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A Convenient Synthesis of Estrone and 11-Methylequilenines based on the Thermal Elimination of β-Ketosulfoxides

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The thermal elimination of β-ketosulfoxides (**3**, **4**, **5**) derived easily from methyl 4-(3-methoxyphenyl)butyrate (**1**) gave 6-(3-methoxyphenyl)hex-1-en-3-one (**6**), which was condensed with 2-methylcyclopentane-1,3-dione (**8**) to yield the triketone (**7**), one of key intermediates of Smith's estrone synthesis. Compound **7** was cyclized to the unsaturated diketone (**9**), which was converted to estrone methyl ether (**13**) by the established procedures. When the mixture of **3** (or **4**) and **8** was heated, **7** was directly formed in a good yield. Moreover, heating of **5** and **8** gave **9**, though in less satisfactory yield. The over-all yield of this simple and short cut synthesis of estrone methyl ether (**13**) from the starting material (**1**) was 34%, nearly twice of the original Smith method. This method also applied for the synthesis of 11α-methylequilenine methyl ether (**20**) and 11α-methylisoequilenine methyl ether (**19**) *via* the prior introduction of a methyl group to **3** yielding the β-ketosulfoxide (**14**) in 40% over-all yield.

Keywords——short cut synthesis; estrone; 11α-methylequilenine; 11α-methylisoequilenine; thermal elimination; β-ketosulfoxide; stereochemistry

The Smith method,[2] as well as Torgov's is well known as an efficient and highly stereospecific synthesis of estrone.[3] However, some processes, especially those to the vinyl ketone (**6**) by the usual Hofmann degradation, still need to be improved. As part of our study on reactions and synthetic applications of β-ketosulfoxides,[4] we report here their thermal elimination to vinly ketones, which may provide a practical improvement of the Smith method.[5]

A β-ketosulfoxide (**2**) prepared quantitatively from methyl 4-(3-methoxy-phenyl)butyrate (**1**) and dimsyl anion by the usual method[6] was treated with methyl iodide in the presence of potassium hydride to give an enone precursor (**3**) in 89% yield. The structural assignment of **3** rests on its spectral data. In its mass spectrum, **3** has no molecular ion, but a peak due to M^+-CH_3SOH at *m/e* 204 corresponding to that of the enone (**6**). Its nuclear magnetic resonance (NMR) spectrum shows that **3** is a diastereomeric mixture in the ratio of 1:2 attributed to the two asymmetric centers of the methine and the sulfoxide. Without further separation into its components, **3** was heated in dioxane–diglyme (1:1) under reflux for 4 hr. The thermal elimination of methanesulfenic acid took place smoothly and, after passing through a short column of silica gel, the pure enone (**6**) was easily isolated in 85% yield.[7]

1) Location: *a) Ishikari-Tobetsu, Hokkaido 061-02 Japan*; *b) Kita-12, Nishi-6, Kita-ku, Sapporo 060, Japan.*
2) G.H. Douglas, J.M.H. Graves, D. Hartley, G.H. Hughes, B.J. McLoughlin, J. Siddall, and H. Smith, *J. Chem. Soc.*, **1963**, 5072.
3) For a review, see: P. Morand and J. Lyall, *Chem. Rev.*, **68**, 85 (1968).
4) Y. Oikawa and O. Yonemitsu, *J. Org. Chem.*, **41**, 1118 (1976); *idem*, *J.C.S. Perkin I*, **1976**, 1479; *idem*, *Heterocycles*, **5**, 233 (1976).
5) The preliminary communication of this paper appeared in Y. Oikawa, T. Kurosawa, and O. Yonemitsu, *Chem. Pharm. Bull.* (Tokyo), **23**, 2466 (1975).
6) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965).
7) The thermal elimination of **3** to **6** in other solvents under similar conditions gave less satisfactory results: xylene (60%), diglyme (62%), dioxane (80%).

