recorded by means of the $\Theta - 2\Theta$ scanning procedure as described previously.[38] From totals of 1650 and 5297 independent measurements for 18 and **20b**, respectively, 1523 reflections for the former were judged to be observed ($I > 2.0\sigma(I)$) whereas only 1603 satisfied this criterion for the latter. The observed data were retained for use in the structure analyses and were corrected for the usual Lorentz and polarization effects but not for absorption. Refined unit cell parameters were derived by least-squares treatment of the diffractometer setting angles for 40 high order reflections from each sample.

Structure Analysis. The crystal structures of 18 and **20b** were solved by use of direct methods and subsequent Fourier syntheses. With regard to 18 the analysis proceeded quite smoothly. The largest $250|E|$ values were input to the MULTAN76[39] suite of programs, and an E map, computed by use of that set of phase angles which yielded the highest combined figure of merit, gave approximate positions for all non-hydrogen atoms. Subsequent full-matrix least-squares adjustment of atomic positional and thermal parameters, with hydrogen atoms included in the later cycles at their calculated positions, converged to $R = 0.043$.

Solution of the crystal structure of the poorly diffracting hydrochloride (**20b**) progressed in a less straightforward manner due to partial site occupation by one of the chloride ions in the asymmetric crystal unit as well as some of the water molecules of crystallization. In this case, an E map, evaluated by use of phase angles which gave rise to the highest combined figure of merit for the 398 highest $|E|$ values, contained one large peak corresponding to a chloride ion, two other peaks of approximately equal magnitude indicating fractional site occupation by a chloride ion and water molecule, and a number of smaller peaks from which it was possible to derive a structure model containing 42 of the 44 non-hydrogen atoms comprising the two cations in the asymmetric crystal unit. An F_0 Fourier synthesis phased by this partial structure ($R = 0.33$) gave positions for the remaining 2 atoms. Several rounds of least-squares adjustment of atomic positional and isotropic thermal parameters decreased R to 0.168. Subsequent F_0 and difference Fourier syntheses revealed four additional significant maxima three of which were ascribed to relatively well ordered water molecules. The fourth peak, somewhat broader and much smaller in magnitude, lay with its maximum on a crystallographic 2-fold axis and was interpreted as representing a further very disordered water molecule. With cation hydrogen atoms included at their calculated positions, continuation of the least-squares iterations, during which the chlorine and ordered water oxygen atoms were allowed to assume anisotropic thermal parameters, led to convergence at $R = 0.084$.

Final atomic positional and thermal parameters for 18 and **20b** are in Tables I–III and Tables V and VI.[34]

Atomic scattering factors for chlorine, carbon, nitrogen, and oxygen were taken from ref 40, and for hydrogen from ref 41, with that for chlorine corrected for anomalous dispersion effects[42]; for the disordered chlorine/oxygen situations, a modified scattering factor $(2f_{\mathrm{Cl}} + f_0)/3$ was employed. In the least-squares iterations, $\sum w\Delta^2$ ($\Delta = ||F_0| - |Fc||$) was minimized with weights, w, assigned according to the scheme: $(w)^{1/2} = 1$ for $|F_0| \leq K$, $(w)^{1/2} = K/|F_0|$ for $|F_0| > K$ ($K = 7.0$ for (**18**), $K = 100.0$ for **20b**), which revealed no systematic dependence of $\langle w\Delta^2\rangle$ values when analyzed in ranges of $|F_0|$ and sin Θ.

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Registry No. (±)-**4**, 91817-15-1; (±)-**4**·HCl, 92007-79-9; **5**, 931-64-6; (±)-**6**, 91877-78-0; **7**, 2716-23-6; (±)-**8**, 91817-16-2; (±)-**9**, 91817-17-3; **10**, 80641-35-6; **11**, 91817-18-4; (±)-**12**, 91817-19-5; (±)-**13**, 91817-20-8; **14**, 91817-21-9; **15**, 91817-22-0; **16**, 91817-23-1; (±)-**17**, 91817-24-2; (±)-**18**, 91817-25-3; (±)-**19**, 91817-26-4; (±)-**20**, 91877-79-1; (±)-**20**·HCl, 91926-14-6; (±)-**21**, 91817-27-5; (±)-**21**·HCl, 91817-14-0; (±)-**22**, 91817-28-6; (±)-**22**·HCl, 91817-29-7; *p*-methoxyphenylacetic acid, 104-01-8; *p*-methoxyphenylacetyl chloride, 4693-91-8.

Supplementary Material Available: Tables of atomic postional and thermal parameters (Tables I–III, V, VI) and interatomic distance and angles (Tables IV and VII) for 18 and **20b** (19 pages). Ordering information is given on any current masthead page.

