proved to be identical with 5 from part A by superimposing the IR spectra.

6,12-Dioxo-2,3,7-trimethoxy-11-methyl-6,8a,9,10-tetrahydro-9,8a-iminoethanophenanthrene (6). A. By Anodic Oxidation. The lactam (**3**, 1.6 g) was electrochemically oxidized in DCM–TFA solution at a constant potential of 1.8 V over a period of 2.5 h. The purple anolyte was treated with Zn dust, filtered, and washed with water (2 × 150 ml), followed by aqueous $NaHCO_3$ (2 × 150 ml). The organic layer was dried (Na_2CO_3), and the solvent was evaporated to leave a brown oil that was redissolved in hot EtOAc–$CHCl_3$. From this solution the lactam spirodienone (**6**) crystallized as a pale yellow solid: 0.6 g; mp 252–254 °C; IR (Nujol) 1690 (C=O for γ-lactam), 1660, 1650 cm^{-1}; UV max (95% EtOH) 239 nm (log ε 4.04), 265 (4.10), 293 (3.92), and 356 (3.89); *m/e* (M^+) 355; NMR δ 6.86 (s, β H in α,β-unsaturated ketone), 6.65 (s, 1, ArH), 6.41 (s, 1, ArH), 5.95 (s, α H in α,β-unsaturated ketone), 3.92 (m, 1, ArC**H**N), 3.84 (s, 6, OCH_3), 3.67 (s, 3, vinyl OCH_3), 2.91 (s, 3, NCH_3), 2.81 (s, 2, ArCH_2CO), 2.78–2.43 (m, 2, ArCH_2).

Anal. Calcd for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.72; H, 6.15; N, 4.17.

B. By Vanadium Oxyfluoride Oxidation of 3. A solution of the lactam **3** (3.6 g) in DCM (100 ml) was cooled to 0 °C and treated with a suspension of VOF_3 (5.5 g) in TFA (30 ml). The red-purple solution was stirred for 4 h and then poured into water (400 ml) containing citric acid (12 g). The organic layer was separated and washed with water, dried (Na_2CO_3), and evaporated. The residue (3.6 g was dissolved in MeOH (40 ml)–$CHCl_3$ (15 ml), an the first crop of crystals, 1.4 g, mp 253–255 °C, was identical with the dienone **6** from anodic oxidation of the lactam **3** by infrared spectral comparison.

2,3,7,8-Tetramethoxy-13-oxo-10,5-(epoxymethano)dibenzo[*a,d*]cycloheptadiene (10). A solution of MeCN (230 ml) containing tetrabutylammonium hydrogen sulfate (10 g) was divided between the compartments of the electrolytic cell. The lactone (**2**, 1.79 g) was dissolved in the anolyte. Electrolysis at 1.3 V (vs. Ag reference electrode) for 4 h gave a red-brown solution. The anode solution was evaporated, and the residual brown oil was washed with water to afford an orange solid that was recrystallized from MeOH as colorless crystals: 0.4 g; mp 242–243 °C; IR spectrum (Nujol) 1740 cm^{-1}; UV max (95% EtOH) 285 nm inflection (log ε 3.89), 288 (3.90), 290 (3.89); NMR δ 6.77 (s, 1, ArH), 6.71 (s, 2, ArH), 6.48 (s, 1, ArH), 5.53 (dd, 1, *J* = 7.0, 1.6 Hz, Ar**C**HO–), 4.41 (s, 1, $Ar_2CHC{=}O$), 3.82 and 372 (2 s, 12, OCH_3), 3.62 (dd, 1, *J* = 24, 4.6 Hz), and 3.21 (dd, 1, *J* = 20, 3 Hz); mass spectrum *m/e* (M^+) 356.

Anal. Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66; O, 26.94. Found: C, 67.64; H, 5.92; O, 26.99.

Acknowledgments. This work was supported in part by Grant RR-08062 from the General Research Support Branch, Division of Research Resources, National Institutes of Health, and by a grant from the Nashville Universities Center for International Study. The author gratefully acknowledges the assistance by Dr. Stanley L. Evans for mass spectra and NMR data.