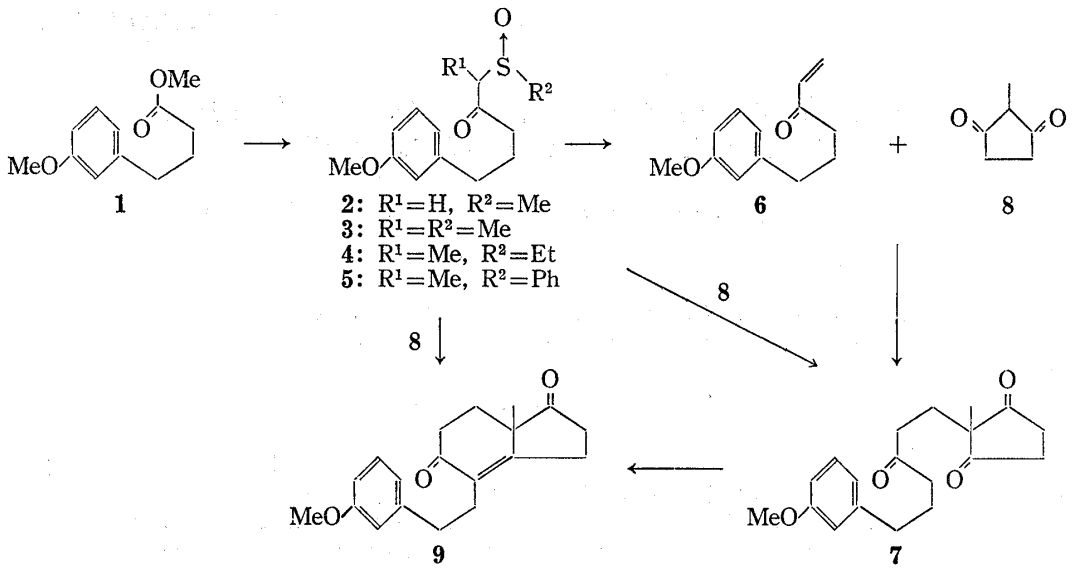


Fig. 1

The condensation of **6** and 2-methylcyclopentane-1,3-dione (**8**) to the trione (**7**) was carried out at room temperature in the presence of triethylamine in 80% yield.[8] As a more convenient way, however, when a diglyme solution of **3** and **8** (1.3 eq) was heated under reflux for 4.5 hr, **7** was formed directly in 70% yield through the thermal elimination of **3** and the subsequent Michael addition.

Moreover, to dispense with the methylation step (**2**→**3**), **1** was condensed with a carbanion prepared from diethyl sulfoxide and lithium diisopropylamide to give **4** in 97% yield. Its NMR spectrum shows that **4** was also a diastereomeric mixture. In its mass spectrum, **4** has again no molecular ion, but has entirely the same peaks as **3**. In analogy with **2**, **4** was heated with the dione in diglyme to yield the trione (**7**) though in less satisfactory yield (41%), probably because the thermal elimination of ethanesulfenic acid took place simultaneously in the unfavorable direction. In order to facilitate the thermal elimination, **5** was next prepared from **1** and a carbanion of ethyl phenyl sulfoxide. This compound

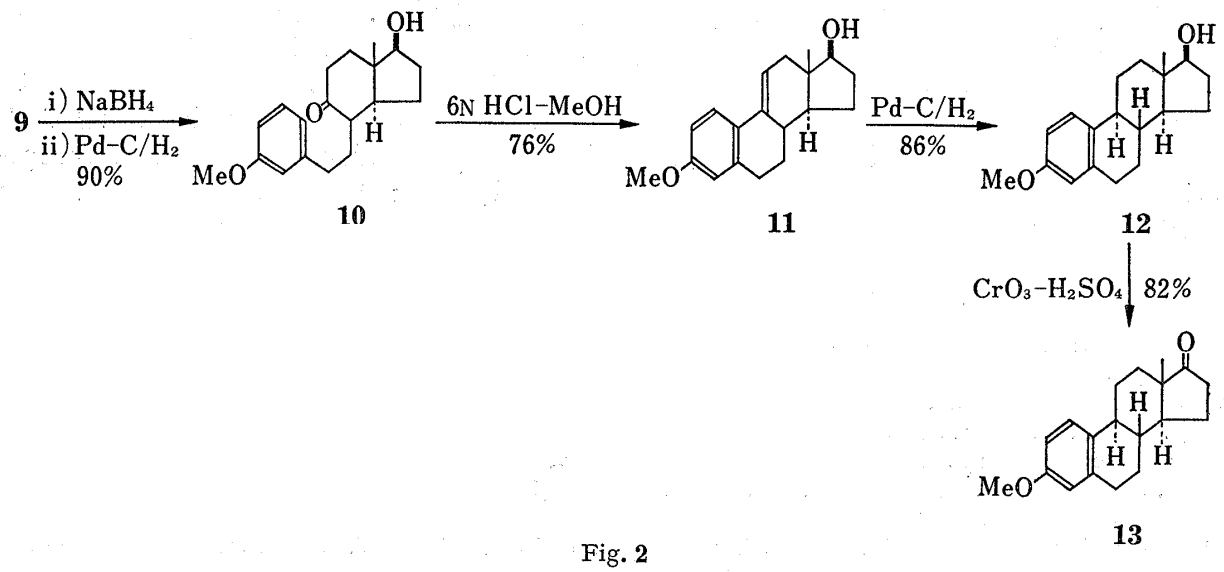


Fig. 2

8) *cf.* S. Danishefsky and P. Cain, *J. Org. Chem.*, **39**, 2925 (1974); G. Bauduin, H. Christol, and Y. Pietrasanta, *Bull. Soc. Chim. Fr.*, **1973**, 359.

