ - \text{HCl}$ )] on refluxing in dilute hydrochloric acid for a short time.

In the same manner as with 2a, the carbinol (2b)<sup>4)</sup> was converted into 3b [mp 123~124°; IR(nujol): 3330, 3150, 1640 and 1595  $\text{cm}^{-1}$ ; NMR( $\text{CDCl}_3$ )  $\tau$ : 2.70 (5H, s), 5.14 (2H, s), 7.21 (4H, s) and 8.26 (6H, s); m/e 302 ( $\text{M}^+$ )] which, on treatment with dilute hydrochloric acid at room temperature, gave the 8-isoquinolone (4b) hydrochloride [mp 304~305° (dec); IR(nujol): 3280, 3200, 1705 and 1640  $\text{cm}^{-1}$ ; NMR( $\text{d}_6$ -DMSO)  $\tau$ : 6.38 (2H, s), 6.65 (2H, s), 7.05 (3H, s) and 7.29 (3H, s); m/e 267 ( $\text{M}^+ - \text{HCl}$ )] in 46.6% overall yield from 2b. Also obtained in 18.1% yield was the 8-isoquinolinol (5b) hydrochloride [mp 304~306°; IR(nujol): 1660 and 1620  $\text{cm}^{-1}$ ; NMR( $\text{d}_6$ -DMSO-TFA)  $\tau$ : 2.20~2.60 (8H), 6.73 (3H, s), and 7.33 (3H, s); m/e 249 ( $\text{M}^+ - \text{HCl}$ )].

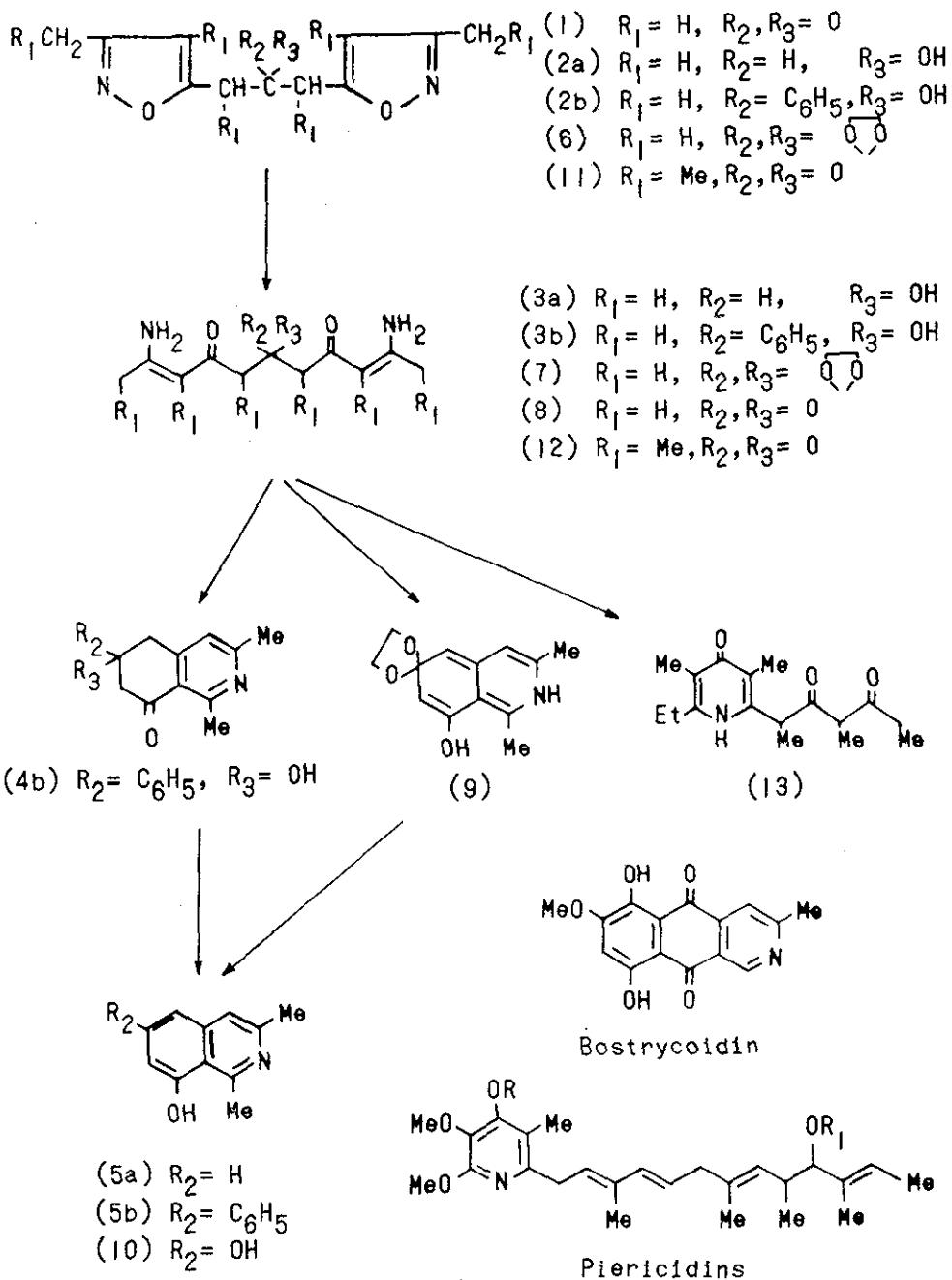
An attempt to obtain the diimino-triketone (8) by acid treatment of the diimino-diketo-ketal (7) [mp 175~176°; IR(nujol): 3300, 3150, 1620 and 1600  $\text{cm}^{-1}$ ; NMR( $\text{CDCl}_3$ )  $\tau$ : 0.08 (2H, bs), 4.80 (2H, s) 4.90 (2H, bs), 6.01 (4H, s), 7.20 (4H, s) and 8.08 (6H, s); m/e 268 ( $\text{M}^+$ )] which was derived from 1 by the conventional ketalization followed by hydrogenolysis resulted in the formation of the 6-isoquinolone-ketal (9) [mp 201~203° (dec); IR(nujol): 3500~2500 (br) and 1620

