Concise Syntheses of the Oxo Derivatives of Benzo[*c*]phenanthridine Bases by *N*-Deformylated Cyclization Based on Vilsmeier–Haack Reaction

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Chelerythrine-type oxobenzo[*c*]phenanthridine bases were effectively synthesized by the action of 1,3-dimethoxybenzene on 2-(2-methoxycarbonylphenyl)-1-(*N*-methylformamido)naphthalenes in the presence of phosphorus oxychloride. The *N*-deformylation based on the Vilsmeier–Haack reaction is also discussed.

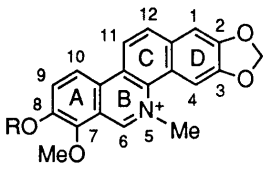
Key words *N*-deformylation; phosphorus oxychloride; Vilsmeier–Haack reaction; benzo[*c*]phenanthridine synthesis; isoquinolone cyclization; selective demethylation

Recently we[1] have reported the synthesis of chelerythrine (**1**), a quaternary benzo[*c*]phenanthridine alkaloid (quaternary base) with a benzene ring having four successive substituents (ring A) in its molecule, by the combination of the cesium fluoride-mediated Claisen rearrangement of an aryl propargyl ether and oxidative cleavage of the furan ring in the intermediary 2-methylarylfuran. However, the last step of the synthesis by *N*-deformylated cyclization of a 2-(2-formylphenyl)-1-(*N*-methylformamido)naphthalene **2** under acidic conditions (*p*-toluenesulfonic acid/xylene) was not entirely satisfactory (46% yield at best). In the course of a synthetic study of decarine (**3**),[2] a naturally occurring phenolic tertiary benzo[*c*]phenanthridine alkaloid (norbase) which has the same substituent pattern as **1**, we succeeded in establishing an effective cyclization method under mild conditions based on the Vilsmeier–Haack (V.H.) reaction.[3] We report here the *N*-deformylation reaction and its application to the syntheses of the oxo derivative of a benzo[*c*]phenanthridine base (oxobase) **4** derived from **3** and oxochelerythrine (**5**).

Results and Discussion

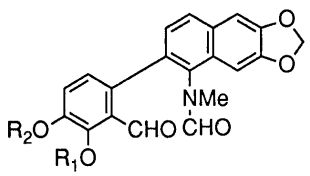
The synthetic route[1] developed for chelerythrine (**1**) was applied to decarine (**3**) by changing the methoxy group at the 7 position of the 2-methylbenzofuran substituent in a furanylformamide **6** to a benzyloxy group. Selective demethylation of the methyl ether function in the presence of the acid-sensitive methylenedioxy group was achieved by using trimethylsilyl iodide (TMSI).[4] However, purification of the demethylated product **7** met difficulty because of low solubility of the product, in addition to the appearance of distinct spots on thin layer chromatography (TLC) due to the presence of geometrical isomers[5] derived from the double bond nature of the tertiary amide structure in the naphthylformamide derivatives. Therefore the phenolic **7** was purified through its benzyl ether. Treatment of **6** with TMSI in quinoline at 180 °C for 4 h followed by conventional benzylation gave a benzyl ether **8** in 55% yield. Although almost the same result was obtained when TMSI, formed *in situ* from trimethylsilyl chloride (TMSCl) and sodium iodide (NaI) in acetonitrile (MeCN), was used, prolonged heating for 5 d and also the use of a large excess of reagents (12—22 mol eq) were needed for the completion of demethylation. The furan ring in **8** was cleaved by successive oxidation[6] with osmium tetroxide and periodic acid to give a crude acetate **9**, which was then converted into the desired aldehydic formamide **11** upon hydrolysis and methylation.

Since acidic treatment of **11** according to the method described for chelerythrine[1] only resulted in the formation of a complex mixture, we then attempted *N*-deformylation under non-acidic conditions (Table 1). Photolysis[7] of **11** under neutral conditions also led to the formation of a complex mixture (run 1). On the other hand, treatment of **11** with either 70% aqueous potassium hydroxide in ethanol (run 2) or 10% sodium ethoxide in ethanol (run 3) followed by acidification with hydrochloric acid afforded the desired quaternary salt **12**,[8] isolated as its chloride, but the yield was low in each case. Our attention was then directed to the development of an *N*-deformylation reaction suitable for the preparation of **12**.