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Tricarbonylcyclohexadienyliron Complexes as Aryl Cation Equivalents: A Formal Synthesis of (±)-*O*-Methyljoubertiamine[1]

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The use of tricarbonyl(4-methoxycyclohexadienyl)iron hexafluorophosphate **1b** as a synthetic equivalent of the *p*-anisyl cation for a formal synthesis of (±)-*O*-methyljoubertiamine is described.

There is already appreciable documentation in the literature[3] showing that cyclohexadienyl–$Fe(CO)_3$ cationic complexes of type **1** may be used as aryl cation equivalents. Thus, **1** reacts with a range of carbon nucleophiles to give diene complexes type **2**, and these can be demetalated and oxidized to aromatic compounds in a number of ways. Of

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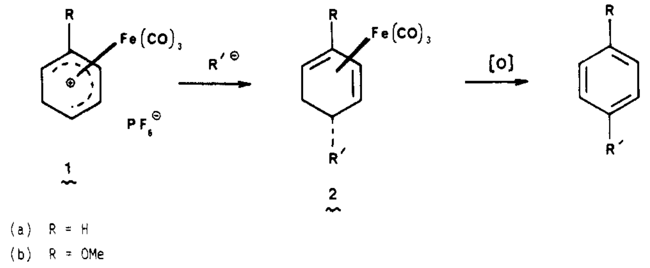


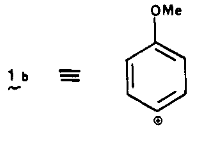
1

2

(a) R = H

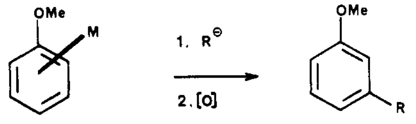
(b) R = OMe

particular interest is the methoxy-substituted complex **1b**, since conversion of this to para-substituted anisoles indicates that it may be used as a *p*-anisyl cation (**3**)



3

equivalent in synthesis of, e.g., natural products. This may be compared with the behavior of both chromium[4] and manganese[5] complexes of anisole (**4**) in which the methoxy



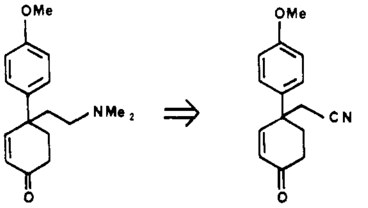
4

(a) M = Cr(CO)$_3$

(b) M = [Mn(CO)$_3$]$^+$

group directs incoming nucleophiles to the meta position leading, after oxidation, to meta-substituted anisoles. Thus, complex **1b** is complementary to complexes **4**, and indeed it can be regarded as the equivalent of anisole showing umpolung at the 4-position.

In order to illustrate the potential applicability of this novel concept to organic synthesis, we chose to examine a synthetic approach to a relatively simple Sceletium alkaloid derivative, *O*-methyljoubertiamine (**5**). These alkaloids, of which there are over thirty, are isolated from plants of the genus *Sceletium*,[6] the species *Sceletium expansum*, *Sceletium tortuosum*, and *Sceletium antomicum* being flora which are indigenous to South Africa. They are said to have pharmacological properties ranging from antihistamine to narcotic.[7] A number of syntheses of *O*-methyljoubertiamine[8] and related alkaloids[9] have appeared in the recent literature; of particular interest for our approach is the synthesis described by Sanchez and co-workers[8a] which proceeded via the anisyl-substituted cyclohexenone **6**, which we considered to be an accessible compound using the readily prepared[10] iron complex **1b**.

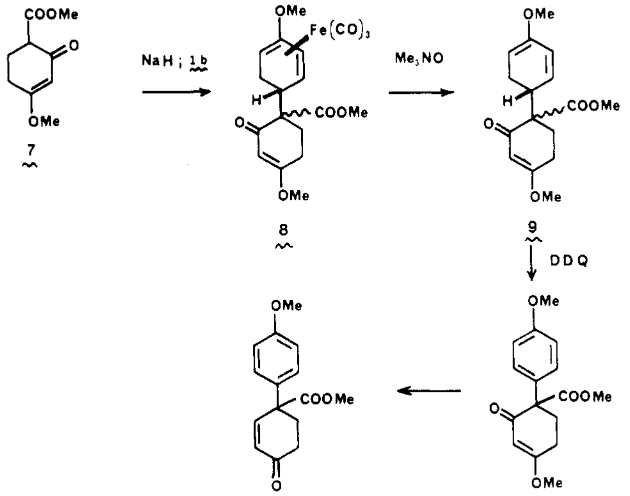


5

6

Results and Discussion

The most appropriate nucleophile, which was to become the cyclohexenone ring of *O*-methyljoubertiamine, was the keto ester **7**, readily prepared in two steps from cyclohexane-1,3-dione. Reaction of the sodium enolate of **7** with the dienyl complex **1b** proceeded without event to give complex **8** as an equimolar mixture of diastereomers in 92% yield, which were separated and individually purified for purposes of characterization but used as a mixture in the subsequent steps. Conversion of **8** to the de-



7

8

9

10

11a

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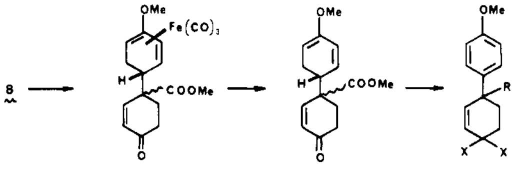
sired aromatic intermediate **10** proved to be more troublesome, the previously described methods for direct conversion[3] (e.g., treatment with Pd–C; direct treatment with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone)) either failing completely or else causing rupture of the carbon–carbon bond formed in the first step.

