with methanol, and **7c** was isolated from the filtrate by preparative TLC ($CHCl_3$–MeOH, 5:1 v/v). The zone immediately above the origin and extending to R_f ~0.45 was removed (the low-intensity absorption of **4c** precludes detection by UV illumination) and extracted with methanol. Removal of the solvent afforded crystalline **4c** (22 mg, 58%) with TLC, melting point, UV, and NMR properties identical with those of authentic **4c**.

The ^{13}C NMR spectrum (H_2O–Me_2SO-d_6, 1:2 v/v) of the lyophilized reaction mixture containing the 225-nm-absorbing intermediate shows, in addition to sodium acetate, a methyl signal at δ 23.1 consistent with structure **13**. Low-field peaks from nonenhanced carbon atoms were not sufficiently clear to assign with any confidence.

Methyl 2,3-Dihydro-5-(hydroxymethyl)-1-methyl-2-oxo-1*H*-imidazole-4-carboxylate (17). A solution of diazomethane in ether (0.5 mmol, assayed with benzoic acid) was added portionwise to a solution of **16** (86 mg, 0.5 mmol) in methanol (10 mL). After 15 min, the reaction mixture was concentrated to a small volume, and the methyl ester **17** was isolated by preparative TLC ($CHCl_3$–MeOH, 9:1 v/v): 50 mg (54%, from ethyl acetate–hexane); mp 195–197 °C; UV (H_2O) λ_{max} 273 nm, λ_{min} 234; UV (pH 13) λ_{max} 292 nm, λ_{min} 247; NMR δ 10.67 (1 H, s, N_3 H), 5.26 (1 H, t, OH), 4.63 (2 H, d, CH_2, $J_{H,OH} = 4.6$ Hz), 3.73 (3 H, s, CO_2Me), 3.19 (3 H, s, N_1 Me).

Anal. Calcd for $C_7H_{10}N_2O_4$: C, 45.16; H, 5.41; N, 15.05. Found: C, 45.18; H, 5.40; N, 14.93.

5,5′-Methylenebis[2,3-dihydro-1-methyl-2-oxo-1*H*-imidazole-4-carboxylic Acid] (18). A solution of 6,6′-methylenebis[1-methyl-5-hydroxyuracil] hemihydrate (**20**; 245 mg, 0.8 mmol) in 50 mL of 0.1 N sodium hydroxide was heated under reflux for 14 h, at which time the shift of the UV spectrum from λ_{max} 325 to λ_{max} 262 nm (0.125-mL sample diluted to 25 mL) was essentially complete. Acidification of the cooled, yellowish reaction mixture afforded 166 mg (70%) of colorless **18**, identical (melting point, UV, NMR) with the material prepared from **4b** as described above.

Methylation of 18. A stirred suspension of **18** (50 mg) in 75% (v/v) aqueous methanol (20 mL) was treated at room temperature with a large excess of ethereal diazomethane. When all the starting material had dissolved (~1 h), the solvents were removed, and a solution of the residue in chloroform was applied to a preparative TLC plate. The plate was developed in $CHCl_3$–MeOH (18:1, v/v), the appropriate zones were removed and extracted with ethyl acetate. The filtrates were evaporated to give the following materials.

(a) 5,5′-Methylenebis[methyl 2,3-dihydro-1,3-dimethyl-2-oxo-1*H*-imidazole-4-carboxylate] (**19**): R_f 0.55; 30 mg (50.5%). Material was crystallized from ethyl acetate: mp 226–228 °C; UV (MeOH) λ_{max} 282.5 nm, λ_{min} 238; NMR ($CDCl_3$) δ 4.83 (1 H, s, CH_2), 3.89 (3 H, s, CO_2Me), 3.49 (3 H, s, NMe), 3.17 (3 H, s, NMe).

Anal. Calcd for $C_{15}H_{20}N_4O_6$: C, 51.13; H, 5.72; N, 15.90. Found: C, 51.22; H, 5.78; N, 15.93.

(b) The product of mixed O- and N-methylation (**21**): R_f 0.67; 14 mg (23.5%). Material was recrystallized from ethyl acetate–*n*-hexane: mp 187–188 °C; UV (MeOH) 276 nm, 265 (sh), λ_{min} 232; NMR ($CDCl_3$) δ 4.93 (2 H, s, CH_2), 4.08 (3 H, s, OMe), 3.91 (3 H, s, CO_2Me), 3.89 (3 H, s, CO_2Me), 3.49 (3 H, s, NMe), 3.26 (3 H, s, NMe), 3.15 (3 H, s, NMe).

Anal. Calcd for $C_{15}H_{20}N_4O_6$: C, 51.13; H, 5.72; N, 15.90. Found: C, 51.16; H, 5.78; N, 15.81.

(c) 5,5′-Methylenebis[methyl 1-methyl-2-methoxyimidazole-4-carboxylate] (**23**): R_f 0.80; 1 mg (1.7%); mp, indistinct at 200–205 °C (dec with shrinkage above 180 °C); UV (MeOH) λ_{max} 264 nm λ_{min} 225–240 (flat); NMR ($CDCl_3$) δ 4.99 (1 H, s, CH_2), 4.06 (3 H, s, OMe), 3.91 (3 H, s, CO_2Me), 3.25 (3 H, s, NMe).