was easily converted to the enone (**6**) in refluxing benzene or monoglyme, and when heated with **8** in diglyme, the unsaturated diketone (**9**), one of key intermediates in the Smith method, was interestingly isolated in 37% yield, that is, the initially formed trione (**7**) further underwent an acid catalyzed cyclization. Benzenesulfenic acid, though unstable, formed as the elimination of **5** proceeded probably acted as a catalyst. If this assumption was correct, an excess of the dione (**8**) was expected to also act as a catalyst in this type of acid catalyzed cyclization, because **8** has almost the same acidity as acetic acid. Actually, when **3** was heated with three-fold excess of **8**, the yield of **9** increased to 52%.

The conversion of **9** to estrone methyl ether (**13**) essentially followed the established procedures as shown in the scheme.[2,9] The overall yield of estrone methyl ether (**13**) from the starting material (**1**) was 34%, nearly twice of the original Smith method.

An additional advantage of the elimination method presented in this paper is that a substituent can be easily introduced at the C-11 position of the steroid skeleton through the prior introduction of the substituent at the active methylene between the sulfinyl and carbonyl groups of the starting β-ketosulfoxides.

As an example illustrating this feature the synthesis of 11-substituted steroids is next described. Treatment of **2** with 2.4 equivalents of methyl iodide in the presence of potassium hydride or sodium hydride gave **14** in 90% yield. In its mass spectrum, a peak owing to the elimination of methanesulfenic acid appears at 218. Its NMR spectrum has two singlets of methyl substituents at δ 1.70 and 2.10 ppm. On heating in dioxane, **14** readily gave an enone (**15**) in 89% yield. Then **15** was condensed with **8** in ethyl acetate containing 5% triethylamine at 70° for 7 days to give a ketol (**17**) in 70% yield accompanied by a small amount (7%) of a triketone (**16**). The mass spectrum of **17**, though without its parent peak, has a fairly strong peak at 312 (M^+—18) from loss of water. The infrared (IR) spectrum, which contains a hydroxy (35000 cm^{-1}) and two carbonyl groups (1740, 1705 cm^{-1}), indicates that **17** is an aldol cyclization product.