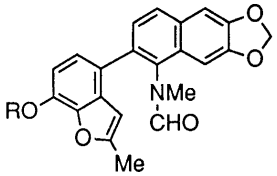


1 : R=Me
3 : R=H (des-*N*-methyl)
12 : R=Bn

Bn=CH_2Ph



2 : R_1=R_2=Me
9 : R_1=Ac, R_2=Bn
10 : R_1=H, R_2=Bn
11 : R_1=Me, R_2=Bn



6 : R=Me
7 : R=H
8 : R=Bn

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The V. H. reaction[3] is one of the most important methods for introduction of a formyl group into nucleophiles, such as electron-rich aromatic compounds, and a combination of *N*,*N*-dimethylformamide (DMF) and phosphorus oxychloride ($POCl_3$) has been most widely used as the formylating mixture. The iminium salt formed *in situ* is regarded as the reactive species. Therefore it should be possible for this reactive species to act as a useful selective deformylating agent for the removal of a formyl group from tertiary formamides if the formamides are used in place of DMF. In other words the aldehydic formamide **11** could be converted into a secondary amine **13** by loss of the formyl group when treated with $POCl_3$ in the presence of an appropriate nucleophile followed by alkaline hydrolysis. The amine **13** would provide a quaternary base **12** through spontaneous intramolecular iminium salt formation between the newly generated amine function and the aldehyde group in the phenyl substituent (Chart 1).

Table 1. Cyclization of an Aldehydic Formamide **11** under Non-acidic Conditions

Run	Reagent/solvent	Conditions		Result
		Temp. (°C)	Time (min)	
1	*hν* in MeCN	r.t.	180	C.M.[a]
2	70% KOH aq. in EtOH	Reflux	90	**12**: 28%
3	10% EtONa in EtOH	Reflux	10	**12**: 25%

a) A complex mixture.

Since aminolysis of **11** in the presence of diethylamine as a nucleophile failed to give any isolable products, we then picked 1,3-dimethoxybenzene in place of diethylamine. Treatment of **11** with 1,3-dimethoxybenzene and $POCl_3$ in chloroform at around 50 °C afforded the desired **12**[8] in 50—60% yield, together with considerable amounts of undefined products in some cases. The inconsistent results forced us to investigate the V. H. type *N*-deformylation reaction with model amide compounds in order to establish the scope and limitations of the reaction (Table 2).

N-Methylformanilide, which can also be used as a formyl source in the V. H. formylation reaction, was deformylated as expected to afford *N*-methylaniline in high yield (run 1).

The presence of a phenolic hydroxyl group did not interfere with the reaction (run 2). Ineffective conversion was observed in the cases of *N*-methylacetanilide (run 3) and formanilide (run 4). Interestingly this reaction was applicable not only to an aliphatic tertiary amide (run 5), but also to a secondary one (run 6). Thus, this *N*-deformylation reaction was established as a useful reaction applicable to a variety of formamide compounds.

On the other hand, a phenolic formamide protected by a methoxymethyl group resulted in the formation of a

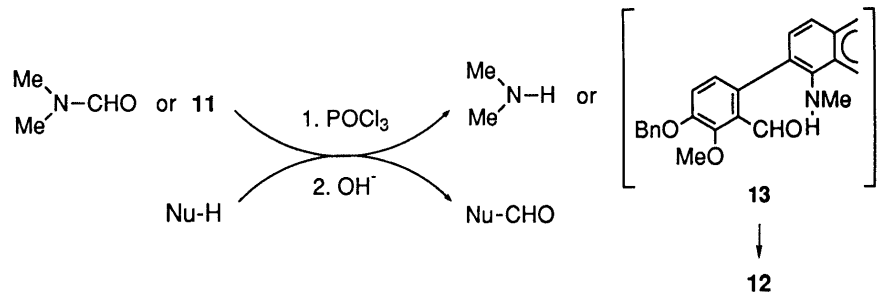
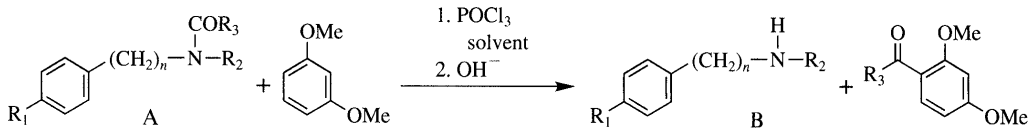


Chart 1

Table 2. *N*-Deacylation by the Action of 1,3-Dimethoxybenzene on Carboxamides in the Presence of $POCl_3$[a]



