Synthesis and Reactions of 3,7-Cycloerythrinans: Skeletal Rearrangement of 2,7,8-Trioxoerythrinans to 4-Oxo-4H-pyrido[2,1-a]isoquinolines¹⁾

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Treatment of 2,7,8-trioxoerythrinan derivatives with anhydrous phosphoric acid or Lewis acids gave 3,7-cycloerythrinan derivatives via an intramolecular aldol condensation. The structures of the products were established by spectroscopic and chemical means. Further treatment of the 3,7-cycloerythrinans with anhydrous phosphoric acid resulted in skeletal rearrangement to yield 6,7-dihydro-4-oxo-4H-pyrido[2,1-a]isoquinolines, whose structures were also determined mainly by spectroscopic means.

Keywords Erythrina alkaloid; 2,7,8-trioxoerythrinan; 3,7-cycloerythrinan; intramolecular aldol reaction; 4-oxo-4H-pyrido[2,1-a]isoquinoline; anhydrous phosphoric acid; Lewis acid; skeletal rearrangement

In a previous paper²⁾ we described high yield cyclization of 1- β -arylethyl-3a-ethoxycarbonyl-2,3,3a,4,5,6-hexahydro-1H-indole-2,3-diones **1** to 6-ethoxycarbonyl-7,8-dioxoerythrinans **2**. The ethoxycarbonyl group in the product can be smoothly removed by heating with MgCl₂ in dimethyl sulfoxide (DMSO) [or in hexamethylphosphoric triamide (HMPA)]. One of the particular advantages in the use of the 3a-ethoxycarbonyl derivative is in the synthesis of oxoerythrinans such as **7a**, because attempted cyclization of the 3a-H derivative **4** to the erythrinan was reported to fail, giving instead the hydroxyisatin **5**.³⁾ On the other hand, cyclization of **6a** proceeded smoothly to give **7a**, but this

product was sometimes accompanied with several by-products which apparently were the products of over-reaction.²⁾ This paper deals with structural elucidations of these by-products and describes a new skeletal rearrangement of 2,7,8-trioxoerythrinans to pyrido[2,1-a]isoquinolines.⁴⁾

Results and Discussion

Formation of 3,7-Cycloerythrinans from 2,7,8-Trioxoerythrinans Treatment of **8a** with anhydrous phosphoric acid at room temperature for 1.5 h resulted only in cleavage of the ethylene acetal group to give **6a**. Further treatment of

Chart 1

Chart 2

6a with the same reagent at 70 °C for 3.5 h produced the trioxoerythrinan **7a** and the 3,7-cycloerythrinan **9a**, while on treatment at 100 °C, **9a** and a new yellow compound **10a** were produced.

Compound **7a** was identical with that reported previously.²⁾ Compound **9a** showed infrared (IR) absorptions at 1760, 1725, 1695 and 3400 cm⁻¹, indicative of five membered ketone, ester, lactam, and hydroxyl moieties, respectively, and showed the presence of three quaternary carbons (δ 65.9, 68.6, 88.2, each s) and one tertiary carbon (δ 54.2, d) in the ¹³C-nuclear magnetic resonance (¹³C-NMR) spectrum.

Treatment of **7a** with BF₃·Et₂O in methylene chloride or with an excess of anhydrous phosphoric acid gave **9a** in 55% or 70% yield. On the other hand, heating of **9a** in 80% AcOH for 1.5 h produced **7a**, though in low yield. All of these results indicate that **7a** and **9a** are interconvertible and **9a** is an intramolecular aldol product of **7a**, i.e., the 3,7-cyclo (**9a**) or 1,7-cyclo (**9'**) derivative.

The structure **9a** was verified by the following chemical correlations. Reduction of **9a** with Zn–AcOH gave a mixture of two stereoisomeric alcohols, **11** and **12**, which on Jones oxidation gave **7a**. Reduction of **9a** with NaBH₄ in ethanol gave a 1:1 mixture of stereoisomeric alcohols, **13** and **14**, which, without separation, was mesylated and treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene to give the olefin **17** and the mesylate **16**. The olefin **17** was identical with the Diels–Alder adduct of the dioxopyrrolone **18** to butadiene.⁵⁾ Since **17** is the product of concerted fragmentation from the β -*O*-mesylate **15**, the structure of **9a** was thus established. The *O*-mesylate **16** must therefore be of α configuration. Treatment of **16** with lithium iodide in dimethylformamide (DMF) followed by heating of the resulting iodide **19** with DBU in benzene afforded the olefin **17** as expected. Reduction of **9a** with LiAlH(*O*-*tert*-Bu)₃ gave a single stereoisomer **14**.