Since the extensive functionality present in complex **8** appeared to result in a sensitive molecule, we elected to proceed to **10** by a two-step sequence. Mild decomplexation of **8** with anhydrous trimethylamine *N*-oxide[11] gave the sensitive diastereomeric dienol ethers **9**. Aromatization of **9** was examined by using a variety of oxidizing agents, the best yields (46% from **8**) being obtained with DDQ in benzene. Use of high temperatures caused rearrangement and/or fragmentation of the molecule. Conversion of **10** to the desired intermediate **11a** was accomplished in 73% yield by using sodium borohydride reduction followed by acidic workup.

In view of the poor yield obtained during aromatization of **9** it was decided to reorganize the sequence of reactions leading to **11a**. Selective 1,2-reduction of the ketone group in complex **8** with diisobutylaluminum hydride (Dibal) in ether at −78 °C to room temperature, followed by mild acid treatment, afforded the complex **12** as an equimolar mixture of diastereomers. Decomplexation of this compound (Me$_3$NO) followed by treatment of the resulting dienol ether **13** with DDQ in boiling xylene proceeded without problems, to generate the key intermediate **11a** in 60% overall yield from complex **12**. This method was easily adapted to preparative scale.

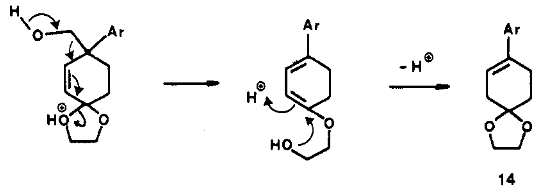


12 **13** **11**

(a) R = CO$_2$Me; X,X = C
(b) R = CO$_2$Me; X,X = OCH$_2$CH$_2$O
(c) R = CH$_2$OH; X,X = OCH$_2$CH$_2$O
(d) R = CH$_2$OTs; X,X = OCH$_2$CH$_2$C
(e) R = CH$_2$CN; X,X = OCH$_2$CH$_2$O

We now required to homologate the ester group of **11a** to give, ultimately, the Sanchez intermediate **8**. Accordingly, the ketone group was protected to give **11b**, and the ester was reduced with lithium aluminum hydride to give **11c**. This compound was extremely acid sensitive, undergoing (acid-catalyzed) fragmentation to give compound **14** even in reagent grade chloroform. Whilst this was vexing from the standpoint of handling the intermediate, it did establish that **11a** indeed had the structure shown, since it is correlated with **14** by vinylogous retroaldol-type of reaction (Scheme I). Immediate conversion of crude **11c** to the tosylate **11d** was therefore necessary, and was readily accomplished under standard conditions. Displacement of the tosylate with cyanide to give **11e** proved to be somewhat capricious, but after considerable experimentation conditions of temperature and reagent concentration (NaCN, HMPA) were found which gave reproducible yields (60%) on small scale (50 mg). Scaleup of this reaction proved difficult mainly owing to the anticipated competing side reaction involving ring expansion of **11d**. With a limited amount of nitrile **11e** in hand we elected to deprotect the enone, giving the Sanchez intermediate **6**, thereby accomplishing a formal synthesis of (±)-*O*-methyljoubertiamine.

Scheme I



14

This work, therefore, illustrates that efficient synthesis of complex para-substituted anisole derivatives is extremely simple using organoiron precursors and that this can be used as an approach to natural products synthesis.

Experimental Section

Melting points were determined on a Kofler block and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1420, mass spectra on A.E.I. MS12 or MS30, and ^{1}H NMR spectra on Varian EM360 (60 MHz), EM390 (90 MHz), XL-200 (200 MHz), or Bruker WH400 (400 MHz) instruments. All synthetic and chromatographic operations with iron complexes were conducted under an atmosphere of dry nitrogen. Solvents were freshly distilled under nitrogen as follows: tetrahydrofuran (THF) from sodium and benzophenone; diethyl ether from lithium aluminum hydride; hexamethylphosphoric triamide (HMPA), benzene, and xylene from calcium hydride.