Run	Substrate (A)				OMe / OMe (mol eq)	$POCl_3$ (mol eq)	Solvent	Conditions		Product (B) yield (%)
	n	R_1	R_2	R_3				Temp. (°C)	Time (d)	
1	0	H	Me	H	1.1	1.2	CH_2Cl_2	40	1	97
2	0	OH	Me	H	2.0	2.1	$CHCl_3$	60	1	55
3	0	H	Me	Me	2.0	2.1	$CHCl_3$	60	3	23
4	0	H	H	H	1.1	1.2	CH_2Cl_2	40	1	38
5	1	H	Me	H	2.0	2.1	CH_2Cl_2	40	1	74
6	1	H	H	H	1.1	1.2	CH_2Cl_2	40	1	68
7	1	OMOM[b]	Me	H	2.0	2.1	$CHCl_3$	60	1	C.M.[c]

a) The conditions of alkaline hydrolysis are not given here. *b*) A methoxymethyl ether. *c*) A complex mixture.

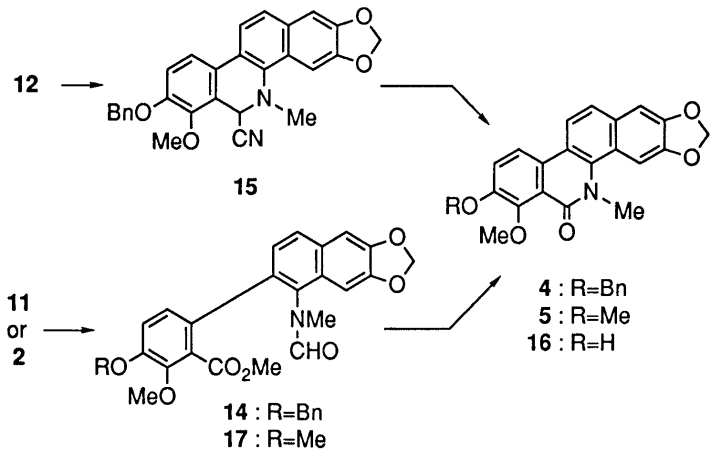


Chart 2

complex mixture of unisolable products (run 7) under the same reaction conditions, suggesting that incomplete cyclization to a quaternary base **12** from **11** described above may be caused by the undesired partial deprotection of the benzyl group in **11** and/or **12** during the *N*-deformylation reaction. Proton nuclear magnetic resonance (^{1}H-NMR) measurements of the reaction solution in the course of the reaction revealed no sign of debenzylation. This fact indicated that the presence of an aldehyde group in the phenyl substituent of **11** might be responsible for the unsatisfactory *N*-deformylated cyclization. Therefore, we changed the substrate from **11** to an ester derivative **14**, which was expected to produce an oxobase **4** in this V. H. type *N*-deformylation reaction.

We[9] have already established a general and practical transformation of norbases into the corresponding oxobases through dihydrobenzo[*c*]phenanthridine bases, quaternary bases and 6-cyano-5, 6-dihydrobenzo[*c*]phenanthridine bases (Ψ-cyanides) by four reaction steps: reductive *N*-alkylation, dehydrogenation, cyanation and oxidation. In order to prepare an authentic sample the quaternary base **12**[8] was firstly converted into the oxobase **4** in high yield by treatment with potassium cyanide followed by air-oxidation of the formed Ψ-cyanide **15** under basic conditions.

Oxidation[10] of **11** with sodium chlorite–hydrogen peroxide in sodium hydrogen phosphate buffer solution followed by methylation afforded the methyl ester **14** in good yield. Application of the newly developed *N*-deformylation reaction to **14** gave the oxobase **4** in 95% yield, and this could be easily debenzylated by catalytic hydrogenation to yield a phenolic oxobase **16**. Independently, the same treatment of the methyl ester **17** afforded oxochelerythrine (**5**), also in high yield (Chart 2). Thus, we have succeeded in establishing a useful and convenient route for the preparation of chelerythrine-type oxobenzo[*c*]phenanthridine alkaloids by applying the V. H. type *N*-deformylation reaction.

Experimental

All melting points were measured on a micro melting-point hot stage (Yanagimoto) and are uncorrected. Infrared (IR) spectra were recorded for Nujol mulls on a Hitachi 260-10 or JASCO IR-700 spectrophotometer. ^{1}H-NMR spectra were recorded in $CDCl_3$ solution with a JEOL JNM GX-270 or GSX-400 or -500α spectrometer, unless otherwise stated, with tetramethylsilane as an internal reference. Electron-impact mass spectra (EIMS) were recorded on a Hitachi M-60 spectrometer with direct inlet system. For column and flash chromatography, Silica gel 60 (70—230 mesh ASTM; Merck) and Silica gel 60 (230—400 mesh ASTM; Merck) were used, while for TLC and preparative TLC (PLC), DC-Fertigplatten SIL-G 25 UV254 (Macherey-Nagel) and Silica gel GF_{254} (Merck) were used. In general, the extract was washed with brine, dried over magnesium sulfate, then filtered, and the filtrate was evaporated to dryness under reduced pressure, unless otherwise stated.

