7.3–8.3 (10 H, m, Ar H and vinylic H).

Anal. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01. Found: C, 72.22; H, 5.48; N, 3.99.

(*Z*)-2-(*o*-Carboxyphenyl)-4-benzylidene-5-oxazolone (6a). A solution of **5a** (5.34 g, 0.015 mol) in 100 mL of CF_3CO_2H/CH_2Cl_2 solution (1:3) was stirred for 2 h at room temperature. The solvent was removed in vacuo and the residue was triturated with ethyl acetate (100 mL) to give 4.2 g (94%) of **6a**: mp 194–195 °C; IR (KBr) 1795, 1775, 1695, 1650 cm^{-1}; NMR (Me_2SO-d_6) δ 7.4 (5 H, m, Ar H), 7.9 (4 H, s, Ar H), 8.1 (1 H, s, vinylic H).

Anal. Calcd for $C_{17}H_{11}NO_4$: C, 69.62; H, 3.78; N, 4.77. Found: C, 69.50; H, 3.84; N, 4.73.

(*Z*)-1-Phenyl-5-[*o*-(methoxycarbonyl)phenyl]-6-oxo-4-azaspiro[2.4]hept-4-en-7-one (7). To a stirred suspension of **6a** (5 g, 0.0172 mol) in methylene chloride (40 mL) was added dropwise a solution of diazomethane in 250 mL of ether, prepared from 32.3 g (0.15 mol) of Diazald. After the reaction mixture was stirred at room temperature for 24 h, the excess of diazomethane was removed under a stream of dry nitrogen and the solvent was evaporated under reduced pressure to give a yellow oil. The residue was dissolved in 20 mL of ether and 2 g (33%) of spiro compound **7** deposited on cooling: mp 93–96 °C; IR (KBr) 1810, 1725, 1630 cm^{-1}; NMR ($CDCl_3$) δ 2.2–2.6 (2 H, m, CH_2), 3.2–3.4 (1 H, m, CH), 3.6 (3 H, s, $COOCH_3$), 7.2–7.9 (9 H, m, Ar H).

Benzyl (*Z*)-1-Phthalimido-2-phenylcyclopropanecarboxylate (9). A mixture of spirooxazolone **7** (1 g, 0.003 mol), DMAP (380 mg, 0.003 mol), and 5 mL of benzyl alcohol was stirred at room temperature of $2^1/_2$ h. The reaction mixture was dissolved in ethyl acetate (25 mL) and the solution was washed with 10% citric acid, water, and saturated sodium chloride and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The residue was crystallized from ether/petroleum ether to yield 838 mg of **9** (68%): mp 143–144 °C; IR (KBr) 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.2–2.6 (2 H, m, CH_2), 3.4–3.6 (1 H, m, CH), 5.3 (2 H, s, $OCH_2C_6H_5$), 7.2 (5 H, s, Ar H), 7.4 (5 H, s, Ar H), 7.8 (4 H, s, Ar H).

Anal. Calcd for $C_{25}H_{19}NO_4$: C, 75.55; H, 4.82; N, 3.52. Found: C, 75.41; H, 4.89; N, 3.48.

Benzyl (*Z*)-1-Amino-2-phenylcyclopropanecarboxylate Hydrochloride (10). A mixture of **9** (795 mg, 2 mmol), hydrazine hydrate (0.2 g, 4 mmol), and methanol (5 mL) was stirred at room temperature for 30 min. The solvent was removed under reduced pressure and the residue was dissolved in 10 mL of 1 N HCl, heated 15 min on a steam bath, and filtered and the filtrate was evaporated to dryness. The residue was crystallized from isopropyl alcohol/ether to yield 379 mg (63%) of **10**, mp 161–63 °C dec, identical with that of the known compound.[3]

(*Z*)-2-(*o*-Carboxyphenyl)-4-(3,4-diacetoxybenzylidene)-5-oxazolone (6b). A mixture of 3,4-diacetoxybenzaldehyde (7.55 g, 0.034 mol), *o*-(*tert*-butoxycarbonyl)hippuric acid (4; 6.3 g, 0.03 mol), NaOAc (5.1 g, 0.068 mol), and Ac_2O (50 mL) was stirred for 2 days at room temperature. Excess acetic anhydride was removed in vacuo and the resulting residual syrup was extracted with AcOEt (3 × 50 mL). The extract was washed with water, 10% Na_2CO_3 solution, and saturated NaCl solution and then dried over anhydrous Na_2SO_4. The solvent was removed in vacuo to give a yellow oil, which was dissolved in CH_2Cl_2 (110 mL), and CF_3COOH (36 mL) was added to the solution. After the solution was stirred overnight at room temperature, the solvents were evaporated in vacuo, and the residue was chromatographed (50 g silica gel, 60–200 mesh, J. T. Baker Chemical Co.) with $CHCl_3$/AcOEt (5:1) to give a pale yellow solid, **6b** (2.0 g). Recrystallization from MeOH/AcOEt (1:1) gave 1.6 g (17.2%) of **6b** as light yellow prisms: mp 214–215 °C; IR (KBr) 1750, 1680, 1630, 1600 cm^{-1}; NMR (Me_2SO-d_6) δ 7.2–8.5 (m, 8 H, Ar H, CH=), 2.22 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3).