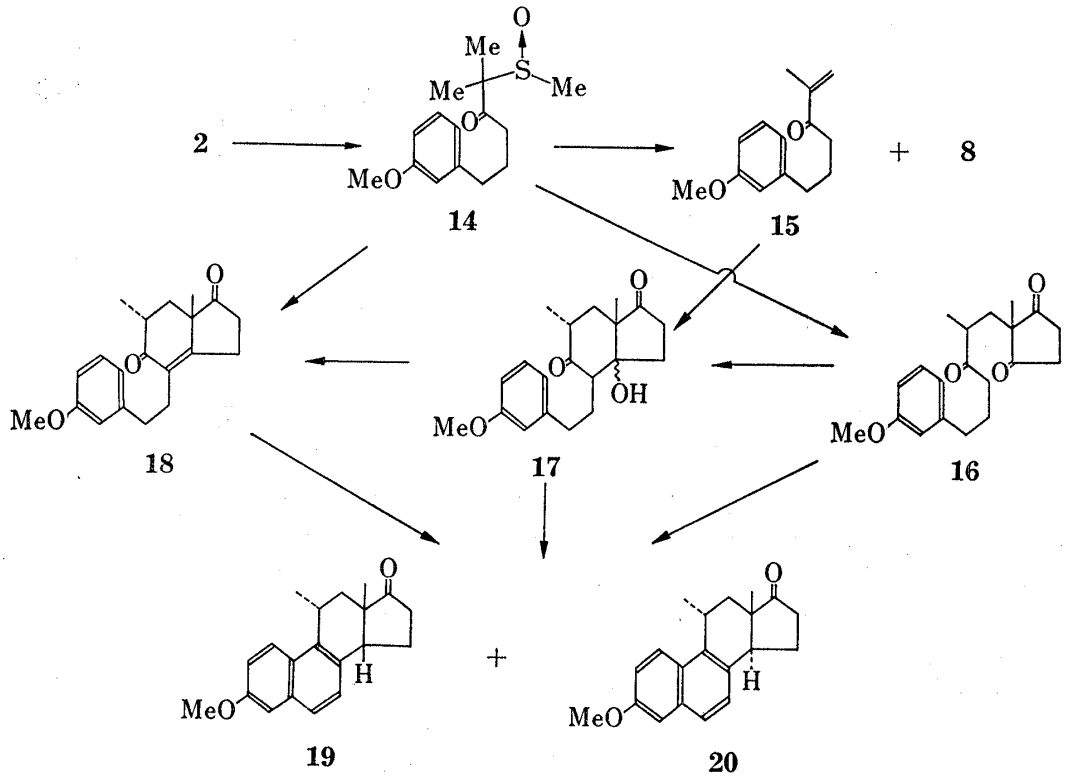


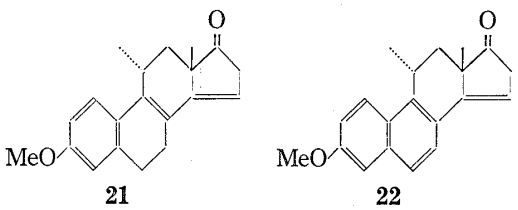
Fig. 3

9) R.P. Stein, G.C. Buzby Jr., G.H. Douglas, and H. Smith, *Tetrahedron Lett.*, **1967**, 3603.

On treatment with polyphosphoric ester (PPE) in refluxing chloroform for 4 hr, **17** readily lost water to yield an unsaturated diketone (**18**) in 80% yield. Its mass spectrum gives the fragmentation pattern identical with that of **17**, in which a strong and characteristic peak formed by the McLafferty rearrangement appears at 178. Its NMR spectrum shows that **18** is not a diastereomeric mixture, but a single product, whose two C-methyl groups must be in the *trans* configuration to avoid an unfavorable 1,3-diaxial interaction in the *cis* configuration. Then **18** was treated with polyphosphoric acid (PPA) in refluxing chloroform for 30 min, and gave two steroidal products, **19** and **20**, which were separated by silica gel column chromatography in 43% and 36% yield, respectively. Under the same conditions, **17** also gave directly **19** (38%) and 20 (30%) without isolation of the intermediary **18**.

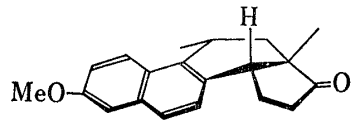
As a more practical way, a mixture of **14** and **8** in diglyme was heated under reflux for 7 hr to give triketone (**16**) in 60% yield. Then **16** was treated with PPA in refluxing chloroform as described above, and interestingly gave **19** (41%) and **20** (33%), which were formed probably *via* **17** and **18**. The over-all yield of combined **19** and **20** from **2** was over 40%. When **14** was heated in the presence of three-fold excess of **8**, a mixture of **16** and **18** was formed, though only in 19% and 30% yield, respectively.

The structural assignment of **19** and **20** was established spectroscopically, and was suported by some chemical reactions and by mechanistic considerations. On the basis of the elemental analyses and the mass spectra, both **19** and **20** have the composition $C_{20}H_{22}O_2$. Their NMR spectra have no vinyl proton. In their UV spectra, both compounds have the chromophore of equilenine type, not **21**-type.[2,10,11] Therefore, they must be isomeric each other with regard to the configuration at C-14. Compound **20** having absorption maxima at a little longer wavelength can be assigned as 11α-methylequilenine methyl ether with C-14 α-hydrogen, and hence **19** is 11α-methylisoequilenine methyl ether with C-14 β-hydrogen.[11] This assignment is supported by the following reactions.

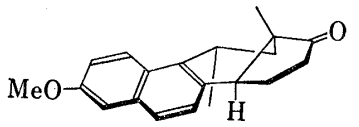


21 **22**

Fig. 4



19a



20a

Fig. 5

Compound **19** was dehydrogenated by the treatment with dichlorodicyanobenzoquinone (DDQ) in refluxing benzene to **22**, which was then subjected to hydrogenation with 5% palladium on carbon to give **20** as well as **19**. On the other hand, **20** was unreactive to DDQ. Three-dimensional drawings (**19a** and **20a**) of **19** and **20** may account for their different reactivities, namely the α-side of **20** being hindered by the C-11 α-methyl group, it is hardly possible to form a charge transfer complex, the formation of which must be the initial step of the DDQ oxidation, between DDQ and the electron-donating naphthalene moiety of **20a**, whereas the β-side of **19a** is open to the attack of DDQ.

