

A NOVEL REARRANGEMENT OF AN 6-ETHOXYCARBONYL-2,7,8-TRIOXOERYTHRINAN
TO AN ISOQUINOLINO- α -PYRIDONE DERIVATIVE¹

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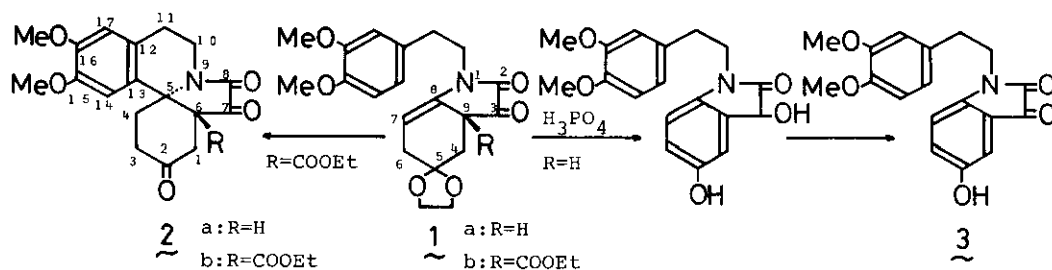
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Acid catalysed cyclization of the dioxopyrroline derivative 1b smoothly gave the 2-oxoerythrinan derivative 2b after deacetalization of the intermediate 5. Further acid treatment of 2b gave the pentacyclic compound 7 which could rearrange into an isoquinolino- α -pyridone derivative 13 on additional treatment with anhyd. H_3PO_4 or PPA. Each compound, 5, 2b, 7, or 13, was isolable in a satisfactory yield by controlling the reaction condition.

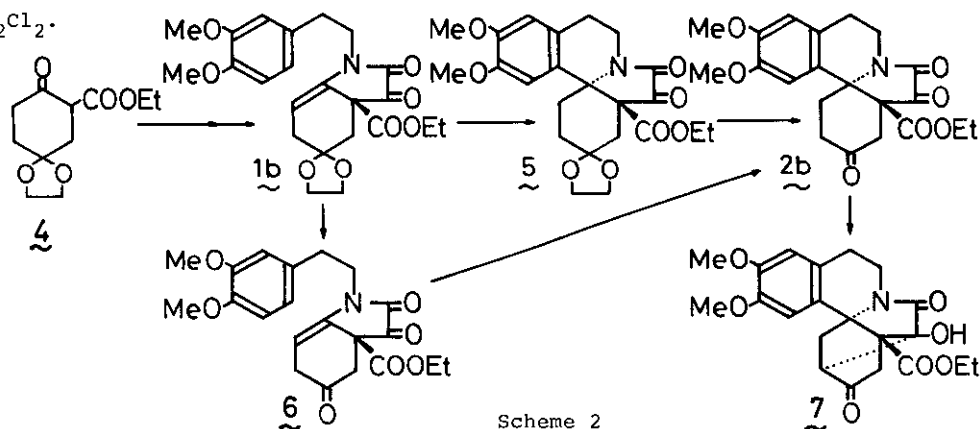
In a previous paper² we showed high yield cyclization of 9-ethoxycarbonyl-1- β -arylethyl-tetrahydroisatins to 6-ethoxycarbonyl-7,8-dioxoerythrinans. A particular advantage in the use of an 9-ethoxycarbonyl derivative rather than that of an 1- β -arylethyl-tetrahydroisatin itself may be in the synthesis of an oxoerythrinan such as 2, because attempted cyclization of 1a failed to yield the corresponding erythrinan 2a; aromatization took place to furnish a hydroxyisatin 3³ instead.

In this communication we show easy cyclization of the ethoxycarbonyl derivative 1b to the corresponding erythrinan 2b, which is smoothly convertible to 2a by decarboxylation with $MgCl_2$ -DMSO⁴, and describe a new rearrangement of 2b to an isoquinolino- α -pyridone derivative 13.



Scheme 1

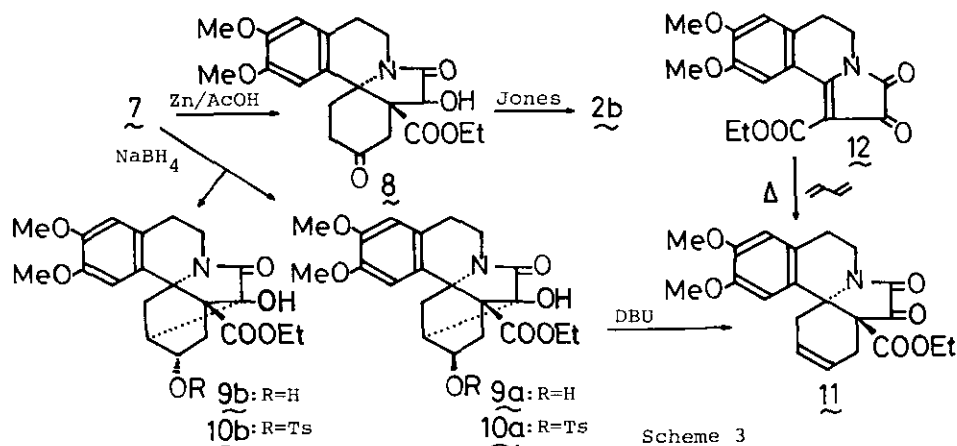
The dioxopyrroline 1b was easily prepared by condensation of 4⁶ with homoveratrylamine followed by oxalylolation as described previously². Treatment of 1b with AgClO₄ in benzene at 90° for 1 hr yielded 5⁵, 2b⁵, and 7⁵ in 25, 32, and 25% yields, respectively. Reaction of 1b with BF₃·Et₂O in CH₂Cl₂ under reflux for 40 min gave a similar result, ratios of 5, 2b, and 7 being ca. 1:1:1. On the other hand, treatment of 1b with anhyd. H₃PO₄ at room temp. for 1.5 hr produced, together with 7 (10%), the deacetalization product 6 (70%) which, on further treatment at 70° with the same reagent, was smoothly converted to 7. The compound 7 was also obtained in high yield from 2b on treatment with excess BF₃·Et₂O in CH₂Cl₂.