Registry No.—1, 26954-85-8; 2, 61140-40-7; 3, 61140-41-8; 5, 61140-42-9; 6, 61140-43-0; 10, 61140-44-1.

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Baeyer–Villiger-Type Oxidation of an Isoindolo[1,2-*b*][3]benzazepine Derivative

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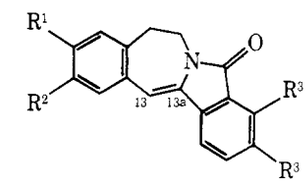
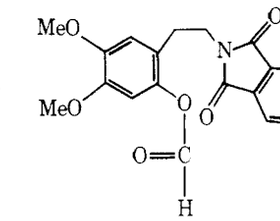
During the course of our work with isoindolo[1,2-*b*][3]-benzazepine derivatives **1a–c**, prepared by a new photo-



1a, $R^1 = R^2 = OMe$; $R^3 = H$
b, $R^1 + R^2 = OCH_2O$; $R^3 = OMe$
c, $R^1 = R^2 = R^3 = OMe$

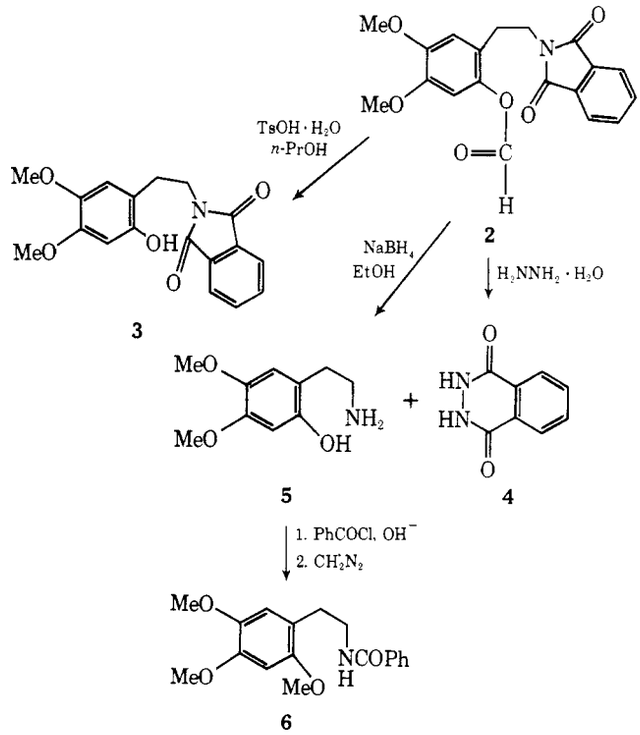


2

chemical method and correlated with rearrangement products of protoberberine and papaverrubine alkaloids,[3] we investigated routes to C-13–C-13a functionalized derivatives of **1a**. We report on the *m*-chloroperbenzoic acid (MCPBA) oxidation of **1a** to the phthalimide derivative **2**, a reaction which, in sum, is the result of oxidative double bond cleavage and Baeyer–Villiger reaction.

Attempts to prepare the epoxide of **1a** using 1 equiv of MCPBA[4] as well as basic,[5] acidic,[6] and neutral[7] conditions were unsuccessful (see Experimental Section). However, treatment of **1a** with 3 equiv of MCPBA resulted in the formation of **2** in 60% yield. The product showed the molecular formula $C_{19}H_{17}NO_6$ indicating incorporation of three oxygen atoms into compound **1a**. Its IR spectrum showed absorption at 1735 and at 1760 and 1710 cm^{-1} consistent with the presence of formyl ester and phthalimide functionality, respectively. The NMR spectrum exhibited a one-proton singlet at