10) G.A. Smith and H. Smith, *Chem. and Ind.*, **1960**, 1022.
11) T. Miki, K. Hiraga, and T. Asako, *Chem. Pharm. Bull.* (Tokyo), **13**, 1285 (1965).

Experimental

5-(3-Methoxyphenyl)-1-methylsulfinylpentan-2-one (2)——To a stirring suspension of KH (0.8 g) washed with dry hexane in THF (5 ml), DMSO (2 ml) was added dropwise at 0° under argon. After evolution of hydrogen ceased, 4-(3-methoxyphenyl)butyrate (**1**, 1.02 g) in THF (5 ml) was added to the solution and the stirring was continued for 30 min at room temperature. The reaction mixture was then poured into sat. NH_4Cl solution and extracted with CH_2Cl_2. The extract was washed with water and sat. NaCl, then dried over Na_2SO_4. The solvent was removed *in vacuo* and the residual oil was purified by silica gel column chromatography to yield 1.25 g of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1700, 1040. NMR ($CDCl_3$) δ: 1.8—2.2 (2H, m), 2.62 (2H, t, J=6 Hz), 2.67 (2H, t, J=6 Hz), 2.69 (3H, s), 3.72 (1H, d, J=14 Hz), 3.77 (1H, d, J=14 Hz), 3.82 (3H, s), 6.6—6.8 (3H, m), 7.20 (1H, t, J=8 Hz).

6-(3-Methoxyphenyl)-2-methylsulfinylhexan-3-one (3)——To a stirring suspension of KH (0.4 g) washed with dry hexane in THF (10 ml), **2** (1.27 g) in THF (10 ml) was added dropwise at 0° under argon. After evolution of hydrogen ceased, MeI (0.79 g) was added and the stirring was continued for 3.5 hr at room temperature. Work-up as described above gave 1.19 g (89%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1700, 1040. NMR ($CDCl_3$) δ: 1.30 (2H, d, J=7 Hz), 1.42 (1H, d, J=7 Hz), 1.8—2.1 (2H, m), 2.3—2.8 (7H, m), 3.74 (0.33H, q, J=6 Hz), 3.80 (3H, s), 3.84 (0.67H, q, J=6 Hz), 6.65—6.8 (3H, m), 7.18 (1H, t, J=8 Hz). MS *m/e* (%): 204 (M^+—MeSOH, 11), 134 (100), 121 (15), 91 (16).

6-(3-Methoxyphenyl)-2-ethylsulfinylhexan-3-one (4)——To a stirring THF solution (8 ml) of diisopropylamine (1.21 g), 7.5 ml of *n*-BuLi (10% in hexane) was added dropwise at −20——−30° under nitrogen and the stirring was continued for 20 min. Then a THF solution (2 ml) of diethylsulfoxide (1.5 g) was added and the solution was stirred for additional 20 min. After the temperature was allowed to raise to −10°, 1.01 g of the ester (**1**) in THF was added and the solution was stirred at room temperature for 1 hr. The reaction mixture was worked up as described above to give 1.33 g (97%) of a colorless oil: IR ν_{max}^{neat} cm^{-1}: 1700, 1040. NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7.5 Hz), 1.35 (1.2H, d, J=7.5 Hz), 1.45 (0.8H, d, J=7.5 Hz), 1.7—2.3 (2H, m), 2.4—2.8 (6H, m), 3.70 (0.6H, q, J=7.5 Hz), 3.73 (0.4H, q, J=7.5 Hz), 3.80 (3H, s), 6.6—6.8 (3H, m), 7.05—7.3 (1H, dd, J=7, 9 Hz). MS *m/e* (%): 204 (M^+—EtSOH, 6), 134 (100), 121 (10), 105 (9), 91 (15).

6-(3-Methoxyphenyl)-2-phenylsulfinylhexan-3-one (5)——To a THF solution (5 ml) of diisopropylamine (1.01 g), 6.4 ml of *n*-BuLi (10% in hexane) was added under nitrogen at −30——−40° and the temperature was gradually raised to 0° during 20 min. Then ethyl phenyl sulfoxide (1.54 g) in THF (2 ml) was added dropwise, and after 20 min the ester (**1**, 0.52 g) was added. The stirring was continued for additional 2 hr and the reaction mixture was worked up as described above to give 0.73 g (88.5%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1700, 1040. NMR ($CDCl_3$) δ: 1.22 (1.35H, d, J=6 Hz), 1.37 (1.65H, d, J=6 Hz), 1.6—2.0 (2H, m), 2.3—2.65 (4H, m), 3.74 (1H, q, J=6 Hz), 3.80 (3H, s), 6.65—6.8 (3H, m), 7.20 (1H, t, J=8 Hz), 7.53 (5H, s). MS *m/e* (%): 218 ($C_6H_5SSC_6H_5$, 7), 204 (M^+—C_6H_5SOH, 7), 134 (100), 121 (9), 110 (25), 104 (9), 91 (8).