Registry No. 1a, 20406-86-4; **2a**, 80029-05-6; **2b**, 28199-47-5; **2c**, 80029-06-7; **4a**, 80029-07-8; **4b**, 80029-08-9; **4c**, 80029-09-0; **5a**, 80029-10-3; **5b**, 80029-11-4; **7a**, 80029-12-5; **7b**, 17374-27-5; **7c**, 616-03-5; **8**, 80029-14-7; **13**, 80029-13-6; **16**, 80029-15-8; **17**, 80029-16-9; **18**, 80029-17-0; **19**, 80029-18-1; **20**, 28199-48-6; **21**, 80029-19-2; **23**, 80029-20-5; 5-hydroxyuracil, 20636-41-3.

Synthesis of Oxoaporphines. An Unusual Photocyclization–Photoreduction of 2,3-Diaryl-Δ^2-pyrroline-4,5-diones[1]

Luis Castedo,* Carlos Saá, José M. Saá, and Rafael Suau

Departamento de Química Orgánica de la Facultad de Química e Instituto de Productos Naturles Orgánicos (Sección de Alcaloides) del CSIC, Santiago de Compostela, Spain

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The photocyclization of substituted 2,3-diaryl-Δ^2-pyrroline-4,5-diones, with a forced *cis*-stilbene geometry, afforded the corresponding phenanthrene derivatives. Concomitant photoreduction of the C-4 carbonyl group to methylene has been observed when triethylamine was used as acid scavenger. The role of the amine in the photocyclization and photoreduction steps is discussed in terms of the results obtained with different amines (triethylamine, pyridine, and *tert*-butylamine). The naturally occurring oxoglaucine, lysicamine, and dicentrinone have been synthesized in good to acceptable yields by Fremy's salt oxidation of the photocyclized products.

Oxoaporphines constitute a small group of isoquinoline alkaloids biogenetically derived from aporphines.[2a] Recently it has been shown that they possess interesting antibacterial as well as antifungal activity against several microorganisms,[2b] thus making them clinically attractive (particularly liriodenine **4c**) as antibiotics.

As a continuation of our work on the synthesis of isoquinoline alkaloids we became interested in devising a short and effective route to oxoaporphines and to noraporphines. Classically oxoaporphines are obtained from aporphines or noraporphines by treatment with several oxidizing agents,[3] including a possible biomimetic-like

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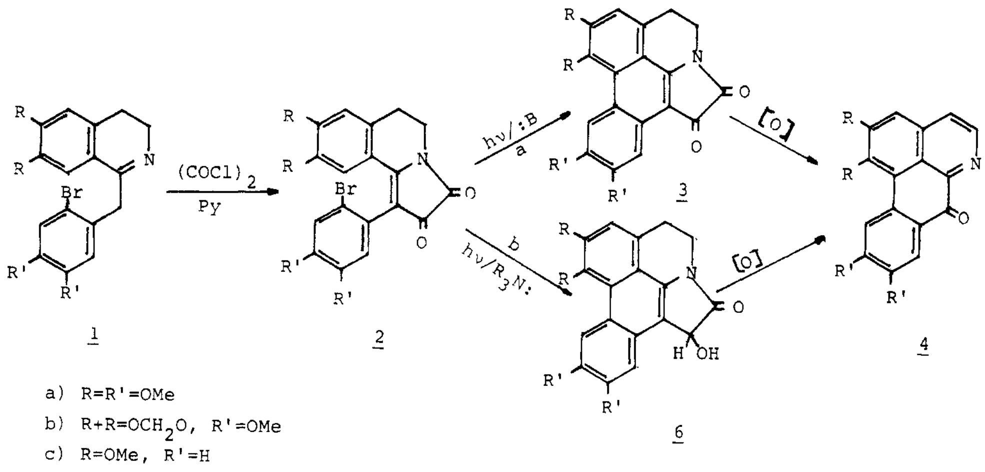
[1] Presented in part at the 10th International Conference on Photochemistry, Creta, Sept 1981.

[2] (a) M. Shamma and J. L. Moniot, "Isoquinoline Alkaloids Research 1972–1977", Plenum Press, New York, 1978. See also M. Shamma "The Isoquinoline Alkaloids", Academic Press, New York, 1972. (b) C. D. Hufford, A. S. Sharma, and B. O. Oguntimein, *J. Pharm. Sci.*, **69**, 1180 (1980), and references therein.

[3] These include CrO_3 in Py, MnO_2, I_2, singlet oxygen, etc. See ref 2a for leading references.

0022-3263/82/1947-0513$01.25/0

Scheme I



oxidant such as Fremy's salt.[4] On the other hand, total synthesis of oxoaporphines usually involves elaboration of a C-2′ or C-6′ functionalized (NO$_2$ or halogen) aromatic benzylisoquinoline, which is then cyclized through a Pschorr or photochemical sequence.[5] Both alternatives usually result in poor yields due to low efficiency in the key cyclization step, an exception being Kupchan's photochemical synthesis of oxoaporphines.[6] Another photochemical approach is that of Cava et al.,[7] whose key step is the photocyclization of an *o*-halo enamide[8] to a dehydroaporphine derivative which is then further oxidized. Cava's sequence[7] also gives low yields in the cyclization as well as in the oxidation steps.