3-Methoxy-2-cyclohexenone. Cyclohexane-1,3-dione (10.6 g), *p*-toluenesulfonic acid (0.46 g), methanol (36 mL), and trimethyl orthoformate (11 mL) were heated under reflux in benzene (180 mL) for 80 min. The cooled reaction mixture was washed with 10% aqueous NaOH saturated with NaCl (4 × 20 mL), dried (MgSO$_4$), and evaporated in vacuo to give 3-methoxy-2-cyclohexenone which was purified by distillation (9.1 g, 76%): bp 52–53 °C (0.7 mmHg); ν_{max} (CHCl$_3$) 1665, 1610 cm^{-1}; δ (CDCl$_3$, 90 MHz) 5.35 (1 H, s, vinyl H), 3.69 (3 H, s, OMe), 2.38 (4 H, m), 2.01 (2 H, m); MS, *m/e* (%) 126 (85), 112 (70), 98 (100), 68 (99). Anal. Found: C, 66.9; H, 7.85. Calcd for C$_7$H$_{10}$O$_2$: C, 66.6; H, 8.00.

Methyl 4-Methoxy-2-oxo-3-cyclohexenecarboxylate (7). To a stirred solution of diisopropylamine (40 mL) in THF (250 mL) at −78 °C, under N$_2$, was added dropwise *n*-butyllithium (15% in hexane, 180 mL) over 30 min. After stirring for 45 min, 3-methoxy-2-cyclohexenone (30 g) in THF (200 mL) was added dropwise over a period of 45 min. The mixture was brought to room temperature and transferred dropwise (via cannular) to a vigorously stirred suspension of sodium hydride (13 g) in dry dimethyl carbonate (250 mL). Stirring was continued for 16 h, the mixture cooled to 0 °C, and excess sodium hydride was destroyed by dropwise addition of methanol (30 mL) followed by water (500 mL). The pH of the mixture was adjusted to arround 7 by slow addition of acetic acid at 0 °C, and the product was extracted with ether in the usual way. The extracts were washed with water, aqueous NaHCO$_3$, and water, dried (MgSO$_4$), and evaporated to give crude product. Purification by flash chromatography (40% EtOAc, hexane) gave unreacted starting material (5.6 g) and the desired keto ester **7** (28 g, 64%): bp 155–158 °C (0.5 mmHg); ν_{max} (CHCl$_3$) 1720, 1655, and 1607 cm^{-1}; δ (CDCl$_3$, 90 MHz) 5.40 (1 H, s vinyl H), 3.75 (3 H, s, CO$_2$Me), 3.72 (3 H, s, OMe), 3.33 (1 H, m), 2.47 (2 H, m), 2.25 (2 H, m); MS, *m/e* (%) 184 (50), 153 (20), 125 (40), 98 (100); found M$^+$ 184.0737, calcd for C$_9$H$_{12}$O$_4$ M$^+$ 184.0736.

Tricarbonyl[methyl 1-((2–5-η)-4-methoxycyclohexa-2,4-dienyl)-4-oxo-3-cyclohexenecarboxylate]iron (8). To a stirred suspension of sodium hydride (90 mg) in dry THF (25 mL), under nitrogen, was added a solution of keto ester **7** (700 mg) in THF (5 mL). After the mixture had stirred for 20 min the reaction flask was opened briefly, with backflushing of nitrogen, while tricarbonyl(2-methoxycyclohexadienylium)iron hexafluorophosphate (**1b**) (1.5 g) was added in one portion, and the mixture was stirred for 15 min. Excess sodium hydride was destroyed by dropwise addition of methanol (1 mL), the mixture was poured into water (200 mL), and the product extracted with ether in the usual way to afford **8** (1.47 g, 92%) as an equimolar mixture of diastereomers. For characterization purposes these were separated

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[11] Shvo, Y.; Hazum, E. *J. Chem. Soc., Chem. Commun.* **1974**, 336.

by fractional crystallization, using ether/pentane/ethyl acetate (7:7:2). Diastereomer A: pale yellow plates, mp 155–156 °C; ν_{max} ($CHCl_3$) 2060, 1985, 1730, 1670, 1615, 1487 cm^{-1}; δ ($CDCl_3$, 90 MHz) 5.30 (1 H, s, vinyl ether), 5.15 (1 H, dd, *J* = 6, 2 Hz, 3-H), 3.70 (3 H, s, CO_2Me), 3.66 (3 H, s, OMe), 3.63 (3 H, s, OMe), 3.66 (1 H, m, 5-H), 3.3 (1 H, m, 2-H), 2.92 (1 H, dd, *J* = 16, 6 Hz, *endo*-6-H), 2.6–1.6 (5 H, m); MS, *m/e* (%) 432 (4), 404 (1), 376 (15), 348 (55), 212 (100). Anal. Found: C, 52.9; H, 4.80. Calcd for $C_{19}H_{20}FeO_8$: C, 52.8; H, 4.80. Crystallization of the mother liquors from 10% ether in pentane gave diastereomer B: mp 144–147 °C; ν_{max} ($CHCl_3$) 2060, 1985, 1730, 1670, 1615, 1487 cm^{-1}; δ ($CDCl_3$, 90 MHz) 5.25 (1 H, s), 5.15 (1 H, dd, *J* = 6, 2 Hz), 3.73 (3 H, s), 3.69 (3 H, s), 3.63 (3 H, s), 3.65 (1 H, m), 3.3 (1 H, m), 2.92 (1 H, dd, *J* = 16, 6 Hz), 2.6–1.6 (5 H, m). Anal. found: C, 52.8; H, 4.70.