2-[4-(7-Hydroxy-2-methylbenzo[*b*]furanyl)]-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (7): (a) With TMSI in Quinoline TMSI (0.11 ml, 0.77 mmol) was added to a solution of **6**[1] (0.199 g, 0.51 mmol) in quinoline (3 ml) at 100 °C under argon and the mixture was stirred at 180 °C. After 1.5 h, additional TMSI [0.04 ml (total 0.15 ml, 1.03 mmol)] was added. The reaction mixture was stirred at the same temperature for 0.5 h and poured into water, then the quinoline was removed by azeotropic distillation. The residue was dissolved in chloroform–methanol, and the solution was washed with 5% hydrochloric acid, 10% aqueous sodium thiosulfate and brine. Work-up gave **7** (0.079 g) as brown prisms (from chloroform–methanol), mp >300 °C. After evaporation of the mother liquor, purification of the residue by column chromatography with chloroform–ethyl acetate (10 : 1, v/v), followed by recrystallization, afforded additional **7** [0.016 g (total 0.095 g, 49%)]. IR ν_{max} cm^{-1}: 3138 (OH), 1666 (CO). ^{1}H-NMR (DMSO-d_6) δ: 2.40 (3H, diffused s, 2′-Me), 2.85 (3H, s, NMe), 6.19 (2H, s, OCH_2O), 6.22 (1H, d, J=1.0 Hz, 3′-H), 6.70 (1H, d, J=8.3 Hz, 6′-H), 6.84 (1H, d, J=8.3 Hz, 5′-H), 7.04 (1H, s, 8-H), 7.33 (1H, d, J=8.3 Hz, 3-H), 7.49 (1H, s, 5-H), 7.86 (1H, d, J=8.3 Hz, 4-H), 7.97 (1H, s, NCHO), 10.04 (1H, s, OH). MS *m/z*: 375 (100%, M$^+$). *Anal.* Calcd for $C_{22}H_{17}NO_5$: C, 70.39; H, 4.57; N, 3.73. Found: C, 70.34; H, 4.49; N, 3.43.

(b) With TMSCl–NaI in MeCN TMSCl (0.49 ml, 3.85 mmol) was slowly added to a suspension of **6** (0.300 g, 0.77 mmol) and NaI (1.73 g, 11.6 mmol) in absolute MeCN (15 ml) at 55—60 °C and the mixture was refluxed. After 22 h, NaI (0.58 g), TMSCl (0.20 ml) and MeCN (5 ml) were added and the reaction mixture was again refluxed. After 33 h, additional NaI [0.23 g (total 2.54 g, 17.0 mmol)] and TMSCl [0.15 ml (total 0.84 ml, 6.6 mmol)] were added. The reaction mixture was refluxed for 11 h, poured into water and extracted with dichloromethane. The organic solution was washed with 10% aqueous sodium thiosulfate and brine. After removal of chloroform-insoluble material, the soluble part was purified by column chromatography on silica gel with chloroform–ethyl acetate (30 : 1, v/v) to give **7** (0.113 g, 39%).

2-[4-(7-Benzyloxy-2-methylbenzo[*b*]furanyl)]-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (8) A mixture of the crude **7** (0.524 g, 1.36 mmol), K_2CO_3 (0.386 g, 2.79 mmol) and benzyl chloride (0.241 ml, 2.09 mmol) in DMF (16 ml) was stirred at 60 °C for 2 h, then poured into water and extracted with ethyl acetate. Work-up afforded **8** (0.609 g, 94%) as colorless prisms (from chloroform–hexane), mp 283—284 °C. IR ν_{max} cm^{-1}: 1675 (CO). ^{1}H-NMR[5] δ: 2.44 and 2.45 (total 3H, s, 2′-Me), 2.82 and 2.95 (toatl 3H, s, NMe), 5.32 and 5.33 (total 2H, s, OCH_2Ph), 6.10 (2H, s, OCH_2O), 6.11 (1H, s, 3′-H), 6.81 (1H, d, J=8.0 Hz, 6′-H), 6.89 (1H, d, J=8.0 Hz, 5′-H), 7.01 and 7.09 (total 1H, s, 8-H), 7.20 and 7.26 (total 1H, s, 5-H), 7.35 (1H, d, J=8.4 Hz, 3-H), 7.26—7.54