Obviously there was still a need for a practical synthesis of oxoaporphines for which the photochemical approach seemed the most promising. Accordingly we decided to work with a modification of Cava's enamide, which should meet the following three conditions: (1) a forced *cis*-stilbene geometry to prohibit undesired modes of cyclization, particularly that leading to the protoberberine skeleton,[8] (2) absorption of most of the light in presence of the cyclized product, and (3) ability to be easily converted into the oxoaporphine stage after cyclization.

Actually our scheme is derived from the observation that "isatins" 3[9] are easily oxidized under a variety of conditions to the corresponding oxoaporphines 4 in variable yields.[10] Consequently our planned short synthesis called for the following: (a) conversion of a dihydrobenzylisoquinoline 1 to a *Z* enamide 2, (b) photochemical closure of 2 to 3 in the presence of a base that would not open up the Δ^2-pyrroline-4,5-dione ring of 2 or 3,[11] and (c) direct oxidation of 3 to 4 (Scheme I, a).

At the outset it was clear that hydroxide or alkoxide bases were of no value in the photochemical closure since they destroy the five-membered Δ^2-pyrrolinedione ring; therefore tertiary amines were the choice for the bases. Furthermore we predicted that with tertiary amines photoreduction of the keto group by the amine might take place, thus allowing the starting enamide 2 to absorb most of the light in the presence of the cyclized product and consequently we expected the reaction to go to completion (Scheme I, b).

As shown below, both pathways (Scheme I, a and b) turn out to be formally feasible although some modifications had to be made (vide infra).

As expected, dihydroisoquinolines 1[12] were converted in high yields into the corresponding red-wine enamides 2 when treated with oxalyl chloride in dry pyridine.[13]

Cyclization of the enamides 2 (450-W Hanovia lamp, Pyrex filter, 8–10 h) took place smoothly in benzene solution, under argon, in the presence of a tertiary amine as an acid scavenger. To our surprise, as the reaction proceeded we observed (TLC) the appearance of a violet spot (proved to be the "isatins" 3) as well as a blue-fluorescent one (under UV light). By the end of the reaction only this latter compound was present. Careful workup yielded the unstable oxindole 5 in variable yields. An independent synthesis of 5 definitely proved its structure. Thus reduction of 3 with sodium hydrosulfite[14] yielded 6, which was hydrogenolyzed[15] to the oxindole 5 found to be identical with the photoproduct.

A literature search for the photoreduction of a carbonyl group to methylene turned up one report, on the photolysis of a 4-acetylquinoline.[23] According to the mechanism,[16] for the photoreduction of carbonyls by amines, a likely explanation for this unusual result would be two consecutive photoreductions following the cyclization step, as shown in Scheme II.[19] The first would lead to a "dioxindole" 6 in tautomeric equilibrium with the "dioxindole" 7,which is then photoreduced to 8. Finally loss of water would produce "oxindole" 5 (Scheme II). It must be emphasized that we have been unable to detect the presence of 6 in the reaction mixture during the whole process. Alternatively, 6 or 7 might first eliminate water

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[4] L. Castedo, A. Puga, J. M. Saá, and R. Suau, *Tetrahedron Lett.*, 2233 (1981).

[5] See ref 2a for leading references.

[6] S. M. Kupchan and P. F. O'Brien, *J. Chem. Soc., Chem. Commun.*, 915 (1973).

[7] M. P. Cava, P. Steen, and K. Wakisaka, *Tetrahedron*, **29**, 2245 (1973); M. P. Cava and S. S. Libsch, *J. Org. Chem.*, **39**, 577 (1974).

[8] G. R. Lenz, *Synthesis*, 489 (1978).

[9] J. M. Saá and M. P. Cava, *J. Org. Chem.*, **43**, 1096 (1978).

[10] J. M. Saá, unpublished results.

[11] W. C. Sumpter and F. M. Miller, "The Chemistry of Heterocyclic Compounds", Interscience, New York, 1954. See also F. D. Popp, *Adv. Heterocycl. Chem.*, **18**, 2 (1975).

[12] M. P. Cava, M. J. Mitchell, S. C. Havlicek, A. Lindert, and R. J. Spangler, *J. Org. Chem.*, **35**, 175 (1970).

[13] W. Ott, G. Kollenz, and E. Ziegler, *Synthesis*, 546 (1976).

[14] C. Marschalk, *Ber. Dtsch. Chem. Ges.*, **45**, 582 (1912).

[15] J. M. Muchowski, *Can. J. Chem.*, 857 (1969); A. H. Beckett, R. W. Daisley, and J. Walker, *Tetrahedron*, **24**, 6093 (1968).