Methyl 4-Methoxy-1-(4-methoxyphenyl)-2-oxo-3-cyclohexenecarboxylate (10). The mixture of diastereomers 8 (450 mg) and anhydrous trimethylamine *N*-oxide (2.5 g) were stirred in benzene (30 mL) at room temperature for 17 h, and the chilled reaction mixture (ca. 10 °C) was filtered through Celite. The filter plug was washed with a small amount of benzene (ca. 5 mL) and DDQ (250 mg) was added. The mixture was stirred at room temperature for 7 h, cooled, poured into ether, washed with water, dried (Na_2CO_3), and evaporated to give crude product, which was subjected to preparative TLC to give pure 10 as a colorless oil (139 mg, 46%): ν_{max} ($CHCl_3$) 1728, 1655, 1615, 1510 cm^{-1}; δ ($CDCl_3$, 90 MHz) 7.28 (2 H, d, *J* = 8 Hz, ArH), 6.88 (2 H, d, *J* = 8 Hz, ArH), 5.51 (1 H, s, vinyl), 3.81 (3 H, s, OMe), 3.75 (3 H, s, CO_2Me), 3.68 (3 H, s, OMe), 2.7–2.3 (4 H, m); MS, *m/e* (%) 290 (30), 192 (100), 184 (15), 98 (35); found M^+ 290.1162, calcd for $C_{10}H_{18}O_5$ M^+ 290.1154. Attempts to improve the aromatization yield by carrying out the DDQ oxidation in boiling benzene only led to rearrangement of the diene without aromatization.

Tricarbonyl[methyl 1-((2-5-η)-4-methoxycyclohexa-2,4-dienyl)-4-oxo-2-cyclohexenecarboxylate]iron (12). The mixture of diastereomers 8 (100 mg) was stirred in dry ether (10 mL) at −78 °C under nitrogen while diisobutylaluminum hydride (1 M solution in hexane, 0.48 mL) was added. The reaction mixture was allowed to reach room temperature (ca. 30 min) and was stirred for 3.5 h, after which time methanol (2 mL) then water (0.5 mL) were added. After stirring for 0.5 h, the mixture was filtered through Celite, the plug was washed with ether, and the filtrate and washings were washed with water (2 × 10 mL), dried ($MgSO_4$), and evaporated to give a yellow gum. This was stirred in methanol (6 mL) and a solution of oxalic acid (100 mg) in water (3 mL) was added. After 7 h the mixture was poured into water and extracted with ether in the usual way to afford crude product which was purified by preparative TLC to give the mixture of diastereomers 12 (67 mg, 74%): mp 143–145 °C; ν_{max} (CCl_4) 2058, 1960, 1725, 1676, 1488 cm^{-1}; δ ($CDCl_3$, 90 MHz) [diastereomer values in parentheses] 6.95 [6.63] (1 H, dd, *J* = 11, 2 Hz), 6.00 [5.92] (1 H, d, *J* = 11 Hz), 5.15 (1 H, m, 3-H), 3.70 [3.63] (3 H, s, CO_2Me), 3.60 [3.61] (3 H, s, OMe), 3.7–3.6 (1 H, m, 5-H), 3.22 (1 H, m, 2-H), 2.6–1.8 (7 H, m); MS, *m/e* (%) 402 (1), 374 (2), 346 (20), 318 (50), 210 (40), 164 (100). Anal. Found: C, 53.3; H, 4.90. Calcd for $C_{18}H_{18}FeO_7$: C, 53.7; H, 4.50. Scaleup of this procedure to 10 g of complex 7 gave a slightly lower yield (65%).