$\text{cm}^{-1}$ ;  $\text{UV} \lambda_{\text{max.}}^{\text{EtOH}}$  nm( $\epsilon$ ): 325(5400), 275(5400), 244(51400) and 223(19700);  $\lambda_{\text{max.}}^{\text{EtOH-0.1N NaOH}}$  nm( $\epsilon$ ): 340(7200), 258(27000);  $\text{NMR}(\text{d}_6\text{-DMSO}) \tau$ : 2.79 (1H, s), 3.36 (1H, d,  $J$  = 2Hz), 3.40 (1H, d,  $J$  = 2Hz), 5.93 (2H, t,  $J$  = 5Hz), 6.23 (2H, t,  $J$  = 5 Hz), 7.04 (3H, s) and 7.55 (3H, s); m/e 233( $M^+$ )] in 73.8 % yield accompanied with trace amounts of the 6,8-isoquinolinediol (10) [mp 188~190° (dec); IR(nujol) 3500~3200 and 1660  $\text{cm}^{-1}$ ; UV  $\lambda_{\text{max.}}^{\text{EtOH}}$  nm( $\epsilon$ ): 328(4500), 278(7300), 264(8500), 245(31600) and 220 (14000);  $\lambda_{\text{max.}}^{\text{EtOH-0.1N NaOH}}$  nm( $\epsilon$ ): 345(5000), 300(5000), 275(sh)(16400) and 263(22000), m/e 189( $M^+$ )].

On the other hand, the sterically hindered carbonyl group in the ketone (11) resisted to hydrogenation using platinum oxide, while smooth cleavage of the isoxazole ring occurred. Crude diimino-triketone (12) obtained was treated with the acid to yield the 4-pyridone (13) [mp 127~129°; IR(nujol): 3270, 3170, 3055, 1740, 1710, 1635 and 1615  $\text{cm}^{-1}$ ;  $\text{UV} \lambda_{\text{max.}}^{\text{EtOH}}$  nm( $\epsilon$ ): 273(11400) and 219(16500); m/e 291( $M^+$ ), 262( $M^+ - \text{C}_2\text{H}_5$ ), 234( $M^+ - \text{COC}_2\text{H}_5$ ), 206( $M^+ - \text{CH}_3\text{CHCOC}_2\text{H}_5$ ) and 178( $M^+ - \text{COCHCH}_3\text{COC}_2\text{H}_5$ )] exclusively.

Although such bis-isoxazole-ketones as 1 and 11 could not make the equivalents of linear  $\beta$ -pentaketones<sup>5)</sup>, the cyclization modes of 1,9-diimino-3,7-dicarbonyl and -3,5,7-tricarbonyl compounds are of interest in connection with the structures of some antibiotics originated from  $\beta$ -polyketides like bostrycoidin<sup>6)</sup> and piericidins<sup>7)</sup>.

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References and Notes

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- 4) This compound was obtained as a by-product of the reaction between 3-methyl-5-isoxazolylmethyl carbanion and methyl benzoate [mp 118~119°; IR(nujol): 3400  $\text{cm}^{-1}$ ; NMR( $\text{CDCl}_3$ )  $\tau$ : 7.80 (6H, s), 6.64 (4H, s), 4.35 (2H, s) and 2.80~2.60 (5H); m/e 298 ( $M^+$ )].
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