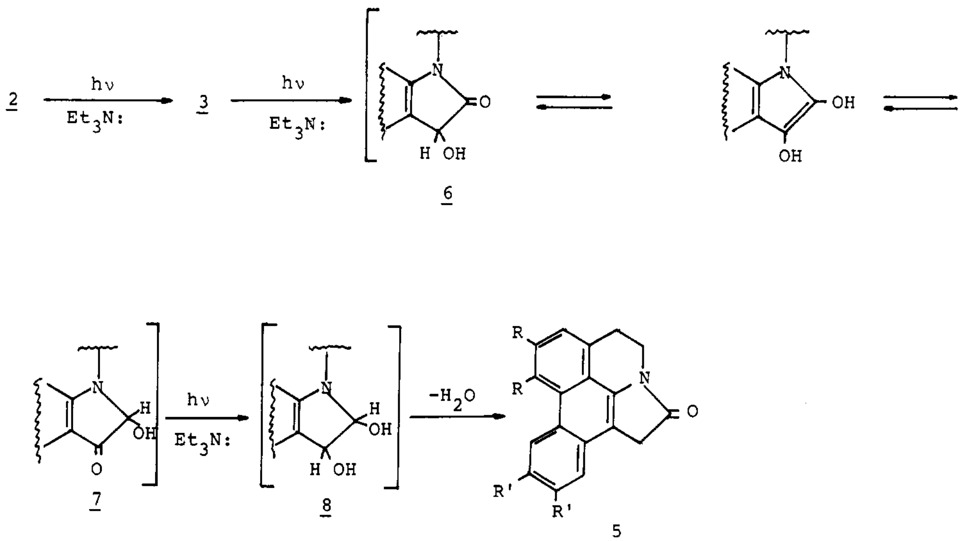
[16] S. G. Cohen, A. Parola, and G. H. Parsons, Jr., *Chem. Rev.*, **73**, 141 (1973).

[17] S. Inbar, H. Linschitz, and S. G. Cohen, *J. Am. Chem. Soc.*, **102**, 1419 (1980).

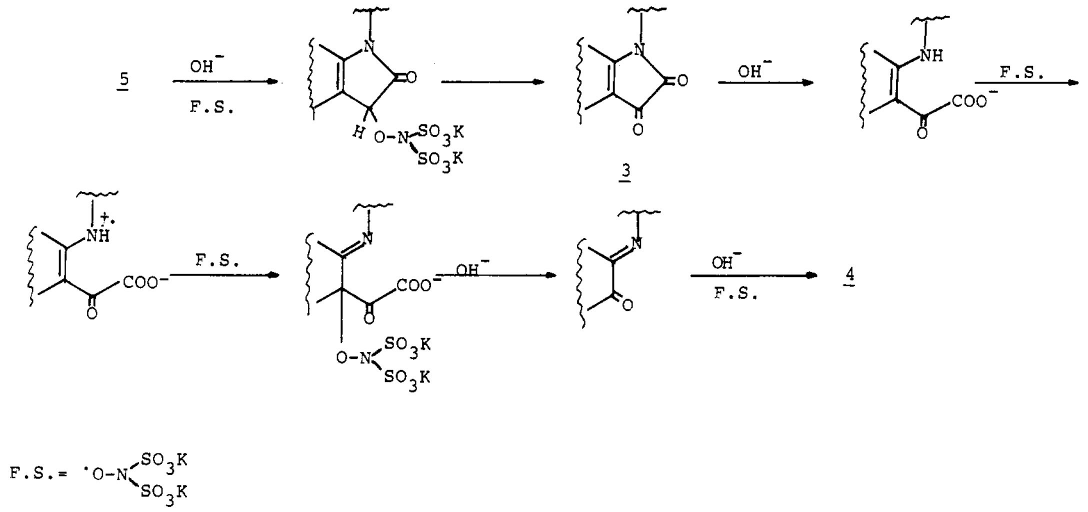
[18] See H. Aoyama, T. Hasegawa, M. Watabe, H. Shiraishi, and Y. Obote, *J. Org. Chem.*, **43**, 419 (1978), and references therein for the typical photochemical behavior of acyclic N,N-disubstituted α-oxo amides.

[19] For an analogous electrochemical CO to CH$_2$ reduction, see W. Pfleiderer and R. Gottlieb, *Heterocycles*, 1603 (1980).

Scheme II



Scheme III



and then be further reduced to **5**.

According to this mechanistic interpretation, "isatins" **3**[9] are photoreduced to **5** in the presence of Et_3N, (i-$Pr)_2NEt$, or other tertiary amines at a higher rate (3 h), therefore suggesting that the slowest step might possibly be that of cyclization. Furthermore the "dioxindole" **6** obtained by hydrosulfite reduction[14] of the "isatins" **3** is also easily photoreduced to **5** in a much shorter time (1.5 h).

Further support for the above reasoning was that "isatins" **3** as well as enamides **2** were recovered totally unchanged after more than 17 h of irradiation[18] in the presence of a 15 M excess of pyridine ($pK_a = 5.25$).

Since photoreduction must depend on the presence of α-hydrogen in the amine, irradiation of **2** in the presence of *tert*-butylamine ($pK_a = 10.83$) was investigated, and cyclization to **3** occurred in 70–90% yields after 24 h.