Methyl 1-(4-Methoxyphenyl)-4-oxo-2-cyclohexenecarboxylate (11a). Method A, from compound 10. The aromatic intermediate 10 (30 mg) and sodium borohydride (100 mg) were stirred in ethanol (5 mL) at room temperature for 17 h. The mixture was poured onto 10% hydrochloric acid (5 mL) and stirred for 20 min; ether (30 mL) was added and the mixture was vigorously shaken for 10 min. The separated ether layer was washed successively with water and aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated to afford crude product. Purification by preparative TLC afforded 11a (19 mg, 73%) as a colorless oil: ν_{max} ($CHCl_3$) 1730, 1680, 1650, 1606, 1582 cm^{-1}; δ ($CDCl_3$, 90 MHz), 7.31 (1 H, d, *J* = 10 Hz), 7.22 (2 H, d, *J* = 9 Hz), 6.86 (2 H, d, *J* = 9 Hz), 6.16 (1 H, d, *J* = 10 Hz), 3.73 (3 H, s, OMe), 3.68 (3 H, s, CO_2Me), 2.6–2.0 (4 H, m); MS, *m/e* (%) 260 (13), 201 (100), 192 (17), 84 (22); found M^+ 260.1042, calcd for $C_{15}H_{16}O_4$ M^+ 260.1048. A minor amount of the isomeric enone, methyl 1-(4-methoxyphenyl)-2-oxo-3-cyclohexenecarb oxylate, arising from 1,4-reduction of 10 was also isolated (4 mg, 13%): ν_{max} ($CHCl_3$) 1725, 1680, 1610, 1580 cm^{-1}; δ ($CDCl_3$, 90 MHz) 7.27 (3 H, d, *J* = 9 Hz, Ar-H and enone β-H), 6.93 (2 H, d, *J* = 9 Hz), 6.23 (1 H, d, *J* = 9 Hz), 3.76 (3 H, s,), 3.75 (3 H, s), 2.6–2.2 (4 H, m); found M^+ 260.1049.

Method B, from complex 12. The complex 12 (7.0 g) and anhydrous Me_3NO (10 g) were stirred in benzene (500 mL) for 17 h. The chilled (ca. 10 °C) mixture was filtered through Celite and the filter plug was washed with benzene (20 mL). The filtrate volume was reduced to 50 mL in vacuo, *p*-xylene (150 mL) was added, and the volume was reduced to 80 mL. The mixture was diluted with *p*-xylene (300 mL) and heated under reflux while a solution of DDQ (3.90 g) in *p*-xylene (600 mL) was added dropwise over 1 h. The reaction mixture was boiled under reflux for 5 h, cooled, filtered, diluted with ether (1000 mL), and washed with aqueous $NaHCO_2$ (3 × 50 mL). The organic phase was dried ($MgSO_4$) and evaporated in vacuo and the residue was purified by flash chromatography (40% ethyl acetate in hexane) to afford 11a (2.08 g, 60%).

8-(Methoxycarbonyl)-8-(4-methoxyphenyl)-1,4-dioxaspiro[4.5]dec-6-ene (11b). The enone 11a (2.9 g), ethylene glycol (15 mL), and *p*-toluenesulfonic acid (0.2 g) were boiled in benzene (250 mL) for 17 h under a reflux condenser fitted with a Dean and Stark trap. The cooled reaction mixture was diluted with ether and washed with aqueous Na_2CO_3, and the organic layer separated, dried (Na_2CO_3), and evaporated in vacuo to give 11b (3.2 g, 97%) as a colorless oil, which was used without further purification in the next step: ν_{max} (CCl_4) 1734, 1650 (w), 1610, 1580 cm^{-1}; δ ($CDCl_3$, 400 MHz) 7.19 (2 H, d, *J* = 8.8 Hz), 6.84 (2 H, d, *J* = 8.8 Hz), 6.30 (1 H, d, *J* = 10.2 Hz), 5.86 (1 H, d, *J* = 10.2 Hz), 3.95 (4 H, m, dioxolane), 3.77 (3 H, s), 3.67 (3 H, s), 2.56 (1 H, ddd, *J* = 12.7, 9.3, 2.9 Hz), 2.02 (1 H, ddd, *J* = 12.7, 9.3, 2.9 Hz), 1.81 (1 H, ddd, *J* = 13.2, 9.3, 2.9 Hz), 1.70 (1 H, ddd, *J* = 13.2, 9.3, 2.9 Hz); MS, *m/e* (%) 304 (10), 245 (100), 173 (80); found M^+ 304.1310, calcd for $C_{17}H_{20}O_5$ M^+ 304.1311.

8-(Hydroxymethyl)-8-(4-methoxyphenyl)-1,4-dioxaspiro[4.5]dec-6-ene (11c). The protected enone 11b (30 mg) was stirred at 23 °C in dry ether (4 mL) with lithium aluminum hydride (5 mg) for 14 h. Methanol (2 drops) and water (1 drop) were added and the mixture was stirred for 30 min before being filtered and evaporated. The crude product was purified by preparative TLC (silica gel, 10% ethyl acetate in benzene) to give 11c (25 mg, 91%) as CH_2O colorless oil: ν_{max} (CCl_4) 3580, 3485 (broad), 1607, 1584 cm^{-1}; δ ($CDCl_3$ pre-filtered through basic Al_2O_3, 90 MHz), 7.23 (2 H, d, *J* = 8 Hz), 6.84 (2 H, d, *J* = 8 Hz), 6.15 (1 H, d, *J* = 11 Hz), 5.84 (1 H, d, *J* = 11 Hz), 3.85 (4 H, m), 3.76 (3 H, s), 3.66 and 3.46, partly obscured (1 H, each AB_q, *J* = 10 Hz, CH_2OH), 3.5 (1 H, exchanges D_2O, OH), 2.2–1.6 (4 H, m); MS, *m/e* (%) 246 (100, M − CH_2O), 245 (80), 173 (87); found $M^+ - CH_2O$ 246.1274, calcd for $C_{15}H_{18}O_3$ 246.1283.