Scheme I

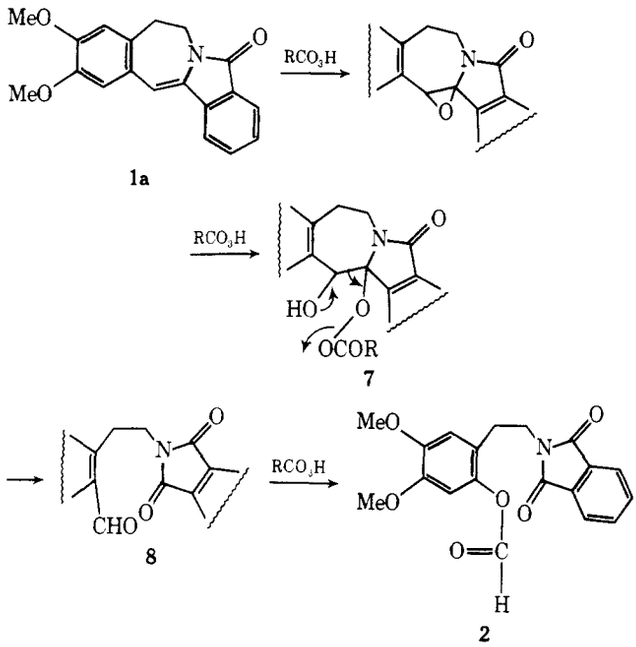


τ 1.59 confirming the presence of a formyl function. The remaining absorptions were fully compatible with the assigned structure (see Experimental Section). Finally, the mass spectrum of **2** showed, besides the correct parent ion at *m/e* 355, a base peak at *m/e* 327 ($M^+ - CO$) indicating facile decarbonylation as may be expected from phenyl formate derivatives.[8]

Structure **2** was confirmed by acid-catalyzed deformylation to **3** and by conversion with NH_2NH_2 to phthalhydrazide and the amino phenol **5**. Compound **5** was obtained in better yield by sodium borohydride reduction of **2**. The structure of **5**[9] is based on spectral evidence (see Experimental Section) and on its transformation into the known **6** by successive benzoylation and methylation.

A plausible mechanism for the MCPBA-promoted rearrangement of **1a** into **2** (Scheme II) incorporates, as the salient

Scheme II



features, the fragmentation (**7** → **8**) and Baeyer–Villiger[10] steps **8** → **2**. Baeyer–Villiger oxidation products have previously been encountered in attempted epoxidations of α,β-unsaturated ketones,[5] α-amino-α,β-unsaturated ketones,[10] enol ethers,[12] and enamides.[13] The proposed mechanism for the oxidative rearrangement of **1a** by MCPBA has analogy in the work of Bagli and Immer.[12] A related rearrangement has been observed in the case of iminium salts.[14]

Experimental Section[15]

Reaction of 7,8-Dihydro-10,11-dimethoxy-5*H*-isoindolo[1,2-*b*][3]benzazepin-5-one (1a) with MCPBA. To a stirred solution of 50 mg (0.16 mmol) of compound **1a** in 20 ml of dry methylene chloride was added 90 mg (0.52 mmol) of 98% *m*-chloroperbenzoic acid and the solution was stirred at room temperature under nitrogen for 6.5 h after which time TLC (silica gel, ethyl acetate–methylene chloride, 1:1) showed the absence of the highly fluorescent spot due to starting material and the potassium iodide–starch test showed the absence of MCPBA. The solution was washed successively with 5% aqueous sodium bicarbonate, dried (Na_2SO_4), and evaporated to dryness. The resulting pale yellow oil solidified upon standing. Recrystallization from 2-propanol gave 35 mg (60%) of **2**: mp 163–164.5 °C; IR 1760, 1735 (OCHO), 1710 cm^{-1}; UV 298 nm (ϵ 2600), 285 (5200), 235 (sh, 15 200); NMR ($CDCl_3$) τ 1.59 (s, 1, OCHO), 2.1–2.3 (m, 4, ArH), 3.20 (s, 1, H-3), 3.35 (s, 1, H-6), 6.06 (t, 2, J = 7 Hz, CH_2N), 6.16 and 6.20 (2 s, 6, 2 OCH_3), 7.13 (t, 2, J = 7 Hz, CH_2CH_2N); mass spectrum *m/e* (rel intensity) 355 (M^+, 8), 327 (100), 180 (67), 167 (96), 160 (30), 149 (30).