The above results show that the cyclization of **8** with

phosphoric acid proceeds firstly with hydrolytic cleavage of the ethylene acetal group, followed by cyclization to **7**, which is further converted to **9** by an intramolecular aldol reaction.

Treatment of **8a** with Lewis acids gave somewhat different results. Lewis acids were found to catalyze the cyclization of **8a** prior to hydrolysis of the ethylene acetal group. Although silver perchlorate did not affect **8a** at room temperature, it gave three products, **20**, **7a**, and **9a**, on heating at 90 °C for 1 h, in the yields of 25, 32, and 25%. Treatment of **8a** with BF₃·Et₂O in methylene chloride produced, at room temperature for 19 h, **20**, **7a**, **9a**, and **21** in the yields of 35, 23, 4, and 4%, and gave **20**, **7a**, and **9a** in a ratio of 1:1:1 on reflux for 40 min. Compound **20** was identical with that previously reported²⁾ and gave **7a** on hydrolysis with 80% AcOH. The structure of **21** was assigned on the basis of spectral data and confirmed by acid hydrolysis to **9a**. The formation of this compound can be rationalized by considering the intermediacy of the enolate **22**, which might be produced by the action of a Lewis acid on **20**.

3,7-Cycloerythrinans from Photochemical Routes The formation of 3,7-cycloerythrinans by intramolecular aldol reaction of 2,7,8-trioxoerythrinans was also observed in photochemical approaches to erythrinans. The photo-adduct **23** of an activated butadiene to **18**, upon thermolysis followed by treatment with potassium fluoride, gave the 3,7-cycloerythrinan derivative **25**.⁶⁾ Obviously, the intermediate enolate anion underwent an intramolecular aldol reaction to yield **25**. Further examples and details of this photochemical approach will be given in a separate paper.

Rearrangement of 3,7-Cycloerythrinans to Pyrido[2,1-*a*]-isoquinolines In the above section we reported that, when **8a** was treated with anhydrous phosphoric acid at 100 °C for 3 h, a new yellow compound **10a** was produced together with **9a**. Compound **10a** was obtained in better yield on treatment of **9a** with hot phosphoric acid or on heating with polyphosphoric acid (PPA) at 70–100 °C.

Chart 3

Chart 4

Chart 5

Chart 6

Compound **10a**, mp 182–183 °C, had the formula $\text{C}_{21}\text{H}_{21}\text{NO}_6$ and showed ultraviolet (UV) absorptions at 286 (ϵ 15600), 303 sh (ϵ 13900) and 380 nm (ϵ 15000), indicating that it has an elongated conjugated system. In the ^{13}C -NMR spectrum, it exhibited signals due to ten aromatic carbons, seven of which were quaternary (δ 151.4, 148.7, 145.5, 144.7, 141.5, 128.9, 121.4) and three tertiary (δ 110.3, 108.2, 94.0), which corresponded to the singlet signals at δ 7.21, 6.76, and 6.82 in the ^1H -nuclear magnetic resonance (^1H -NMR) spectrum. In the IR spectrum, **10a** showed absorptions at 1720 and 1653 cm^{-1} . The ^1H -NMR chemical shifts of the three aromatic protons and the IR absorption at 1653 cm^{-1} are in agreement with the data for the pyrido-isoquinoline **29** reported by Mondon *et al.*⁷⁾ Reduction of **10a** with NaBH_4 gave two alcohols, **27** and **28**. The UV spectrum [λ_{max} nm (ϵ): 269 (9000), 348 (24800)]

of the major product (stereochemistry was not determined). mp 199–201 °C, was again in good agreement with that of **29** [λ_{max} nm (ϵ): 267(6760), 343 (18200)].⁷⁾ We therefore consider that the product is the 6,7-dihydro-4-oxo-4*H*-pyrido[2,1-*a*]isoquinoline (**10a**), which was produced from the 3,7-cycloerythrinan **9a** through acid-catalyzed fragmentation as illustrated in Chart 6.