8-(4-Methoxyphenyl)-1,4-dioxaspiro[4.5]dec-7-ene (14). When compound 11c was allowed to stand in reagent grade chloroform for a few hours, considerable formation of 14 occurred. This compound was also prepared as follows. Compound 11c (20 mg) was boiled under reflux for 5 h in dry benzene (5 mL) containing *p*-toluenesulfonic acid (2 mg). The cooled reaction mixture was diluted with ether, washed (aqueous Na_2CO_3), dried (Na_2CO_3), and evaporated in vacuo. Preparative TLC (silica gel, ether) gave 14 (15 mg) as white plates: mp 87–89 °C; ν_{max} ($CHCl_3$) 1660, 1608, 1580 cm^{-1}; δ ($CDCl_3$, 90 MHz), 7.32 (2 H, d, *J* = 9 Hz), 6.83 (2 H, d, *J* = 9 Hz), 5.88 (1 H, m, vinyl H), 4.01 (4 H, m), 3.79 (3 H, s), 2.45–1.8 (6 H, m); MS, *m/e* (%) 246 (33), 173 (25), 160 (100); found M^+ 246.1278, calcd for $C_{15}H_{18}O_3$ M^+ 246.1283.

8-(4-Methoxyphenyl)-8-[[(4-tolylsulfonyl)oxy]methyl]-1,4-dioxaspiro[4.5]dec-6-ene (11d). The alcohol 11c (85 mg) and *p*-toluenesulfonyl chloride (200 mg) were dissolved in pyridine (2 mL) at 0 °C. The solution was set aside in the refrigerator (ca. 1 °C) for 64 h. The mixture was then stirred at room temperature while water (0.25 mL) was added. After 0.5 h the mixture was poured into ether (50 mL) and washed with aqueous $NaHCO_3$ (3 × 50 mL). The organic phase was dried (Na_2CO_3) and evaporated in vacuo. Remaining traces of pyridine were removed by addition of toluene (2 mL) and evaporation under vacuum (0.1 mmHg). Preparative TLC (silica gel, 1:1 ether/pentane) afforded the tosylate 11d (110 mg, 95%): ν_{max} ($CHCl_3$) 1611, 1602, 1585, 1510, 1500, 1365, 1175 cm^{-1}; δ ($CDCl_3$, 90 MHz), 7.68 (2 H, d, *J* = 8 Hz), 7.36 (2 H, d, *J* = 8 Hz), 7.13 (2 H, d, *J* = 9 Hz), 6.79 (2 H, d, *J* = 9 Hz), 5.98 (1 H, d, *J* = 10 Hz), 5.80 (1 H, d, *J* =

10 Hz), 4.15 and 4.03 (1 H, each, AB_q, J = 10 Hz, CH_2OTs), 3.93 (4 H, m), 3.72 (3 H, s), 2.40 (3 H, s), 2.0–1.4 (4 H, m); MS, *m/e* (%) 258 (40, M − TsOH), 2.45 (60, M − CH_2OTs), 107 (100).

8-(Cyanomethyl)-8-(4-methoxyphenyl)-1,4-dioxaspiro[4.5]dec-6-ene (11e). The tosylate **11d** (50 mg) and sodium cyanide (250 mg) were dissolved in HMPA (5 mL) in a tightly stoppered flask, purged with nitrogen, and heated at 155 °C for 17 h (oil bath). The cooled mixture was diluted with ether, washed thoroughly with water, dried (Na_2CO_3), and evaporated. The crude product was subjected to preparative TLC (10% ethyl acetate in benzene) to give pure nitrile **11e** (19 mg, 60%): ν_{max} ($CHCl_3$) 2260, 1650, 1605, 1585 cm^{-1}; δ ($CDCl_3$, 400 MHz) 7.25 (2 H, d, J = 9 Hz), 6.87 (2 H, d, J = 9 Hz), 6.09 (1 H, d, J = 10 Hz), 5.89 (1 H, d, J = 10 Hz), 4.05–3.9 (4 H, m), 3.79 (3 H, s, OMe), 2.78 and 2.67 (1 H each AB_q, J = 16.6 Hz, CH_2CN), 2.08 (2 H, m), 1.75 (1 H, m), 1.67 (1 H, m); MS, *m/e* (%) 285 (1), 284 (11), 245 (85), 173 (100); found M^+ 285.2651, calcd for $C_{17}H_{19}NO_3$ M^+ 285.2667.