Anal. Calcd for $C_{19}H_{17}NO_6$: C, 64.22; H, 4.82; N, 3.93. Found: C, 64.29; H, 4.74; N, 3.87.

When the above reaction was carried out with 1 equiv of MCPBA for 14 days, TLC (EtOH–PhH, 5:95) showed only starting material (major, R_f 0.49), trace amounts of two other components (R_f 0.31 and 0.22), and the absence of compound **2**. The minor components were in insufficient amounts for characterization.

When the above reaction was carried out at room temperature using hydrogen peroxide under basic,[5] acidic,[6] and neutral[7] conditions only starting material (>80%) was recovered. Under acidic conditions[6] at 100 °C for 30 min, there was obtained compound **2** (60%) which was shown to be identical by UV and NMR spectral comparison with a sample obtained above.

***N*-[β-(2-Hydroxy-4,5-dimethoxyphenethyl)]phthalimide (3).** A solution of 35 mg (0.10 mmol) of compound **2** in 5 ml of 1-propanol containing a catalytic amount of *p*-toluenesulfonic acid hydrate was refluxed for 5 h and evaporated to dryness. The residue was taken up in chloroform and the solution was extracted with $NaHCO_3$ solution. The organic layer was evaporated to dryness to give 25 mg (78%) of compound **3**. Recrystallization from ethyl acetate gave an analytical sample: mp 214–215 °C; IR 1760, 1705 cm^{-1}; NMR (acetone-d_6) τ 1.97 (br s, 4, ArH), 2.04 (s, 1, exchangeable with D_2O, OH), 3.13 (s, 1, H-6), 3.33 (s, 1, H-3), 5.93 (t, 2, J = 7 Hz, CH_2N), 6.15 and 6.27 (2 s, 6, 2 OCH_3), 6.93 (t, 2, J = 7 Hz, CH_2CH_2N); mass spectrum *m/e* (rel intensity) 327 (M^+, 39), 180 (26), 167 (100), 160 (29), 149 (29).

Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.67; H, 5.41; N, 4.00.

The acetate of **3** was prepared under standard conditions using acetic anhydride in pyridine. Recrystallization from ethyl acetate gave an analytical sample: mp 188.5 °C; IR 1755 (ester and imide CO), 1720 cm^{-1} (imide CO); NMR($CDCl_3$) τ 2.1–2.3 (m, 4, ArH), 3.18 (s, 1, H-3), 3.39 (s, 1, H-6), 6.15 (t, 2, J = 7 Hz, CH_2N), 6.15 and 6.18 (2 s, 6, 2 OCH_3), 7.20 (t, 2, CH_2CH_2N), 7.82 (s, 3, $OCOCH_3$); mass spectrum *m/e* (rel intensity) 369 (M^+, 10), 327 (70), 180 (34), 167 (100).

Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 65.04; H, 5.14; N, 3.74.

Reaction of Compound 2 with Hydrazine Hydrate. A solution of 50 mg (0.14 mmol) of **2** and 25 mg of hydrazine hydrate (85%) in 2 ml of 95% ethanol was refluxed for 2 h according to an established literature procedure.[16] Normal workup gave 6 mg (27%) of **phthalhydrazide (4)**, identical by melting point and mixture melting point with an authentic sample[17] and 7 mg (26%) of **2-(2-aminoethyl)-4,5-dimethoxyphenol (5)** which was shown to be identical by TLC and NMR with the $NaBH_4$ reduction product of **2** described below.