The non-methoxy derivative **8b** similarly gave the 3,7-cycloerythrinan **9b** and the pyrido-isoquinoline **10b** on heating with phosphoric acid, thus revealing that this rearrangement is a general one for 3,7-cycloerythrinans. In support of this consideration, compound **2**, which can not form an intramolecular aldol, was recovered unchanged on heating with PPA at 100–110 °C. Mondon⁸⁾ reported a pyrido-isoquinoline **31** (which is structurally isomeric to **29**) as one of the products of Wolff-Kishner reduction of the

bromo-ketone **30**. Apparently our pyrido-isoquinoline **10** is different from **31**-type product in substitution pattern and formation mechanism.

The pyrido[2,1-*a*]isoquinoline structure of the type **29** has been found in natural alkaloids such as alamarine,⁹ so the above described transformation should provide a synthetic route to these alkaloids.

Experimental

General Unless otherwise stated, the following procedures were adopted. Melting points were determined on a Yanaco micro hot stage melting point apparatus and are uncorrected. IR spectra were taken in KBr disks, recorded on a Jasco IR-G spectrometer, and the data are given in cm^{-1} . UV spectra were taken in ethanol solution and λ_{max} values are given in nm (ϵ). $^1\text{H-NMR}$ spectra were taken with a JNM PMX-60 (60 MHz) or a JEOL FX-100 (100 MHz) spectrometer in chloroform-*d* solution with tetramethylsilane as an internal standard, and the chemical shifts are given in δ values (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). High resolution mass spectra (HR-MS) were taken with a Hitachi M-80 spectrometer. Column chromatography was performed on Wakogel C-200 (silica gel). For thin layer chromatography (TLC), Merck precoated plates GF₂₅₄ were used and spots were monitored by UV (254 nm), then developed by spraying 1% $\text{Ce}(\text{SO}_4)_2$ in 10% H_2SO_4 and heating the plates at 100°C until coloration took place. All organic extracts were washed with brine and water, dried over anhydrous sodium sulfate, and concentrated. Identities were confirmed by mixed melting point determination (for crystalline compounds) and also by comparisons of TLC behavior and $^1\text{H-NMR}$ and IR spectra.

Anhydrous H_3PO_4 was prepared from P_2O_5 (7 g) and 80% H_3PO_4 (15 g), and PPA was prepared from 80% H_3PO_4 (33 g) and P_2O_5 (25 g), by heating each mixture at 110°C for 6 h.

Treatment of Dioxopyrrolone **8a with Phosphoric Acid** 1) Compound **8a**²¹ (0.31 g) was stirred with an excess of anhydrous H_3PO_4 for 1.5 h at room temperature. The mixture was decomposed with ice-water and extracted with CHCl_3 . Chromatography of the product gave **6a** (0.22 g, 80%) and the ketol **9a** (0.03 g, 11%) from the CHCl_3 -AcOEt eluate. Compound **6a** was obtained as a yellow gum. $^1\text{H-NMR}$: 6.70 (3H, s, ArH), 5.28 (1H, t, $J=4.7$ Hz, =CH), 4.09 (2H, q, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$), 3.81, 3.78 (each 3H, s, OMe), 1.10 (3H, t, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$). HR-MS: Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_7$ (M^+) m/z : 401.1473. Found: 401.1422.

2) Crude **8a** prepared from 13 g of ethyl 5,5-ethylenedioxy-2-oxocyclohexanecarboxylate by the reported method,²¹ was heated with anhydrous H_3PO_4 (80 ml) at 70°C for 3.5 h. The mixture was decomposed with ice-water and the separated precipitate was collected by filtration, and washed with hot benzene to give the 2,7,8-trioxo derivative **7a** (5.7 g, 25%), as colorless prisms from CHCl_3 , mp 282–283°C. This product was identical with **7a** previously reported.²¹

Concentration of the hot benzene washings gave a solid which was recrystallized from MeOH then from benzene to give the ketol **9a** (12.6 g, 53%) as colorless prisms, mp 279–282°C (dec.). IR: 3400, 1760, 1725, 1695. $^1\text{H-NMR}$: 6.75, 6.67 (each 1H, s, ArH), 4.01 (2H, q, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$), 3.89, 3.88 (each 3H, s, OMe), 0.94 (3H, t, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$). $^{13}\text{C-NMR}$: 207.1 s, 169.1 s, 168.2 s, 149.2 s, 148.4 s, 128.1 s, 122.8 s, 112.1 d, 108.7 d, 88.2 s, 68.6 s, 65.9 s, 61.3 t, 56.5 q, 56.0 q, 54.2 d, 39.2 t, 36.7 t, 34.9 t, 28.7 t, 13.8 q. Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_7$: C, 62.83; H, 6.02; N, 3.63. Found: C, 62.54; H, 5.75; N, 3.37.