(5H, m, CH_2Ph), 7.73 (1H, d, J=8.4 Hz, 4-H), 8.10 and 8.29 (total 1H, s, NCHO). MS m/z: 465 (94%, M^+), 91 (100%). *Anal.* Calcd for $C_{29}H_{23}NO_5$: C, 74.82; H, 4.98; N, 3.01. Found: C, 74.64; H, 4.88; N, 2.89.

Direct Preparation of the Benzyl Ether 8 from the Methyl Ether 6: (a) Through Demethylation with TMSI in Quinoline TMSI (0.27 ml, 1.87 mmol) was added to a solution of **6** (0.499 g, 1.28 mmol) in quinoline (7.5 ml) at 100 °C under argon and the mixture was stirred at 180 °C. After 4 h, additional TMSI [0.17 ml (total 0.44 ml, 2.19 mmol)] was added, and the reaction mixture was stirred at the same temperature for 0.5 h. After work-up as above, the crude **7** (0.448 g) was benzylated using K_2CO_3 (0.355 g, 2.57 mmol), benzyl chloride (0.22 ml, 1.93 mmol) and DMF (15 ml) to give **8** (0.327 g, 55%).

(b) Through Demethylation with TMSCl–NaI in MeCN TMSCl (0.98 ml, 7.71 mmol) was slowly added to a suspension of **6** (0.600 g, 1.54 mmol) and NaI (2.31 g, 15.4 mmol) in absolute MeCN (30 ml) at 55—60 °C and the mixture was refluxed. After 7 h and 25 h, additional NaI [0.69 g and 2.08 g (total 5.08 g, 33.9 mmol)] and TMSCl [0.39 ml and 1.17 ml (total 2.54 ml, 20.0 mmol)] were added, respectively, and the reaction mixture was refluxed for 35 h. After work-up as above, the crude **7** (0.699 g) was benzylated using K_2CO_3 (0.426 g, 3.08 mmol), benzyl chloride (0.266 ml, 2.31 mmol) and DMF (20 ml) to give **8** (0.418 g, 58%).

Cleavage of the Furan Ring in 8 [2-(4-Benzyloxy-2-formyl-3-hydroxyphenyl)-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (10)] A mixture of **8** (0.400 g, 0.86 mmol) and osmium tetroxide (0.306 g, 1.20 mmol) in pyridine (12 ml) was stirred at room temperature for 3 h, after which a solution of sodium hydrogen sulfite (0.537 g, 2.26 mmol) in pyridine (3 ml) and water (6 ml) was added to it. The whole was stirred at room temperature for 3 h, poured into water and extracted with ethyl acetate. The organic solution was washed with 5% hydrochloric acid, saturated aqueous cupric sulfate and brine. After work-up, the residue was purified by column chromatography with chloroform–ethyl acetate (3 : 1, v/v) followed by recrystallization from chloroform–hexane to give 2-[4-(7-benzyloxy-2,3-dihydroxy-2-methyl-2,3-dihydrobenzo[*b*]-furanyl)]-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene[11] (0.356 g, 83%) as slightly brown prisms, mp 238—241 °C. IR ν_{max} cm^{-1}: 3350 (OH), 1665 (CO). *Anal.* Calcd for $C_{29}H_{25}NO_7$: C, 69.73; H, 5.05; N, 2.80. Found: C, 69.48; H, 4.79; N, 2.70.