6-(3-Methoxyphenyl)hex-1-en-3-one (6)——a) A dioxane–diglyme (1: 1) solution (50 ml) of **3** (1.34 g) was refluxed for 4 hr. After removal of the solvent *in vacuo*, the residual pale yellow oil was purified passing through a silica gel column to give 0.87 g (85%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}; 1695 (sh), 1680. NMR ($CDCl_3$) δ: 1.9—2.15 (2H, m), 2.45—2.8 (4H, m), 3.80 (3H, s), 5.77 (1H, dd, J=4, 9 Hz), 6.23 (1H, d, J=4 Hz), 6.28 (1H, d, J=9 Hz), 6.65—7.2 (4H, m). MS *m/e* (%): 204 (M^+, 6), 134 (100), 121 (10), 105 (9), 91 (11).

b) A xylene solution (50 ml) of **4** (1.41 g) was refluxed for 4 hr. The xylene was distilled off *in vacuo* and the residual oil was worked up as described above to yield of 0.55 g (54%) of **6**.

c) A benzene solution (5 ml) of **5** (1.65 g) was refluxed for 7 hr. Work-up as described above gave 0.63 g (62%) of **6**.

2-(6-3′-Methoxyphenyl-3-oxohexyl)-2-methylcyclopentane-1,3-dione (7)——a) A solution of **6** (204 mg; 1 mmol) and 2-methylcyclopentane-1,3-dione (**8**, 123 mg; 1.1 mmol) in EtOAc (4 ml) containing 5% Et_3N was stirred at room temperature for 36 hr. The reaction mixture was concentrated *in vacuo* and the residual oil was purified passing through a silica gel column to give 253 mg (80%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1760, 1720. NMR ($CDCl_3$) δ: 1.08 (3H, s), 1.7—2.0 (4H, m), 2.2—3.0 (10H, m), 3.80 (3H, s), 6.6—6.8 (3H, m), 7.14 (1H, t, J=8 Hz). MS *m/e* (%): 316 (M^+, 16), 134 (100), 121 (45).

b) A diglyme solution (3.5 ml) of **3** (100 mg; 0.37 mmol) and **8** (55 mg; 0.49 mmol) was heated under reflux for 4.5 hr. Work-up as described above gave 83 mg (70.4%) of **7**.

c) A xylene solution (10 ml) of **3** (536 mg; 2 mmol) was refluxed for 4 hr. After removal of the solvent, the residue was dissolved in EtOAc (6 ml) containing Et_3N (0.4 ml), and to the solution **8** (246 mg; 2.2 mmol) was added. The mixture was stirred for 36 hr at room temperature, then the solvent was removed *in vacuo* and the residue was chromatographed to give 447 mg (71%) of **7**.

d) A diglyme solution (8 ml) of **4** (282 mg; 1 mmol) and **8** (134 mg; 1.03 mmol) was refluxed for 6 hr. Work-up as described above gave 130 mg (41%) of **7**

5,6,7,7a-Tetrahydro-4-(3-methoxyphenethyl)-7a-methylindane-1,5-dione (9)——a) A diglyme solution (5 ml) of **5** (330 mg; 1 mmol) and **8** (115 mg; 1.03 mmol) was refluxed for 7 hr. After removal of the solvent, the residue was chromatographed on a silica gel column to yield 109 mg (36.6%) of a colorless oil. IR ν_{max}^{neat}

cm^{-1}: 1740, 1660. NMR ($CDCl_3$) δ: 1.20 (3H, s), 1.6—2.8 (12H, m), 3.79 (3H, s), 6.5—6.8 (3H, m), 7.14 (1H, t, J=8 Hz). MS *m/e* (%): 298 (M^+, 45), 164 (100), 134 (66), 121 (90).

b) A diglyme solution (5 ml) of **3** (268 mg; 1 mmol) and **8** (336 mg; 3 mmol) was refluxed for 10 hr. Work-up as described above gave 155 mg (52%) of **9**.

c) A benzene solution (15 ml) of **7** (316 mg) was treated with trifluoroacetic acid (1.5 ml) at 80° for 4 hr. The solution was washed with 5% $NaHCO_3$, water, and sat. NaCl and dried over Na_2SO_4. The benzene was evaporated and the residual oil was purified by silica gel chromatography to yield 210 mg (70.5%) of **9**.