Once we had achieved both types of cyclization (Scheme I, a and b), we looked for ways of converting either the "isatins" **3** or the "oxindoles" **5** to the corresponding oxoaporphines **4**. Finally we have found that Fremy's salt[20] (FS) oxidation of both **3** or **5** proceeds directly to the desired compounds in 65–85% and 70% yields, respectively. Direct Fremy's salt oxidation of the crude photoproducts **3** and **5** yielded also the corresponding oxoaporphines but in much lower yields. A mechanistic interpretation for the conversion **3** or **5** → **4** is shown in Scheme III.

Also as mentioned before, treatment of **3** in basic solution with hydrogen peroxide afforded oxoaporphines in 40–50% yield.

In summary, we have achieved a short and efficient synthesis of oxoaporphines based on a photochemical ring closure of a *cis* *o*-halo enamide key step, which is accompanied by a double reduction of a ketone grouping to a CH_2 when a tertiary amine is used, followed by a new oxidative transformation to the oxoaporphine stage. Another important conclusion of this work is that photoreduction of a carbonyl group during a photocyclization may turn out to be a useful way to solve the problems derived from the fact that photoproducts may absorb at lower wavelengths than the starting materials.

Experimental Section

General Procedures. All melting points were taken on a Koffler apparatus and are uncorrected. Proton magnetic resonance spectra were recorded on a Varian Model CFT-20 (80 MHz) spectrometer. Chemical shifts (δ) are expressed in parts per million downfield from internal Me_4Si. Infrared spectra were taken in KBr pellets with a Pye-Unicam 1100 spectrometer.

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[20] H. Zimmer, D. C. Lankin, and S. W. Horgan, *Chem. Rev.*, 71, 229 (1971).

Ultraviolet–visible spectra were run on a Pye-Unicam 1700 instrument and mass spectra were recorded on a Kratos MS-25 instrument operating at 70 eV. Combustion analyses were performed with a Perkin-Elmer Model 240 B at the Inorganic Chemistry Department.

Dry pyridine was prepared by reflux with commercially available material (E. Merck) with solid KOH for 8 h and final distillation. Fremy's salt (FS) was prepared and stored as indicated.[20] Dry benzene was obtained by refluxing 6 h with H_2Ca and then distilling from H_2Ca. It was stored with sodium wire. All other chemicals, NEt_3, $(i\text{-}Pr)_2NEt$, oxalyl chloride, etc., were used as obtained from the suppliers.

Preparative Photochemistry. Reactions were carried out at near room temperature, using a Hanovia 450-W, medium-pressure mercury lamp in a Pyrex immersion well. Solutions were degassed by flushing through argon before (1 h) and during irradiation.

Enamides 2. General Method. To a cold and stirred solution of 6′-bromo dihydroisoquinoline[12] **1** in a minimum amount of dry pyridine was added a slight excess (10 M) of oxalyl chloride dropwise. Stirring was continued for an additional 2 h at room temperature. Workup was carried out as follows: three volumes of Cl_2CH_2 were added to the deep-red solution, which was then washed 5 times with a 5% $CuSO_4$ aqueous solution to remove pyridine. After the mixture was dried, evaporation at reduced pressure yielded a crude product which normally crystallized to give analytically pure samples of the enamides **2**. Enamide **2a** was obtained in 84% yield as deep-red crystals: mp 236–238 °C (from EtAc); IR (KBr) 1750, 1700 cm^{-1}; UV (EtOH) λ_{max} 234 nm (log ϵ 4.00), 260 (sh, 3.80), 292 (3.64), 322 (3.59), 380 (3.67), 450 (3.54), 510 (3.40); NMR ($CDCl_3$) δ 7.11 (s, 1 H), 6.77 (s, 1 H), 6.73 (s, 2 H), 3.92 (s, 3 H), 3.86 (s, 3 H), 3.80 (s, 3 H), 3.36 (s, 3 H), 3.07 (t, 2 H, *J* = 6.2 Hz); mass spectrum, *m/e* 474 (32, M^+), 394 (80), 366 (100), 197 (28).

Anal. Calcd for $C_{22}H_{20}NO_6Br$: C, 55.69; H, 4.21; N, 2.95. Found: C, 55.21; H, 4.11; N, 2.76.

Enamide **2b** was obtained in 86% yield. It crystallized (EtAc) as red prisms: mp 150–152 °C; IR (KBr) 1750, 1700 cm^{-1}; UV (EtOH) λ_{max} 236 nm (log ϵ 4.17), 260 (sh, 3.96), 290 (sh, 3.81), 312 (sh, 3.67), 386 (3.83), 450 (3.62), 510 (3.47); NMR ($CDCl_3$) δ 7.13 (s, 1 H), 6.78 (s, 1 H), 6.71 (s, 1 H), 6.67 (s, 1 H), 6.00 (s, 2 H), 3.91 (s, 3 H), 3.83 (s, 3 H), 3.06 (t, 2 H, *J* = 6.2 Hz); mass spectrum, *m/e* 458 (38, M^+), 378 (82), 350 (100), 189 (33). Enamide **2c** was obtained in 80% yield as red prisms: mp 176–178 °C (benzene); IR (KBr) 1750, 1700 cm^{-1}; UV (EtOH) λ_{max} 232 nm (log ϵ (4.04), 262 (3.92), 322 (3.79), 390 (3.80), 450 (3.67), 510 (3.43); NMR ($CDCl_3$) δ 7.70 (m, 1 H), 7.39–7.20 (m, 3 H), 6.76 (s, 1 H), 6.66 (s, 1 H), 3.94 (s, 3 H), 3.29 (s, 3 H), 3.88 (t, 2 H, *J* = 6.5 Hz), 3.09 (t, 2 H, *J* = 6.5 Hz); mass spectrum, *m/e* 414 (31, M^+), 386 (24), 334 (24), 306 (100), 193 (9).