A solution of periodic acid dihydrate (0.127 g, 0.60 mmol) in dioxane (2.2 ml) and water (0.8 ml) was added to a solution of the diol (0.200 g, 0.40 mmol) in dioxane (8 ml) under argon. The whole was stirred at room temperature for 1.5 h, poured into water and extracted with ethyl acetate. Work-up gave the crude acetate **9** (0.209 g), which was dissolved in dioxane (8 ml) and then treated with 5% aqueous sodium hydroxide (1.5 ml) at room temperature for 5 min. After work-up, the crude product was purified by column chromatography with chloroform–ethyl acetate (5 : 1, v/v) followed by recrystallization from chloroform–hexane to give **10** (0.118 g, 65%) as yellow prisms, mp 212—215 °C. IR ν_{max} cm^{-1}: 1678, 1666, 1650 (CO). ^{1}H-NMR[5] δ: 2.93 and 3.09 (total 3H, s, NMe), 5.17—5.26 (2H, m, OCH_2Ph), 6.12 (2H, s, OCH_2O), 6.64 and 6.65 (total 1H, d, J=8.2 Hz, 6′-H), 7.04 and 7.06 (total 1H, s, 8-H), 7.11 and 7.13 (total 1H, d, J=8.2 Hz, 5′-H), 7.23 (1H, d, J=8.3 Hz, 3-H), 7.23—7.49 (6H, m, CH_2Ph and 5-H), 7.73 (1H, d, J=8.3 Hz, 4-H), 7.97 and 8.16 (total 1H, s, NCHO), 9.60 and 9.64 (total 1H, s, ArCHO), 11.97 and 11.99 (total 1H, s, OH). *Anal.* Calcd for $C_{27}H_{21}NO_6$: C, 71.20; H, 4.65; N, 3.08. Found: C, 71.48; H, 4.42; N, 2.99.

2-(4-Benzyloxy-2-formyl-3-methoxyphenyl)-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (11) A mixture of **10** (0.100 g, 0.22 mmol), benzyltributylammonium chloride (0.015 g, 0.05 mmol), sodium hydroxide (0.021 g, 0.53 mmol), and dimethyl sulfate (0.14 ml, 1.48 mmol) in dichloromethane (2 ml) and water (2 ml) was stirred at room temperature for 15 min, poured into water and extracted with dichloromethane. The dichloromethane solution was washed with 5% ammonium hydroxide and brine. Work-up afforded **11** (0.096 g, 95%) as colorless prisms (from dichloromethane–ether), mp 211.5—214.5 °C. IR ν_{max} cm^{-1}: 1693, 1667 (CO). ^{1}H-NMR[5] δ: 2.89 and 3.05 (total 3H, s, NMe), 4.03 (3H, s, OMe), 5.19—5.30 (2H, m, OCH_2Ph), 6.08 (2H, s, OCH_2O), 6.82—6.83 (1H, m, 5′-H), 7.02 and 7.03 (total 1H, s, 8-H), 7.09 (1H, d, J=8.3 Hz, 3-H), 7.26 (1H, s, 5-H), 7.19—7.22 (1H, m, 6′-H), 7.35—7.48 (5H, m, CH_2Ph), 7.67 (1H, d, J=8.3 Hz, 4-H), 7.96 and 8.15 (total 1H, s, NCHO), 10.37 and 10.38 (total 1H, s, ArCHO). *Anal.* Calcd for $C_{28}H_{23}NO_6$: C, 71.63; H, 4.94; N, 2.98. Found: C, 71.42; H, 4.65; N, 2.83.

Cyclization of 11 under Basic Conditions: (a) With 70% Aqueous KOH in EtOH A solution of **11** (0.03 g, 0.06 mmol) in 70% aqueous KOH in EtOH (1 ml) was treated as shown in Table 1 (run 2). After work-up, acidification of the residue with 10% hydrochloric acid gave **12**[8] (0.008 g, 28%) as a chloride.

(b) With 10% EtONa in EtOH Treatment of **11** (0.03 g, 0.06 mmol) with 10% EtONa in EtOH (7 ml) as shown in Table 1 (run 3) gave **12**[8] (0.007 g, 25%).

Conversion of Aldehydic Formamides into Ester Formamides A mixture of aqueous sodium phosphate monobasic dihydrate, 30% hydrogen peroxide and aqueous sodium chlorite (80%) was added to a solution of an aldehydic formamide in MeCN at *ca.* 10 °C. The reaction mixture was stirred at the same temperature for 4 h and then a small amount of sodium sulfite was added to it. The whole was poured into water, acidified with 10% hydrochloric acid to *ca.* pH 6 and extracted with ethyl acetate. Work-up gave an acid, which was recrystallized from chloroform–methanol.

A mixture of the acid, dimethyl sulfate and potassium carbonate in DMF was stirred at room temperature for 10 min. Work-up gave an ester formamide, which was recrystallized from chloroform–methanol.

(a) 2-(4-Benzyloxy-3-methoxy-2-methoxycarbonylphenyl)-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (14) For oxidation of **11** (0.070 g, 0.15 mmol), MeCN (2 ml), a solution of sodium phosphate monobasic dihydrate (0.005 g, 0.03 mmol) in water (0.1 ml), 30% hydrogen peroxide (0.01 ml) and a solution of sodium chlorite (0.020 g, 0.22 mmol) in water (0.1 ml) were used. Work-up afforded a carboxylic acid (0.072 g, quant.) as colorless prisms, mp 265—267 °C. IR ν_{max} cm^{-1}: 1716, 1632 (CO).