Sodium Borohydride Reduction of Compound 2. A solution of 50 mg (0.14 mmol) of **2** and 100 mg of sodium borohydride in 10 ml of dry ethanol was refluxed for 7.5 h and evaporated to dryness. The residue was partitioned in methylene chloride–water and the organic layer was separated, dried (Na_2SO_4), and evaporated to give 21 mg (76%) of **2-(2-aminoethyl)-4,5-dimethoxyphenol (5)**: mp 123–126 °C; NMR ($CDCl_3$) τ 3.45 (br s, 2, ArH), 4.96 (br s, 3, exchangeable with D_2O, OH and NH_2), 6.20 and 6.24 (2 s, 6, 2 OCH_3), 6.95 (t, 2, J = 5.5 Hz, CH_2N), 7.34 (t, 2, J = 5.5 Hz, CH_2CH_2N); mass spectrum *m/e* (rel intensity) 197 (M^+, 80), 180 (65), 168 (97), 167 (100), 163 (25), 153 (59). Compound **5** was further characterized as described below.

***N*-Benzoyl-β (2,4,5-trimethoxyphenethyl)amine (6).** Compound **5** (21 mg, 0.11 mmol) was benzoylated according to Senoh and Witkop[18] to give 21 mg (65%) of ***N*-benzoyl-β-(4,5-dimethoxy-2-hydroxyphenethylamine,** NMR ($CDCl_3$) τ 1.7–1.9 (m, 2, ArH), 2.1–2.6 (m, 4, ArH and OH, exchangeable with D_2O), 2.7–2.95 (br s, 1, exchangeable with D_2O, NH), 3.35 and 3.40 (2 s, 2, H-3 and H-6), 6.20 (s, 6, 2 OCH_3), 6.28 (t, 2, J = 7 Hz, CH_2N), 7.08 (t, 2, J = 7 Hz, CH_2CH_2N), which, without purification, was subjected to reaction with an excess of diazomethane in ether–methanol. Normal workup followed by PLC on silica gel (benzene–methanol–acetone, 8:1:1) gave a sample of **6** which was recrystallized from aqueous methanol: mp 106–107 °C (lit.[18] 106 °C); IR 3350 (NH), 1655 cm^{-1}; (CO); NMR ($CDCl_3$) τ 1.7–1.9 (m, 2, ArH), 2.1–2.6 (m, 3, ArH), 2.7–2.95 (br s, 1, exchangeable with D_2O, NH), 3.40 and 3.43 (2 s, 2, H-3 and H-6), 6.16, 6.19, and 6.22 (3 s, 9, 3 OCH_3), 6.33 (t, 2, J = 7 Hz, CH_2N), 7.12 (t, 2, J = 7 Hz, CH_2CH_2N).

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Registry No.—**1a**, 35611-54-2; **2**, 61177-89-7; **3**, 61177-90-0; **3** acetate, 61177-91-1; **4**, 1445-69-8; **5**, 61177-92-2; **6**, 61177-93-3; *N*-benzoyl-β-(4,5-dimethoxy-2-hydroxy)phenethylamine, 61177-94-4.

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Nitrogen-15 Nuclear Magnetic Resonance. Structure of Sulfaguanidine[1]

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Sulfaguanidine (**1**)[2] is unusual compared to the many derivatives of sulfanilamide (4-aminobenzenesulfonamide) that contain the grouping $-SO_2HN-$ in being insoluble in aqueous alkali. Its 4-amino group is comparably basic to the other sulfanilamides (pK_B = 11.25) but its guanidino group is only very weakly basic (pK_B = 13.52).[3] The nonacidic character of the compound caused Schwenker[4] to investigate its infrared and ^1H NMR spectra and, by comparison of the infrared spectra in KBr pellets with those of several model compounds, it appeared that **1** had no infrared absorption which could be ascribed to the N–H bond of an $-SO_2NH-$ group. The ^1H NMR spectrum in dimethyl sulfoxide solution was less decisive because of serious overlap of the downfield N–H resonances with the resonances of the aromatic ring, but nonetheless, there appeared to be no evidence for the three different kinds of $-SO_2NHC(=NH)NH_2$ proton resonances predicted for the conventional guanidine structure. It was concluded therefore that the correct structure for sulfaguanidine is not **1a**, but instead the tautomer **1b**. Schwenker's work seems to have been largely, if not totally, ignored, and as recently as 1975, a ^{13}C investigation[5] formulates sulfaguanidine as **1a** in accord with the standard reference works.[6]