Anal. Calcd for $C_{20}H_{16}NO_4Br$: C, 57.97; H, 3.86; N, 3.38. Found: C, 57.45; N, 3.95; N, 3.19.

"Oxindoles" 5 from Irradiation of Enamides 2. General Method. To a degassed solution (approximately 0.001 M) of the enamides **2** in dry benzene continuously flushed with a slow stream of argon was added a 15 M excess of triethylamine. The above solution was irradiated until the starting material had disappeared (TLC). By the end of the reaction (8–10 h) TLC observation showed the presence of "oxindole" **5** sometimes contaminated with a violet spot due to the "isatins" **3**, in which case further irradiation lead to total consumption of **3**.

For isolation of pure samples of **5**, careful workup was needed, avoiding air contamination of its solutions. Thus the well argon-flushed solution coming from irradiation was washed 3 times with 5% HCl and then with water. Evaporation of the dried solution usually yielded a crude sample of **5** already contaminated with the corresponding "isatin" **3**. Further purification was usually needed and that was done by preparative TLC or crystallization. We have obtained an analytical sample of **5a** (by crystallization in EtAc) only, but compounds **5b** and **5c** gave the expected spectroscopic data as shown below.

"Oxindole" **5a** was obtained (82%) as prisms (EtAc): mp 243–245 °C; IR (KBr) 1700 cm^{-1}; UV (EtOH) λ_{max} 258 nm (log ϵ 4.47), 286 (sh, 4.18), 342 (3.81), 388 (3.33); NMR ($CDCl_3$) δ 9.18 (s, 1 H), 7.15 (s, 1 H), 6.96 (s, 1 H), 4.04 and 3.98 (s, 6 H each), 3.82 (s, 2 H), 3.30 (t, 2 H, *J* = 6.2 Hz); mass spectrum, *m/e* 379 (100, M^+), 364 (28), 189, 5 (15).

Anal. Calcd for $C_{22}H_{21}NO_5{\cdot}0.5H_2O$: C, 68.04; H, 5.67; N, 3.60. Found: C, 68.46; H, 5.50; N, 3.56.

"Oxindole" **5b** was obtained (70%) as an amorphous solid: IR (KBr) 1700 cm^{-1}; UV (EtOH) λ_{max} 264 nm (log ϵ 4.32), 284 (sh, 4.10), 346 (3.73), 396 (7.28); NMR ($CDCl_3$) δ 8.42 (s, 1 H), 7.04 (s, 1 H), 6.92 (s, 1 H), 6.24 (s, 2 H), 4.04 (s, 6 H), 3.91 (t, 2 H, *J* = 6.3 Hz), 3.78 (s, 2 H), 3.26 (t, 2 H, *J* = 6.3 Hz); mass spectrum, *m/e* 363 (100, M^+), 348 (46), 181.5 (20).

"Oxindole" **5c** (84%): amorphous solid; IR (KBr) 1700 cm^{-1}; UV (EtOH) λ_{max} 250 nm (log ϵ 4.26), 330 (3.72), 386 (3.32); NMR ($CDCl_3$) δ 9.63 (m, 1 H), 7.64–7.57 (m, 3 H), 7.20 (s, 1 H), 4.04 (s, 3 H), 3.97 (s, 3 H), 3.84 (s, 2 H), 3.31 (t, 2 H, *J* = 6.2 Hz); mass spectrum, *m/e* 319 (100, M^+), 304 (26), 159 (16).

Independent Synthesis of 5a. 1. Reduction of 3a to 6a. To a refluxing solution of 100 mg of **3a**[9] in THF was added an aqueous solution of 5 equiv of sodium hydrosulfite dropwise. Immediately the violet solution turned yellow. The solvent was partially evaporated, water was added, and the mixture was extracted several times with Cl_2CH_2. The organic solution was then evaporated to yield **6a**, which crystallized from ethanol (95%): mp 210–212 °C; IR (KBr) 3340, 1700 cm^{-1}; UV (EtOH) λ_{max} 258 nm (log ϵ 4.83), 280 (sh, 4.40), 354 (3.87), 366 (3.80), 388 (3.65); NMR ($CDCl_3$) δ 9.12 (s, 1 H), 7.42 (s, 1 H), 7.12 (s, 1 H), 5.51 (s, 1 H), 4.05 and 3.96 (s, 6 H each), 3.84 (t, 2 H, *J* = 6.5 Hz), 3.28 (t, 2 H, *J* = 6.5 Hz); mass spectrum, *m/e* 395 (12, M^+), 379 (100), 364 (37), 189, 5 (18).

Anal. Calcd for $C_{22}H_{21}NO_6{\cdot}0.5H_2O$: C, 65.34; H, 5.44; N, 3.46. Found: C, 65.42; H, 5.36; N, 3.04.