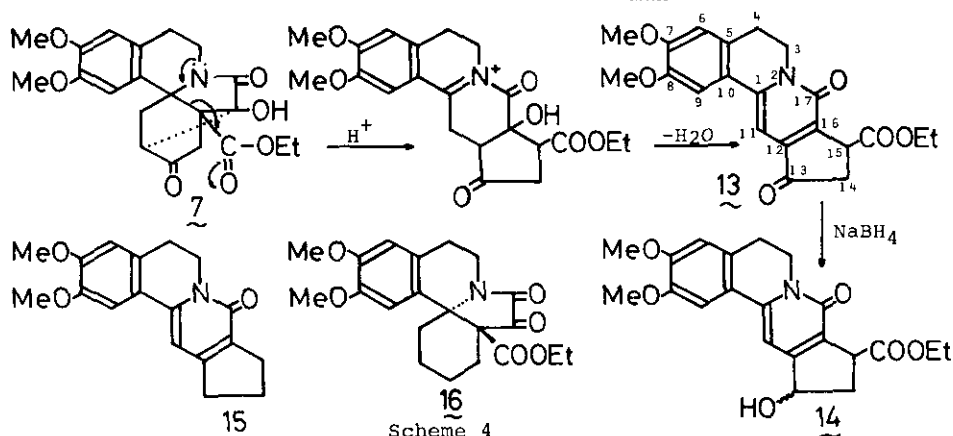
Scheme 2

The structure of 5, 6, and 2b are based on the spectroscopic evidences and usual interconversions. The compound 7 was suggested as the pentacyclic ketol having resulted from an intramolecular aldol condensation of 2b, since it exhibited ¹³C-NMR signals of three -C- (δ 65.9, 68.6, and 88.2) and one -CH (δ 54.2), and the IR absorptions of a 5-membered ring ketone (1760), an ester (1715), a lactam (1695), and a hydroxyl group (3400 br cm⁻¹). This assignment was verified by the following reactions.

Zn-AcOH reduction of 7 yielded a mixture of the keto-alcohol (8) which on Jones oxidation furnished a trioxo-compound identical with 2b in all respects (IR, TLC, and mp). NaBH₄ reduction of 7 afforded a mixture of the epimeric alcohols (9a and 9b) which was tosylated and the resulting mixture of the tosylates was treated with DBU in benzene for 5 min at 80°. Thus the β-tosylate (10a)⁵ was changed into the olefin (11)⁵, and the α-tosylate (10b)⁵ remained unchanged. Identity of the olefin with the Diels-Alder product (11) of isoquinolinopyrrolinedione (12) and butadiene was confirmed by direct comparisons (mp, TLC, IR, and NMR).



Treatment of the compound 7 with anhyd. H_3PO_4 or PPA at $70-100^\circ$ produced a new compound, yellow prisms, mp $182-183^\circ$, $\text{C}_{21}\text{H}_{21}\text{NO}_6$, UV(EtOH): λ_{max} (E) nm 286 (15600), 303sh(13900), 380(15000). IR(KBr): 1720, 1653, 1605cm^{-1} . $^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.21(1H,s), 6.82(1H,s), 6.76(1H,s), 4.26(2H,q, $J=7$ Hz), 3.95(6H,s), 1.32(3H,t, $J=7$ Hz). $^{13}\text{C-NMR}(\text{CDCl}_3)$: δ 204.7s, 172.3s, 160.7s, 151.4s, 148.7s, 145.5s, 144.7s, 141.5s, 128.9s, 121.4s, 110.3d, 108.2d, 94.0d, 61.6t, 56.3q, 56.1q, 41.7d, 41.0t, 39.9t, 27.5t, 14.1q. The same compound was obtained directly from 1b on heating with anhyd. H_3PO_4 at 100° for 1.5 hr. The spectral data indicated that the compound is an isoquinolino- α -pyridone 13. The assigned structure was supported by the UV spectrum of the alcohol 14⁵ (λ_{max} 269 and 348 nm) derived from 13 by NaBH_4 reduction which was similar to that reported for 15 (λ_{max} 267 and 343 nm)⁸.