6-(3-Methoxyphenyl)-2-methyl-2-methylsulfinylhexan-3-one (14)——To a suspension of KH (0.8 g) washed with dry hexane in THF (10 ml), **2** (2.54 g) in THF (10 ml) was added dropwise at 0° under nitrogen. After evolution of hydrogen ceased, MeI (3.4 g) in THF (5 ml) was added and the solution was stirred for 2 hr at room temperature. The reaction mixture was poured into ice-water and extracted with CH_2Cl_2. The extract was washed with water and sat. NaCl, then dried over Na_2SO_4. The solvent was evaporated and residual oil was purified by silica gel column chromatography to give 2.53 g (89.7%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1700, 1040. NMR ($CDCl_3$) δ: 1.32 (3H, s), 1.54 (3H, s), 1.8—2.1 (2H, m), 2.36 (3H, s), 2.5—2.8 (4H, m), 3.80 (3H, s), 6.65—6.8 (3H, m), 7.20 (1H, t, J=8 Hz). MS *m/e* (%): 218 (M^+—MeSOH, 8), 134 (100), 121 (13), 103 (13), 91 (2).

6-(3-Methoxyphenyl)-2-methylhex-1-en-3-one (15)——A dioxane solution (30 ml) of **14** (2.82 g) was heated under reflux for 4.5 hr. After evaporation of the solvent, the residue was purified as described above to give 1.95 g (89.4%) of a colorless oil. IR ν_{max}^{neat} cm^{-1}: 1680. NMR ($CDCl_3$) δ: 1.85 (3H, d, J=1 Hz), 1.75—2.1 (2H, m), 2.61 (2H, t, J=7 Hz), 2.70 (2H, t, J=7 Hz), 3.78 (3H, s), 5.73 (1H, q, J=1 Hz), 5.89 (1H, s), 6.7—6.8 (3H, m), 7.1—7.2 (1H, m). MS *m/e* (%): 218 (M^+, 8), 134 (100).

3a,4,5,6,7,7a-Hexahydro-6α,7aβ-dimethyl-3a-hydroxy-4-(3-methoxyphenethyl)indane-1,5-dione (17), 2-(6-3′-Methoxyphenyl-3-oxo-2-methylhexyl)-2-methylcyclopentane-1,3-dione (16), and 5,6,7,7a-Tetrahydro-6α,7aβ-dimethyl-4-(3-methoxyphenethyl)indane-1,5-dione (18)——a) A EtOAc solution (5 ml) containing 5% Et_3N of **15** (2.18 g) and **8** (1.23 g) was heated at 70° for 7 days. The solution was concentrated and the residual oil was purified by silica gel chromatography to give two fractions. The first fraction was 231 mg (7%) of a colorless oil of **16**. IR ν_{max}^{neat} cm^{-1}: 1760, 1720. NMR ($CDCl_3$) δ: 1.04 (3H, d, J=7 Hz), 1.08 (3H, s), 1.2—2.0 (4H, m), 2.1—2.9 (9H, m), 3.80 (3H, s), 6.6—6.8 (3H, m), 7.20 (1H, t, J=8 Hz). MS *m/e* (%): 330 (M^+, 1), 178 (8), 134 (100), 121 (28).

The second fraction was 2.31 g (70%) of a colorless oil of **17**. IR ν_{max}^{neat} cm^{-1}: 3500, 1740, 1705. NMR ($CDCl_3$) δ: 0.95 (3H, d, J=6 Hz), 0.96 (3H, s), 1.1—2.9 (12H, m), 3.80 (3H, s), 6.6—6.8 (3H, m), 7.16 (1H, t, J=8 Hz). MS *m/e* (%): 312 (M^+-H_2O, 29), 178 (65), 134 (49), 121 (100), 91 (99).

b) A $CHCl_3$ solution (15 ml) of **17** (660 mg) and PPE (2.2 g) was heated under reflux for 4 hr. After the addition of sat. $NaHCO_3$ (75 ml), the mixture was stirred for 12 hr. The organic layer was dried and evaporated to leave an oil, which was purified by passing through a silica gel column to give 500 mg (80%) of a colorless oil of **18**. IR ν_{max}^{neat} cm^{-1}: 1740, 1660. NMR ($CDCl_3$) δ: 1.20 (3H, s), 1.20 (3H, d, J=6.5 Hz), 1.4—2.9 (10H, m), 3.1—3.4 (1H, m), 3.80 (3H, s), 6.6—6.8 (3H, m), 7.16 (1H, t, J=8 Hz). MS *m/e* (%): 312 (M^+, 29), 178 (64), 134 (48), 121 (100).