3) Compound **8a** (2.6 g) was heated with an excess of anhydrous H_3PO_4 at 100°C for 3 h and worked up as described in 1). Chromatography of the product gave the pyridone **10a** (0.55 g, 25%) from the benzene-AcOEt eluate and the ketol **9a** (0.5 g, 21%) from the CHCl_3 -MeOH eluate. Compound **10a** formed yellow prisms from ether, mp 182–183°C. UV: 286 (15600), 303 sh (13900), 380 (15000). IR: 1720, 1653, 1605. $^1\text{H-NMR}$: 7.21, 6.82, 6.76 (each 1H, s, ArH), 4.26 (2H, q, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$), 3.95 (6H, s, OMe $\times 2$), 1.32 (3H, t, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$). $^{13}\text{C-NMR}$: 204.7 s, 172.3 s, 160.7 s, 151.4 s, 148.7 s, 145.5 s, 144.7 s, 141.5 s, 128.9 s, 121.4 s, 110.3 d, 108.2 d, 94.0 d, 61.6 t, 56.3 q, 56.1 q, 41.2 d, 41.0 t, 39.9 t, 27.5 t, 14.1 q. Anal. Calcd for $\text{C}_{21}\text{H}_{21}\text{NO}_6$: C, 65.78; H, 5.52; N, 3.65. Found: C, 65.70; H, 5.59; N, 3.20.

Treatment of Dioxopyrrolone **8a with Lewis Acids** 1) Compound **8a** (79 mg) and AgClO_4 (ca. 50 mg) in dry benzene (10 ml) were heated at 90°C for 1 h. The mixture was decomposed with water and extracted with CHCl_3 . The product was triturated with MeOH to give the trioxo derivative **7a** (25 mg, 32%) as insoluble crystals. Chromatography of the mother

liquor gave **20** (20 mg, 25%) and **9a** (20 mg, 25%). Compound **20** formed colorless needles from ether, mp 185–186°C, and was identical with the compound reported previously.²¹

2) Compound **8a** (475 mg) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (420 mg, 3 mol eq) in CH_2Cl_2 (15 ml) were stirred for 20 h at room temperature. Work-up of the mixture as described above gave **7a** (110 mg, 23%). Chromatography of the mother liquor gave **20** (164 mg, 35%) from the CHCl_3 -AcOEt (5:1) eluate, and **9a** (20 mg, 4%) and **21** (22 mg, 4%) from the CHCl_3 -AcOEt (1:1) eluate; the latter compounds were separated by preparative TLC. Compound **21** formed colorless needles from ether, mp 176–177°C. IR: 3300, 1730, 1708. $^1\text{H-NMR}$: 6.86, 6.63 (each 1H, s, ArH), 3.91, 3.87 (each 3H, s, OMe), 4.2–3.8 (overlapped m, $\text{COOCH}_2\text{CH}_3$, $\text{OCH}_2\text{CH}_2\text{O}$), 0.95 (3H, t, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$). $^{13}\text{C-NMR}$: 169.4 s, 168.8 s, 148.8 s, 148.0 s, 128.3 s, 123.6 s, 116.3 s, 111.9 d, 109.2 d, 90.3 s, 71.3 s, 65.5 s, 65.2 t, 64.5 t, 60.8 t, 56.3 q, 55.9 q, 46.9 d, 38.4 t, 37.2 t, 34.6 t, 28.7 t, 13.9 q. Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_8$: C, 62.01; H, 6.11; N, 3.14. Found: C, 62.11; H, 5.98; N, 3.20.

3) Compound **8a** in CH_2Cl_2 was heated with 3 mol eq of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ under reflux for 40 min to give a mixture of **20**, **7a**, and **9a** in a ratio of ca. 1:1:1 (TLC detection).

Deacetalization of **21** Compound **21** (400 mg) in 80% AcOH (10 ml) was heated under reflux for 1.5 h and the solvent was evaporated off to leave a mixture of **9a** and **7a** (4:1, 337 mg), which were separated by fractional crystallizations and chromatography.

The Ketol **9a from the Trioxo Derivative **7a**** 1) Compound **7a** (3.8 g) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (20.5 g, 15 mol eq) in CH_2Cl_2 (200 ml) were stirred overnight at room temperature. The mixture was washed with saturated NaHCO_3 solution and concentrated to ca. 10 ml. The separated starting material **7a** was removed by filtration. The mother liquor was treated with hot benzene to obtain a further crop of **7a**. Chromatography of the mother liquor gave a further crop of **7a** (total recovery, 2.08 g, 54.7%) together with **9a** (1.3 g, 34.2%).