The formation of 13 from the 2,7,8-trioxoerythrinan derivative 2b, through the intramolecular aldol product 7, is well explained as shown in Scheme 4: 5,6-bond cleavage of 7 by retro-Mannich reaction followed by dehydration gives 13 without

any difficulty. Supporting this mechanism, the erythrinan 16^2 was found to be stable to anhyd. H_3PO_4 at 100° .

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References and Notes

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2. Syntheses of Erythrina and Related Alkaloids(1): Y. Tsuda, Y. Sakai, M. Kaneko, Y. Ishiguro, K. Isobe, J. Taga, and T. Sano, Heterocycles, **15**
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5. 1b. mp $106-107^\circ$, yellow prisms. IR(KBr): $1770, 1720, 1690cm^{-1}$. 1H -NMR($CDCl_3$): δ 6.80(3H, s, ArH), 5.20(1H, t, $J=4Hz$, $-CH=$), 3.9-4.0(4H, ethyleneketal), 4.09(2H, q, $J=7Hz$, $COOCH_2CH_3$), 3.82, 3.80(each 3H, s, OCH_3), 1.24(3H, t, $J=7Hz$, $COOCH_2CH_3$).
5. mp $185-186^\circ$. IR(KBr): $1765, 1735, 1710cm^{-1}$. 1H -NMR($CDCl_3$): δ 6.55(2H, s, ArH), 3.88(4H, s, ethyleneketal), 3.81(6H, s, $OCH_3 \times 2$), 3.57(2H, q, $J=7Hz$, $COOCH_2CH_3$), 0.68(3H, t, $J=7Hz$, $COOCH_2CH_3$).
6. gum. 1H -NMR($CDCl_3$): δ 6.70(3H, s, ArH), 5.28(1H, t, $J=5Hz$, $-CH=$), (2H, q, $J=7Hz$, $COOCH_2CH_3$), 3.81, 3.78(each 3H, s, OCH_3), 1.13(3H, t, $J=7Hz$, $COOCH_2CH_3$).
2b. mp $282-283^\circ$. IR(KBr): $1770, 1742, 1720, 1703cm^{-1}$. 1H -NMR($CDCl_3$): δ 6.62, 6.56(each 1H, s, ArH), 3.87, 3.86(each 3H, s, OCH_3), 3.66(2H, qd, $J=7, 1.5Hz$, $COOCH_2CH_3$), 3.32(2H, s, $-COCH_2-$), 0.73(3H, t, $J=7Hz$, $COOCH_2CH_3$).
7. mp $279-282^\circ$ (decomp.). IR(KBr): $1760, 1715, 1695cm^{-1}$. 1H -NMR($CDCl_3$): δ 6.75, 6.67(each 1H, s, ArH), 4.01(2H, q, $J=7Hz$, $COOCH_2CH_3$), 3.89, 3.88(each 3H, s, OCH_3), 0.94(3H, t, $J=7Hz$, $COOCH_2CH_3$). ^{13}C -NMR($CDCl_3$): δ 207.1s, 169.1s, 168.2s, 149.2s, 148.4s, 128.1s, 122.8s, 112.1d, 108.7d, 88.2s, 68.6s, 65.9s, 61.3t, 56.5q, 56.0q, 54.2d, 39.2t, 36.7t, 34.9t, 28.7t, 13.8q.
9a + 9b. gum. IR($CHCl_3$): $1715cm^{-1}$. 1H -NMR($CDCl_3$): ArH 7.03(0.5H), 6.72(0.5H), 6.58(1H).
10a. 1H -NMR($CDCl_3$): δ 7.70, 7.25(each 2H, d, $J=8Hz$, Ts), 6.83, 6.52(each 1H, s, ArH).
10b. 1H -NMR($CDCl_3$): δ 7.77, 7.26(each 2H, d, $J=8Hz$, Ts), 6.61, 6.54(each 1H, s, ArH).
11. mp $176-180^\circ$, pale yellow prisms. IR(KBr): $1765, 1730, 1715cm^{-1}$. 1H -NMR($CDCl_3$): δ 6.63, 6.52(each 1H, s, ArH), 6.2-5.6(2H, $-CH=CH-$), 3.80(6H, s, $OCH_3 \times 2$), 3.57(2H, q, $J=7Hz$, $COOCH_2CH_3$), 0.67(3H, t, $J=7Hz$, $COOCH_2CH_3$).
14. mp $199-201^\circ$. $UV\lambda_{max}(\epsilon)$ in EtOH: 269(9000), 348(24800). IR(KBr): $1720, 1655, 1608, 1595cm^{-1}$. 1H -NMR($CDCl_3$): δ 7.21, 6.80, 6.73(each 1H, s, ArH), 4.95-5.15(1H, $CH-OH$), 4.25(2H, q, $J=7Hz$, $COOCH_2CH_3$), 3.95, 3.94(each 3H, s, OCH_3), 3.57(1H, d, $J=11Hz$, $-OH$), 1.34(3H, t, $J=7Hz$, $COOCH_2CH_3$).
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