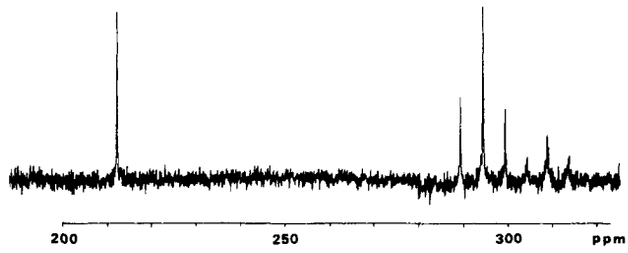
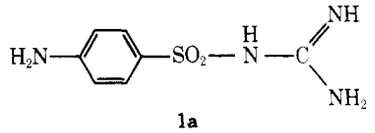
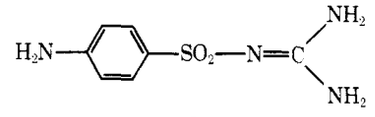


Figure 1. Natural-abundance ^{15}N NMR spectrum of sulfaguanidine in dimethyl sulfoxide with no proton decoupling. The chemical shifts are in parts per million upfield of $D^{15}NO_3/D_2O$.



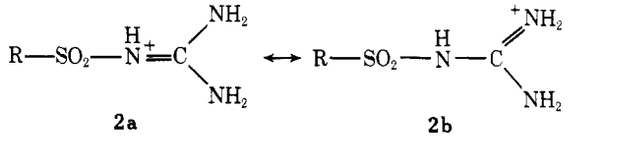
1a



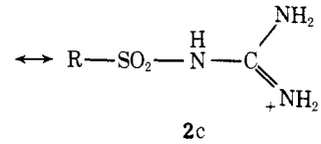
1b

Because the structure of **1** may not be the same in solution as it is in the solid, we have taken the natural-abundance ^{15}N spectrum with a Bruker WH-180 spectrometer at 18.23 MHz (8 g of **1** in 18 ml of dimethyl sulfoxide) *without* proton decoupling, using a 65° flip angle, a repetition rate of 20 s, and an accumulation time of 12 h. The upfield portion (Figure 1) of the resulting spectrum showed two triplet resonances, one over twice the intensity of the other, consistent with a structure having three $-NH_2$ groups. The lower intensity triplet (309.3 ppm upfield of $D^{15}NO_3$) arises from the 4-amino group and the larger intensity triplet (295.0 ppm) from the $=C(NH_2)_2$ amino groups of **1b**. The N–H coupling constants for the two triplets were 85 and 91 Hz, respectively. A downfield singlet resonance at 212.3 ppm upfield of $D^{15}NO_3$ corresponded to the $-SO_2N=C<$ nitrogen.

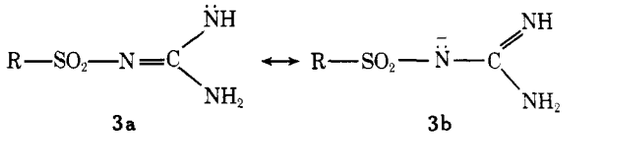
Why does structure **1b** correspond to a substance with a weakly basic and weakly acidic guanidine group? One can write the usual resonance forms for both the conjugate acid, **2**, and the conjugate base, **3**, of **1b**. To be sure, **2a** will be rendered less favorable by the close proximity of the RSO_2^- group to the positively charged nitrogen, but **2b** and **2c** should be



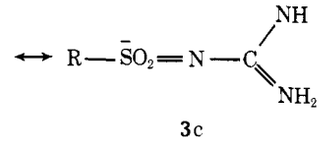
2a **2b**



2c



3a **3b**



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