2. Hydrogenolysis of 6a to 5a. To a solution of 92 mg of **6a** containing 92 mg of 10% Pd/C was added 1.5 mL of concentrated HCl. The heterogeneous mixture, heated at 60 °C, was shaken in a Parr instrument under a H_2 pressure of 4.5 atm for 2 h. The mixture was rapidly filtered, water was added, and the mixture was extracted with Cl_2CH_2. The combined organic phases were washed with water, dried over anhydrous Na_2SO_4, and evaporated to yield a semisolid material, which was found to be identical with "oxindole" **5a**, after crystallization.

"Isatins" 3 from Irradiation of Enamides 2. General Method. To a degassed solution (approximately 0.001 M) of enamide **2** in dry benzene was added a 20 M excess of *tert*-butylamine. After 24 h of irradiation, no starting enamide **2** could be detected (TLC). The solution was washed with dilute HCl and water. After drying, the solution was evaporated under reduced pressure to yield crude **3** in 70–90% yield. An analytical sample of **3** was obtained by crystallization (usually ethanol) of the crude material.

"Isatin" **3a** was obtained (60% yield) as violet prisms: mp 279–280 °C (EtOH); IR (KBr) 1750, 1700 cm^{-1}; UV (EtOH) λ_{max} 266 nm (log ϵ 4.85), 284 (sh, 4.46), 344 (4.37), 370 (sh, 3.94), 540 (3.30); NMR ($CDCl_3$) δ 9.00 (s, 1 H), 8.03 (s, 1 H), 7.11 (s, 1 H), 4.08 (s, 6 H), 4.03 (s, 3 H), 3.95 (s, 5 H), 3.32 (t, 2 H, *J* = 5.8 Hz); mass spectrum, *m/e* 393 (100, M^+), 365 (68), 350 (26), 322 (14), 182.5 (10).

Anal. Calcd for $C_{22}H_{19}NO_6{\cdot}0.5H_2O$: C, 65.67; H, 4.97; N, 3.48. Found: C, 65.74; H, 4.76; N, 3.36.

"Isatin" **3c** was obtained (66% yield) as violet prisms: mp 229–231 °C (EtOH); IR (KBr) 1750, 1700 cm^{-1}; UV (EtOH) λ_{max} 256 nm (log ϵ 4.75), 284 (sh, 4.32), 324 (sh, 4.24), 336 (4.29), 354 (sh, 4.00), 510 (3.38); NMR ($CDCl_3$) δ 9.42 (dd, 1 H, *J* = 1.1 and *J′* = 7.7 Hz), 8.60 (dd, 1 H, *J* = 1.1 and *J′* = 7.7 Hz), 7.66–7.39 (m, 2 H), 7.17 (s, 1 H), 4.09 (s, 3 H), 3.95 (s, 3 H), 3.95 (t, 2 H, *J* = 6.2 Hz), 3.34 (t, 2 H, *J* = 6.2 Hz); mass spectrum, *m/e* 333 (100, M^+), 305 (65), 290 (10), 262 (15), 152.5 (10).

Independent Synthesis of 3a.[9] To a cold, stirred solution of dehydroglaucine[21] (500 mg) in dry THF was added oxalyl chloride (10 M excess) dropwise. Immediately the yellowish solution turned dark red-violet. Stirring was continued for an additional 2 h. Then THF was removed under reduced pressure. The residue was dissolved in Cl_2CH_2 and the solution washed with water, dried over anhydrous Na_2SO_4, and then evaporated to yield crude "isatin" **3a**, which crystallized as fine crystals from EtOH (90% yield), mp 279–280 °C. This compound was found to be

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(21) L. Castedo, T. Iglesias, A. Puga, J. M. Saá, and R. Suau, *Heterocycles*, 15, 915 (1981).

identical with the "isatin" **3a** obtained by irradiation of enamide **2a** in the presence of *tert*-butylamine (see above).

Fremy's Salt Oxidation of "Isatins" 3 to Oxoaporphines 4. To a stirred solution of pure "isatins" **3** in pyridine–water (1:1) was added an excess of Fremy's salt[20] in 4% aqueous sodium carbonate. The amount of pyridine was increased if necessary for obtaining an homogeneous solution. Generally the reaction was over after 30–40 h. The mixture was then acidified (pH 5) with 10% HCl and extracted several times with Cl_2CH_2. The combined extracts were washed once with water, dried over anhydrous Na_2SO_4, and then evaporated to dryness. The yellow residue crystallized from EtOH to yield the corresponding oxoaporphines **4** in 65–85% yields.

The oxoaporphines[22] **4a** (oxoglaucine) and **4c** (lysicamine) thus obtained were found to be totally identical (IR, NMR, MS, melting point) with authentic samples of these compounds previously obtained by us.[4]

On the other hand crude, "isatin" **3c** obtained from irradiation of 360 mg of enamide **2c** in the presence of *tert*-butylamine by simple evaporation to dryness was submitted to Fremy's salt oxidation as above. The crude product obtained was purified by preparative TLC (silica gel plates, Cl_2CH_2 + 1% H_2O) to give 46 mg of lysicamine **4c**,[22] mp 210–211 °C (18% overall yield).