2) Compound **7a** (6.1 g) was heated with a mixture of anhydrous H_3PO_4 (20 ml) and 80% H_3PO_4 (10 ml) at 50–60°C for 2 h. The reaction mixture was decomposed with ice-water and extracted with CHCl_3 . Concentration of the extract and treatment of the residue with MeOH recovered **7a** (1.85 g, 30%). Chromatography of the mother liquor gave the ketol **9a** (4.3 g, 70%).

The 6,7-Dihydro-9,10-dimethoxy-4-oxo-4H-pyrido[2,1-*a*]isoquinoline **10a from the Ketol **9a**** The ketol **9a** (100 mg) was heated with an excess of PPA at 100°C for 1 h. The mixture was decomposed and extracted with CHCl_3 . Chromatography of the product gave the pyridone **10a** (57 mg, 60%).

Zn-AcOH Reduction of the Ketol **9a** Zn powder (3 g) was added in portions to a stirred and refluxed solution of the ketol **9a** (200 mg) in AcOH (15 ml). After being refluxed for 2 h, the mixture was filtered, and the filtrate was diluted with water and extracted with CHCl_3 . Chromatography of the extract gave a mixture of **11** and **12** (180 mg) from the CHCl_3 -MeOH (30:1) eluate. Although this mixture gave a single spot on TLC, the $^1\text{H-NMR}$ spectrum showed two triplets of $\text{COOCH}_2\text{CH}_3$ at δ 0.80 and 0.75, of which the former was identical with that of **11**²¹ as judged from a detailed inspection of the spectrum.

This mixture (50 mg) in acetone (15 ml) was oxidized with Jones reagent at 0°C and worked up as usual to give the trioxo derivative **7a** (40 mg).

The Olefin **17 from the Ketol **9a**** The ketol **9a** (5 g) and NaBH_4 (200 mg) in EtOH-tetrahydrofuran (THF) (1:1, 300 ml) were stirred at 0°C for 1 h. After evaporation of the solvent, the mixture was extracted with CHCl_3 to give a mixture of **13** and **14** [$^1\text{H-NMR}$: ArH δ 7.03 (0.5H), 6.72 (0.5H), 6.53 (1H)]. Although these products could be partially separated by fractional crystallizations after conversion to the tosylates (2 β -O-tosylate: colorless needles from EtOH, mp 133–142°C, and 2 α -O-tosylate: colorless prisms from EtOH, mp 102–112°C), they were used without separation for the next step.

The mixture of **13** and **14** was mesylated with methanesulfonyl chloride (4.2 g) and pyridine (50 ml) for 1 h at room temperature, then the mixture was poured into water and extracted with CHCl_3 to yield the mesylates, **15** and **16**.

The mixture of mesylates was dissolved in benzene (100 ml) and treated with DBU (5 g) at 80°C for 15 min. The cooled mixture was diluted with CH_2Cl_2 (300 ml), washed with 1 N HCl and water, dried, and concentrated. The residue was treated with benzene to give the 2 α -O-mesylate **16** (2.8 g, 46.7% from **8a**) as an insoluble mass, which was recrystallized from acetone as colorless prisms, mp 192.5–193.5°C. IR: 1720, 1700. $^1\text{H-NMR}$: 6.70, 6.62 (each 1H, s, ArH), 5.19 (1H, d, $J=7.5$ Hz, CHOMs), 3.90, 3.87 (each 3H, s, OMe), 3.12 (3H, s, Ms), 0.91 (3H, t, $J=7$ Hz, $\text{COOCH}_2\text{CH}_3$).

Anal. Calcd for $C_{22}H_{27}NO_9S$: C, 54.88; H, 5.65; N, 2.91. Found: C, 54.72; H, 5.88; N, 2.80.