For esterification of the acid (0.050 g, 0.10 mmol), dimethyl sulfate (0.01 ml, 0.11 mmol), K_2CO_3 (0.034 g, 0.24 mmol) and DMF (2 ml) were used. Work-up gave **14** (0.047 g, 92%) as colorless prisms, mp 179—180 °C. IR ν_{max} cm^{-1}: 1728, 1676 (CO). ^{1}H-NMR[5] δ: 2.90—3.30 (3H, br, NMe), 3.55 (3H, s, OMe), 3.95 (3H, s, OMe), 5.16 (2H, s, OCH_2Ph), 6.09 (2H, s, OCH_2O), 6.83 (1H, d, J=8.5 Hz, 5′-H), 7.04 (1H, d, J=8.3 Hz, 4-H), 7.06 (1H, s, 5-H), 7.18 (1H, s, 8-H), 7.24 (1H, d, J=8.5 Hz, 6′-H), 7.35 (1H, t, J=7.3 Hz, CH_2Ph), 7.42 (2H, t, J=7.3 Hz, CH_2Ph), 7.47 (2H, d, J=7.3 Hz, CH_2Ph), 7.65 (1H, d, J=8.3 Hz, 3-H), 8.05—8.15 (1H, br, NCHO). MS m/z: 499 (100%, M^+). *Anal.* Calcd for $C_{29}H_{25}NO_7$: C, 69.73; H, 5.05; N, 2.80. Found: C, 69.78; H, 4.98; N, 2.90.

(b) 2-(3,4-Dimethoxy-2-methoxycarbonylphenyl)-6,7-methylenedioxy-1-(*N*-methylformamido)naphthalene (17) For oxidation of **2** (0.080 g, 0.20 mmol), MeCN (2 ml), a solution of sodium phosphate monobasic dihydrate (0.006 g, 0.04 mmol) in water (0.1 ml), 30% hydrogen peroxide (0.01 ml) and a solution of sodium chlorite (0.028 g, 0.31 mmol) in water (0.1 ml) were used. Work-up afforded an acid (0.079 g, 94%) as colorless prisms, mp 281—283 °C. IR ν_{max} cm^{-1}: 1716, 1631 (CO).

For esterification of the acid (0.077 g, 0.19 mmol), dimethyl sulfate (0.02 ml, 0.21 mmol), K_2CO_3 (0.063 g, 0.45 mmol) and DMF (1 ml) were used. Work-up gave **17** (0.73 g, 92%) as colorless prisms, mp 201—203 °C. IR ν_{max} cm^{-1}: 1730, 1667 (CO). ^{1}H-NMR[5] δ: 2.80—3.00 (3H × 2/5, br, NMe), 3.01 (3H × 3/5, s, NMe), 3.55 and 3.58 (total 3H, s, OMe), 3.91, 3.92, 3.927 and 3.934 (total 6H, s, OMe × 2), 6.05 and 6.08 (each 1H × 2/5, d, J=0.9 Hz, OCH_2O), 6.09 (2H × 3/5, s, OCH_2O), 6.87 (1H, d, J=8.5 Hz, 5′-H), 6.97 and 6.98 (total 1H, d, J=8.5 Hz, 6′-H), 6.98 and 7.05 (total 1H, s, 5-H), 7.16 and 7.18 (total 1H, s, 8-H), 7.22 and 7.24 (total 1H, d, J=8.5 Hz, 4-H), 7.63 and 7.65 (total 1H, d, J=8.5 Hz, 3-H), 8.10—8.30 (1H × 3/5, br, NCHO), 8.33 (1H × 2/5, s, NCHO). MS m/z: 423 (51.4%, M^+), 223 (100%). *Anal.* Calcd for $C_{23}H_{21}NO_7$: C, 65.24; H, 5.00; N, 3.31. Found: C, 65.02; H, 4.89; N, 3.46.

8-Benzyloxy-6-cyano-7-methoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (15) According to the reported method,[9] a mixed solution of **12**[8] (0.280 g, 0.66 mmol) in water (56 ml) and MeOH (28 ml) was treated with potassium cyanide (0.101 g, 1.55 mmol) at 50 °C for 1.5 h. Work-up gave **15** (0.227 g, 70%) as colorless prisms (from chloroform–methanol), mp 235—239 °C. ^{1}H-NMR (60 MHz) δ: 2.62 (3H, s, NMe), 4.03 (3H, s, OMe), 5.18 (2H, s, OCH_2Ph), 5.63 (1H, s, 6-H), 6.04 (2H, s, OCH_2O), 7.00—7.80 (11H, m, ArH). *Anal.* Calcd for $C_{28}H_{22}N_2O_4$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.38; H, 4.99; N, 6.06.