Anal. Calcd for $C_{21}H_{15}NO_8$: C, 61.61; H, 3.70; N, 3.42. Found: C, 61.56; H, 3.99; N, 3.28.

1-(3,4-Diacetoxyphenyl)-7-[*o*-(methoxycarbonyl)-phenyl]-8-oxa-3,4,6-triazaspiro[4.4]nona-3,6-dien-9-one (11). To a suspension of **6b** (1.3 g, 3.18 mmol) in CH_2Cl_2 (10 mL) was added dropwise an ethereal diazomethane solution prepared from Diazald (5.25 g, 245 mol) with ice cooling over a period of 45 min. After stirring was continued for 24 h at room temperature, the solvent was evaporated in vacuo and the resulting syrup was column chromatographed (silica gel 20 g, 60–200 mesh Baker Analyzed Reagent), using $CHCl_3$. The syrup obtained was triturated with Et_2O/*n*-hexane and the resulting solid was collected by suction to give **11** (1.4 g, 94.6%). Recrystallization from AcOEt/*n*-hexane gave colorless prisms: 1.2 g (81.1%); mp 82–83 °C; NMR ($CDCl_3$) δ 7.75 (s, 4 H, Ar H), 6.8–7.0 (m, 3 H, Ar H), 5.2–5.45 (m, 2 H, CH_2N), 4.4–4.6 (m, 1 H, CH), 3.95 (s, 3 H, OCH_3), 2.2 (s, 6 H, $2CH_3CO_2$).

2-[*o*-(Methoxycarbonyl)phenyl]-4-[1-(3,4-diacetoxyphenyl)ethylidene]-5-oxazolone (12). A mixture of **11** (1.2 g, 2.6 mmol) and toluene (20 mL) was stirred at 95–100 °C (bath temperature) for 1.5 h. The solvent was evaporated in vacuo and the residual syrup was triturated with *n*-hexane (20 mL). The crystals were filtered by suction to give **12** (1.1 g, 97.3%), which was recrystallized from AcOEt/*n*-hexane to give colorless prisms: mp 136–138 °C; NMR ($CDCl_3$) δ 7.65–7.9 (m, 4 H, Ar H), 7.00–7.25 (m, 3 H, Ar H), 3.77 (s, 3 H, OMe), 2.70 (s, 3 H, CH_3), 2.20 (s, 6 H, $2CH_3CO_2$).

Anal. Calcd for $C_{23}H_{19}NO_8$: C, 63.16; H, 4.38; N, 3.20. Found: C, 62.98; H, 4.40; N, 3.16.

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Registry No. *cis*-**2**, 87483-06-5; *trans*-**2**, 87483-05-4; **4**, 87483-07-6; **5a**, 87483-08-7; **6a**, 87483-09-8; **6b**, 87483-10-1; **7**, 87483-11-2; **9**, 87483-12-3; **10**, 87483-13-4; **11**, 87483-14-5; **12**, 87483-15-6; *tert*-butyl hydrogen phthalate, 33693-84-4; glycine, 56-40-6; benzaldehyde, 100-52-7; 3,4-diacetoxybenzaldehyde, 67727-64-4; diazomethane, 334-88-3.

Nitration of Estrone into 2-Nitroestrone by Clay-Supported Ferric Nitrate[1]

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The large spectrum of potential biological activities[2-6] of estrone derivatives functionalized in ring A explains the major preparative interest in 2- and 4-nitroestrone as starting materials. The classic procedure, via concentrated nitric acid dissolved in glacial acetic acid,[7,8] suffers from a lack of discrimination, hence the importance of developing a regiospecific mononitration. The recent report by Santaniello et al.[9] of their new procedure, using either silver nitrate or *N*-nitropyrazole as nitrating agents in association with boron trifluoride etherate, prompts us to disclose our results with inexpensive reagents (clay-supported ferric nitrate, "clayfen",[10] a reagent which we have introduced for oxidation of alcohols[10] and used also for oxidative coupling of thiols[1]) under very mild and straightforward conditions (room temperature, toluene suspension, ease of setup and of workup). We obtained the best isolated yields (>55%) reported so far in the nitration of estrone (**1**) in the 2-position. The remainder of the reaction mixture is adsorbed into the clay, and we are hoping to

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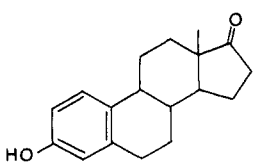
find a means to improve its recovery. Our procedure using "clayfen" has been applied to nitration of phenols in general with excellent results,[11] comparable to those of Kagan et al.[12] but requiring only ferric nitrate[11] as compared to the much more expensive lanthanum nitrate.[12]