The mother liquor was chromatographed to give the olefin **17** (1.7 g, 34% from **9a**), as pale yellow prisms from MeOH, mp 176–180°C. This product was identical with **17** previously reported.⁵⁾

Reduction of the Ketol 9a with $LiAlH(O\text{-}tert\text{-}Bu)_3$ Compound **9a** (0.5 g) and $LiAlH(O\text{-}tert\text{-}Bu)_3$ (1 g) in THF (30 ml) were stirred for 1 h at room temperature. After decomposition of excess reagent with a small amount of water, the mixture was filtered and washed thoroughly with CH_2Cl_2 . The combined filtrate and washings were concentrated and the residue was chromatographed to give the starting material **9a** (0.1 g) from the $CHCl_3$ -AcOEt (3:1) eluate and the 2 α -alcohol **14** (0.4 g), as a gum, from the $CHCl_3$ -AcOEt (1:1) eluate. Mesylation of this in a usual way gave the 2 α -O-mesylate **16**, mp 192–193°C.

Reduction of the Ketol 9a with $Zn(BH_4)_2$ Reduction of **9a** with zinc borohydride in THF gave a 1:1 mixture of **13** and **14**.

Conversion of the 2 α -O-Mesylate 16 to the Olefin 17 Compound **16** (1.15 g) and LiI (2 g) in DMF (50 ml) were stirred and heated at 130°C for 5 h. After addition of water, the mixture was extracted with $CHCl_3$. The extract was washed with dilute $Na_2S_2O_3$ solution and water, dried, and concentrated. The residue in benzene (30 ml) was heated with DBU (5 g) at 90°C for 1 h and worked up as usual. Chromatography of the product gave the olefin **17** (420 mg, 45.6%) from the benzene- $CHCl_3$ (1:1) eluate and the starting material **16** (340 mg) from the $CHCl_3$ -AcOEt (2:1) eluate.

Hydride Reduction of the Pyridone 10a The pyridone **10a** (100 mg) and $NaBH_4$ (10 mg) in THF-EtOH (1:1, 20 ml) were stirred at 0°C for 1 h. After addition of water, the product was taken into $CHCl_3$. Concentration of the extract gave a mixture of two alcohols (**27** and **28**), which were separated by chromatography. The major product obtained from the $CHCl_3$ -AcOEt (1:1) eluate crystallized in colorless plates from benzene, mp 199–201°C. UV: 269 (9000), 348 (24800). IR: 1720, 1608, 1595. 1H -NMR: 7.21, 6.80, 6.73 (each 1H, s, ArH), 4.95–5.15 (1H, m, $CH(OH)$), 4.25 (2H, q, $J=7$ Hz, $COOCH_2CH_3$), 3.95, 3.94, (each 3H, s, OMe), 3.57 (1H, d, $J=11$ Hz, OH, disappeared on addition of D_2O), 1.34 (3H, t, $J=7$ Hz, $COOCH_2CH_3$). *Anal.* Calcd for $C_{21}H_{23}NO_6$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.66; H, 6.04; N, 3.57.

Elution of the column with AcOEt gave a mixture of the major and minor products (41 mg).

The 6,7-Dihydro-4-oxo-4H-pyrido[2,1-a]isoquinoline 10b from 8b

Compound **8b** was prepared from phenylethylamine by condensation with 5,5-ethylenedioxy-2-oxocyclohexanecarboxylate followed by oxalylolation in the manner described previously.²⁾ Crude **8b** (2.38 g) thus obtained was heated with a large excess of PPA at 110°C for 4 h. After decomposition with water, the mixture was extracted with $CHCl_3$. Chromatography of the product gave the pyridone **10b** (0.26 g, 11.2%) and the ketol **9b** (0.17 g, 7%).

The pyridone **10b** formed yellow prisms from ether, mp 159–161°C. IR: 1725, 1650. 1H -NMR: 7.1–7.9 (4H, m, ArH), 6.89 (1H, s, ArH), 4.23 (2H, q, $J=7$ Hz, $COOCH_2CH_3$), 1.30 (3H, t, $J=7$ Hz, $COOCH_2CH_3$). *Anal.* Calcd for $C_{19}H_{17}NO_4$: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.28; H, 5.10; N, 4.43.

The ketol **9b** formed colorless prisms from MeOH-ether, mp 174–176°C. IR: 3200, 1765, 1700. 1H -NMR: 7.1–7.5 (4H, m, ArH), 0.87 (3H, t, $J=7$ Hz, $COOCH_2CH_3$). ^{13}C -NMR: 206.5 s, 169.0 s, 168.4 s, 135.4 s, 129.5 d, 128.4 d, 127.3 d, 125.5 d, 88.4 s, 68.7 s, 65.9 s, 61.4 t, 54.0 d, 39.5 t, 36.6 t, 34.8 t, 29.2 t, 13.7 q. *Anal.* Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.58; H, 5.58; N, 3.98.

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