8-Benzyloxy-7-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5*H*)-one (4) According to the reported method[9] a solution of **15** (0.219 g, 0.49 mmol) in hexamethylphosphoric triamide (11 ml) was treated with sodium hydride (52.9%: 0.155 g, 3.42 mmol) at room temperature for 5.5 h. After work-up, purification of the crude product

by PLC with benzene–ethyl acetate (2:1, v/v) gave **4** (0.176 g, 82%) as colorless prisms (from chloroform–methanol), mp 190—192 °C. IR ν_{max} cm^{-1}: 1640 (CO). ^{1}H-NMR (60 MHz) δ: 3.87 (3H, s, NMe), 4.11 (3H, s, OMe), 5.22 (2H, s, OC$\underline{H}_2$Ph), 6.04 (2H, s, OCH_2O), 7.09 (1H, s, 1-H), 7.30—7.70 (8H, m, ArH), 7.86 (1H, d, J=9.0 Hz, 10- or 11-H), 7.90 (1H, d, J=9.0 Hz, 11- or 10-H). *Anal.* Calcd for $C_{27}H_{21}NO_5$: C, 73.79; H, 4.82; N, 3.19. Found: C, 73.56; H, 4.84; N, 3.17.

***N*-Deacylation of Carboxamides** A *ca.* 30% solution (w/v) of a carboxamide in either chloroform or dichloromethane was treated with 1,3-dimethoxybenzene and $POCl_3$ under the conditions shown in Table 2. When the starting material was no longer detectable on TLC, the reaction mixture was treated with 5% aqueous sodium hydroxide in ethanol at room temperature. After extraction, the extract was repeatedly washed with 5% hydrochloric acid. The washings were combined and basified with 5% aqueous sodium hydroxide. Work-up gave the corresponding amine.

(a) The Oxobase 4 As above, a solution of **14** (0.040 g, 0.08 mmol) in chloroform (0.5 ml) was treated with 1,3-dimethoxybenzene (0.014 ml, 0.09 mmol) and $POCl_3$ (0.01 ml, 0.10 mmol) at 40 °C for 1 d. After hydrolysis, recrystallization of the crude product from chloroform–methanol gave **4** (0.034 g, 95%) as colorless prisms, mp 189—190 °C. This product was identical with the sample prepared above.

(b) Oxochelerythrine (5) As above, a solution of **17** (0.050 g, 0.12 mmol) in chloroform (0.5 ml) was treated with 1,3-dimethoxybenzene (0.017 ml, 0.13 mmol) and $POCl_3$ (0.013 ml, 0.14 mmol) at 60 °C for 1 d. After hydrolysis, recrystallization of the crude product from chloroform–methanol gave **5** (0.040 g, 93%) as colorless prisms, mp192—194 °C (lit.[9] mp 199—203 °C).

8-Hydroxy-7-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5*H*)-one (16) A suspension of **4** (0.050 g, 0.14 mmol) and 5% Pd–C (0.056 g) in ethanol (50 ml) was hydrogenated at room temperature and atmospheric pressure until the reaction ceased. After removal of the catalyst by filtration, the filtrate was evaporated. Recrystallization of the residue afforded colorless prisms (0.035 g, 88%), mp 225—228 °C. IR ν_{max}^{KBr} cm^{-1}: 3200 (OH), 1630 (CO). ^{1}H-NMR ($CDCl_3+CD_3OD$) δ: 3.92 (3H, s, NMe), 3.99 (3H, s, OMe), 6.11 (2H, s, OCH_2O), 7.18 (1H, s, 1-H), 7.41 (1H, d, J=8.5 Hz, 9- or 12-H), 7.56 (1H, s, 4-H), 7.57 (1H, d, J=8.5 Hz, 12- or 9-H), 7.98 (1H, d, J=8.5 Hz, 10- or 11-H), 8.01 (1H, d, J=8.5 Hz, 11- or 10-H). *Anal.* Calcd for $C_{20}H_{15}NO_5$: C, 68.76; H, 4.33; N, 4.01. Found: C, 68.86; H, 4.40; N, 3.95.

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References and Notes

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