Experimental Section

"Clayfen" was prepared as previously described[13] from a mixture of 45 g of iron(III) nitrate nonahydrate, 60 g of K-10 bentonite clay (Süd-Chemie, Munich), and 750 mL of acetone. Freshly prepared "clayfen" (2 g) was added to a mixture of 1 (2 mmol)



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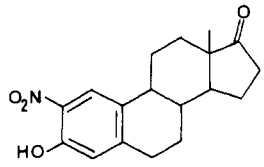

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and toluene (150 mL). The resulting suspension was stirred overnight at room temperature and filtered under vacuum. The crude yellow filtrate was then purified by column chromatography on silica gel (70–230 mesh) by using an 80:20 (v/v) mixture of *n*-hexane and ethyl acetate as the liquid phase. 2-Nitroestrone (**2**) was the sole eluted product, obtained as pure crystals by mere solvent evaporation: 0.347 g (55% isolated yield); mp 178–180 °C (lit. mp 176–178 °C,[9] 183.5–184 °C[8]). ^{1}H NMR ($CDCl_3$) δ 7.96 (s, 1 H_1), 6.82 (s, 1 H_4), 0.93 (s, 3 H_{18}); IR (KBr) 3300 (br, OH), 1738, 1525, 1310 cm^{-1} (lit.[14] 3315, 1736, 1525, 1310 cm^{-1}); MS, *m/e* 315 (M^+), 297, 279, 271. Anal. Calcd (^{12}C = 12.00): C, 68.57; H, 6.71; N, 4.44. Found: C, 69.00; H, 6.80; N, 4.33.

Results

A likely mechanish involves NO_2^+ formation from ferric nitrate on the clay. We are now examining whether the observed regiospecificity is dictated by the steroid or by the clay structure.

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Registry No. 1, 53-16-7; 2, 5976-73-8; ferric nitrate, 10421-48-4.

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Periodination of Benzene with Periodate/Iodide[1]

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Periodination of benzene was recently described in this journal by Levitt and Iglesias,[2] who added C_6H_6 to a chilled solution of H_5IO_6 in concentrated H_2SO_4 and reported a 48% yield of C_6I_6 upon crystallization of the resulting yellow-tan precipitate. I thought that this reaction might be of use in functionalizing some biaryls. The above procedure was unsuccessful in my hands, however: the reaction appeared to proceed according to the description but upon workup gave highly impure material in yields of only a few percent. I report here a modified procedure for this reaction that gives hexaiodobenzene in acceptable yield under vigorous conditions but gives *tetra*iodobenzene at room temperature.

Levitt and Iglesias propose the following stoichiometry for their reaction:

$$2C_6H_6 + 3\ IO_4^- + 9\ I^- + 12H_3O^+ \rightarrow 2C_6I_6 + 24H_2O \quad (1)$$

They suggest that the iodide is generated from periodate during oxidation of benzene to carbon dioxide. If this is true, much of the starting arene must be expended in creating iodide. The overall reaction equation would then be

$$11C_6H_6 + 30IO_4^- + 30H_3O^+ \rightarrow 5C_6I_6 + 36CO_2 + 78H_2O \quad (2)$$

For this reaction, only 45% of the starting C_6H_6 can be converted to C_6I_6.

The aromatic substrate might be conserved if iodide were added directly to the reaction mixture, instead of being generated in situ. Therefore, potassium iodide was added to a solution of periodic acid in concentrated sulfuric acid (making a deep brown solution suggestive of the formation of molecular iodine[3]), followed by addition of benzene, according to the stoichiometry of eq 1. Crystallization of the resulting precipitate gave a product whose melting point (249–252 °C) corresponded to Levitt and Iglesias's melting point of "~260 °C". However, this cannot be hexaiodobenzene. Although the melting point for C_6I_6 was once thought to be 248 °C,[4] it has, like the melting points of many of the polyiodoarenes, undergone repeated revision. A recent preparation of C_6I_6[5] resulted in orange crystals with a melting point of ">360 °C". The melting point obtained here suggested rather the literature value (253 °C) of another likely product: 1,2,4,5-tetraiodobenzene.[6] NMR spectra confirmed that $C_6I_4H_2$ was, in fact, the compound in hand: ^{1}H NMR showed a single aromatic signal; ^{13}C NMR showed two carbon signals, one coupled to H. (The preparation of $C_6I_4H_2$ was subsequently made more efficient by reducing the quantities of periodate and iodide to stoichiometric amounts.)

Only trace amounts of C_6I_6 were obtained at the reaction temperatures used by Levitt and Iglesias. C_6I_6 was finally prepared by heating the reaction mixture at 100 °C with a twofold excess of periodate/iodide. The orange product was crystallized in 45% yield, mp 430 °C (dec with loss of I_2 starting about 370 °C); NMR and mass spectra were consistent with C_6I_6. While the modified periodination procedure described here is not so elegant as the original report, it is still quite simple to perform and avoids the need for the fuming sulfuric acid used in more conventional iodinations.[7,8]

(1) Dedicated to Dr. Kurt D. Kaufman of Kalamazoo College on the occasion of his designation as Emeritus Professor of Chemistry.

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