Fremy's Salt Oxidation of "Oxindoles" 5 to Oxoaporphines 4. To a stirred solution of crystalline **5a** (100 mg) in 10 mL of pyridine–water (1:1) was added an excess of Fremy's salt in the minimum amount of 4% aqueous sodium carbonate. After 48 h the reaction was quenched by addition of 10% HCl and the mixture was extracted with Cl_2CH_2. Evaporation of the solvent yielded crude oxoglaucine **4a**, which was purified by a short-column chromatography on neutral alumina (Woelm), activity IV, using Cl_2CH_2 + 1% EtOH as eluent. Oxoglaucine[22] **4a**, mp 225–226 °C (EtOH) was obtained in 70% yield.

On the other hand, crude **5b** obtained from irradiation of 20 mg of **2b** in the presence of triethyl amine by simple evaporation to dryness was submitted to Fremy's salt oxidation as above. After the usual workup, dicentrinone[22] **4b**, mp 300 °C dec, was obtained in 20% overall yield.

Under analogous conditions crude **5c** obtained from irradiation of 600 mg of enamide **2c** gave 114 mg (27.1% overall yield) of lysicamine[22] **4c**, mp 210–211 °C.

Hydrogen Peroxide Oxidation of "Isatin" 3a to Oxoglaucine 4a. A 50-mg sample of "isatin" **3a** was dissolved in 10 mL of hot dioxane and 6 mL of 10% NaOH. To this stirred yellow solution was added 6 mL of 3% hydrogen peroxide dropwise. The mixture was kept with stirring until an aliquot showed the disappearance of starting material (3 h). The solution was diluted with water and then extracted with Cl_2CH_2 several times. The combined extracts were washed with water and dried over anhydrous Na_2SO_4. Evaporation of solvent yielded crude oxoglaucine **4a**, which crystallized from EtOH, mp 225–226 °C (43% yield).

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Registry No. 1a, 41823-67-0; **1b**, 80041-80-1; **1c**, 80041-81-2; **2a**, 80041-82-3; **2b**, 80041-83-4; **2c**, 80041-84-5; **3a**, 78178-94-6; **3c**, 64938-92-7; **4a**, 5574-24-3; **4b**, 16408-78-9; **4c**, 15444-20-9; **5a**, 80041-85-6; **5b**, 80041-86-7; **5c**, 80041-87-8; **6a**, 80041-88-9; oxalyl chloride, 79-37-8; dehydroglaucine, 22212-26-6.

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Unusual Reaction of *N*-Hydroxyphthalimido Ethers Leading to Oxygen–Nitrogen Heterocycles[1]

Nourdine Amlaiky, Gérard Leclerc,* and Alain Carpy

Institut de Pharmacologie, ERA 142 du CNRS, U.206 de l'INSERM, Faculté de Médecine, 67000 Strasbourg, France, and Laboratoire de Chimie Analytique, ERA 890 du CNRS, Faculté de Pharmacie, 33000 Bordeaux, France

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Treatment of *N*-[(2,3-epoxypropyl)oxy]phthalimide (**1**) with alcohols under basic catalysis yields a new 3-[*o*-(carbomethoxy)phenyl]-5-(hydroxymethyl)-6*H*-1,4,2-dioxazine (**4a**) compound, whose structure was determined by X-ray crystallography. Similarly, the behavior of the higher [(epoxybutyl)oxy]phthalimide (**13**) and [(epoxypentyl)oxy]phthalimide (**18**) derivatives were investigated and compared to that of their *N*-[(3-halo-2-hydroxyalkyl)oxy]phthalimides. Formation of **4a**, *N*-[*o*-(carbomethoxy)benzoyl]-3-(hydroxymethyl)isoxazolidine (**15**), *N*-[*o*-(carbomethoxy)benzoyl]-4-hydroxy-1,2-oxazepine (**19**), and *N*-[*o*-(carbomethoxy)benzoyl]-3-(hydroxymethyl)-1,2-oxazine (**20**) from the corresponding epoxides **1**, **13**, and **18** is discussed in the light of Baldwin's rules.

During our studies relating to the synthesis of oximinopropanol derivatives[2] with β-adrenergic blocking activity[3] we considered hydroxyphthalimido ethers as possible synthons for the preparation of 3-(aminooxy)-2-hydroxypropanamine derivatives **7**.

Treatment of epoxy derivative **1**, readily available from *N*-hydroxyphthalimide and epibromohydrin, with an excess of *tert*-butylamine in MeOH failed to give the expected amino alcohol **3**. Instead, compound **4a** was formed in excellent yield in a few minutes. The ^1H NMR spectra of **4a** lacked a *tert*-butyl group but contained a methyl peak indicative of a methyl ester. The presence of an ester was further confirmed by a 1715-cm^{-1} absorption band in the IR spectrum. Additionally, the IR spectrum showed an OH function at 3400 cm^{-1}. The elemental analysis and mass spectral analysis of this material indicated a composition of $C_{12}H_{13}NO_5$, which could correspond to struc-

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* G.L. and N.A., Institute de Pharmacologie; A.C., Laboratoire de Chimie Analytique.

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