4-(Cyanomethyl)-4-(4-methoxyphenyl)-2-cylohexenone (6). A stock solution of dioxane (5 mL), methanol (3 mL), water (1 mL), and concentrated hydrochloric acid (2 drops) was prepared. The nitrile **11e** (10 mg) was dissolved in this solution (2 mL) and stirred at room temperature for 6 h. The mixture was diluted with ether (20 mL), washed with water (3 × 10 mL), dried ($MgSO_4$), evaporated, and purified by preparative TLC to afford **6** (6 mg, 72%): ν_{max} ($CHCl_3$) 2250, 1685, 1625 cm^{-1}; δ ($CDCl_3$, 200 MHz), 7.26 (1 H, d, J = 10 Hz), 7.14 (2 H, d, J = 9 Hz), 6.90 (2 H, d, J =9 Hz), 6.25 (1 H, d, J = 10 Hz), 3.79 (3 H, s), 2.80 (2 H, close AB_q, CH_2CN), 2.0–1.6 (4 H, m); MS, *m/e* (%) 241 (17), 201 (100), 173 (50), 149 (30); found M^+ 241.1120, calcd for $C_{15}H_{15}NO_2$ M^+ 241.1103.

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Registry No. **1b**, 51508-59-9; (±)-**6**, 79214-94-1; (±)-**7**, 91817-43-5; (±)-**8** (isomer 1), 83917-60-6; (±)-**8** (isomer 2), 83875-21-2; (±)-**10**, 91817-44-6; (±)-**11a**, 83925-42-2; (±)-**11b**, 83925-44-4; (±)-**11c**, 83925-45-5; (±)-**11d**, 83925-46-6; (±)-**11e**, 83925-47-7; (±)-**12** (isomer 1), 83917-59-3; (±)-**12** (isomer 2), 83875-22-3; **14**, 67019-46-9; methyl (±)-1-(4-methoxyphenyl)-2-oxo-3-cyclohexenecarboxylate, 91817-45-7; 3-methoxy-2-cyclohexenone, 16807-60-6.

Selective Reductions. 35. Reaction of Representative Organic Functional Groups with Lithium Borohydride in the Presence of *B*-Methoxy-9-borabicyclo[3.3.1]nonane. A Simple, Convenient Procedure for the Catalyzed Selective Reduction of Esters

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The rate of reduction of esters by lithium borohydride is considerably enhanced by a number of Lewis acids of boron. The remarkable catalytic effect of *B*-MeO-9-BBN and $(MeO)_3B$ in enhancing the reactivity of lithium borohydride toward the reduction of other representative functional groups has been explored. Alkyl halides are not reduced. Epoxides are readily reduced in 0.25 h. Carboxylic acids are reduced rapidly up to 50%, with further reaction being very slow. Acid salts are not reduced. Tertiary amides are slowly reduced in the presence of 100 mol % of *B*-MeO-9-BBN, 40% in 24 h. Nitriles, under the same conditions, are reduced completely in 5 h. Pyridine and nitrobenzene are not significantly affected by this system. Sulfides, sulfoxides, and sulfones are also inert. However, tosylates are reduced rapidly. These results indicate the utility of this catalytic effect for the ready reduction of esters by lithium borohydride, as well as the ability of this reducing system to tolerate many substituents in such reductions.

Sodium borohydride is a mild reducing agent.[1] However, the reducing potential of borohydride can be modified by proper choice of reaction conditions.[1] The important factors which affect the reactivity of borohydride are (1) solvent, (2) cation, (3) use of catalysts, and (4) the presence of activating substituents. We have studied the effect of solvent and cation on the rate of reduction of esters by borohydride.[2] The results indicated that lithium borohydride in ethyl ether is a powerful reducing system for esters. We successfully employed this system for the synthesis of alcohols from esters.[2] However, attempts to reduce unsaturated esters to the corresponding alcohols were not successful. A more systematic study of the reduction of an unsaturated ester, ethyl 10-undecenoate, revealed that the uptake of hydride by this ester was far faster than the uptake by the saturated ester, ethyl caproate.[3] Also, 3 mmol of hydride are utilized per mmol of ester, compared to 2 mmol of hydride utilized by ethyl caproate and similar saturated carboxylic esters. The reduction product, following oxidation, was a mixture of 1,11-undecandiol (85%) and 1,10-undecandiol (15%) (eq 1).

$$CH_2{=}CH(CH_2)_8COOEt + LiBH_4 \xrightarrow[\text{(2) } H_2O_2/NaOH]{\text{(1) } Et_2O,\ 2\ h,\ 25\ ^\circ C} \underset{85\%}{HOCH_2(CH_2)_9CH_2OH} + \underset{15\%}{CH_3CHOH(CH_2)_8CH_2OH}\ (90\%\ \text{overall yield}) \quad (1)$$

This unexpected greater reactivity of the unsaturated ester prompted us to investigate this phenomenon in detail, resulting in the discovery of new powerful catalysts for enhancing the reactivity of lithium borohydride.[4] We

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