c) A diglyme solution (3 ml) of **14** (296 mg; 1.05 mmol) and **8** (140 mg; 1.25 mmol) was refluxed for 7 hr. Work-up as described above gave 209 mg (60%) of **16**.

d) A diglyme solution (10 ml) of **16** (564 mg; 2 mmol) and **8** (672 mg; 6 mmol) was refluxed for 44 hr. Work-up as described above gave 125 mg (19%) of **16** and 188 mg (30%) of **18**.

11α-Methylisoequilenine Methyl Ether (19) and 11α-Methylequilenine Methyl Ether (20)——a) A $CHCl_3$ solution (30 ml) of **18** (624 mg) and PPA (2.0 g) was refluxed for 30 min. After the reaction mixture was washed with sat. $NaHCO_3$ and water, the organic layer was dried and evaporated to leave a gummy product, which was chromatographed on a silica gel column to give two fractions. The first fraction was a crude solid of **19**, which was recrystallized from MeOH to give 253 mg (43%) of colorless needles, mp 104—106°. UV λ_{max}^{MeOH} nm (log ε): 230 (4.84), 254 (3.94), 264 (3.83), 274 (3.82), 285 (3.60), 304 (3.00), 318 (3.29), 327 (3.25), 334 (3.38). NMR ($CDCl_3$) δ: 1.28 (3H, s), 1.45 (3H, d, J=7 Hz), 1.4—2.5 (6H, m), 3.0—3.3 (1H, m), 3.5—3.8 (1H, m), 3.90 (3H, s), 7.1—7.3 (3H, m), 7.56 (1H, d, J=8 Hz), 7.88 (1H, d, J=10 Hz). MS *m/e* (%): 294 (M^+, 100), 279 (33), 235 (25), 221 (33), 208 (18). *Anal.* Calcd. for $C_{20}H_{22}O_2$: C, 81.63; H, 7.48. Found: C, 81.58; H, 7.49.

The second fraction was crude **20**, which was recrystallized from MeOH to give 212 mg (36%) of colorless prisms, mp 142.5—144°. UV λ_{max}^{EtOH} nm (log ε): 235 (5.83), 254 (3.79), 265 (3.76), 275 (3.76), 286 (3.57), 307 (3.01), 321 (3.26), 328 (3.25), 335 (3.38). NMR ($CDCl_3$) δ: 1.13 (3H, s), 1.24 (3H, d, J=8 Hz), 1.4—2.7 (6H, m), 3.2—3.3 (1H, m), 3.4—3.8 (1H, m), 3.90 (3H, s), 7.1—7.3 (3H, m), 7.58 (1H, d, J=8 Hz), 7.86 (1H, d, J=10 Hz). MS *m/e* (%): 294 (M^+, 100), 279 (39), 237 (18), 235 (18), 223 (32), 208 (21). *Anal.* Calcd. for $C_{20}H_{22}O_2$: C, 81.63; H, 7.48. Found: C, 81.62; H, 7.47.

b) A $CHCl_3$ solution (15 ml) of **17** (240 mg) and PPA (900 mg) was refluxed for 30 min. Work-up as described above gave 83 mg (38%) of **19** and 65 mg (30%) of **20**.

c) A $CHCl_3$ solution (5 ml) of **16** (135 mg) and PPA (450 mg) was refluxed for 30 min. Work-up as described above gave 49 mg (41%) of **19** and 40 mg (33%) of **20**.

14-Dehydro-11α-methylequilenine Methyl Ether (22)——A benzene solution (5 ml) of **19** (28 mg) and DDQ (25 mg) was refluxed for 3 hr. The reaction mixture was washed with 10% NaOH and sat. NaCl, then dried over Na_2SO_4. The organic layer was evaporated *in vacuo* to yield a gummy product, which was chromatographed on silica gel to give 19 mg of crude **22**. Recrystallization from MeOH gave 14 mg of pale yellow plates, mp 140.5—142°. IR ν_{max}^{Nujol} cm^{-1}: 1755, 1620, 1600. NMR ($CDCl_3$) δ: 1.06 (3H, s), 1.34 (3H, d, J=5 Hz), 1.5—2.6 (2H, m), 3.1—3.3 (2H, m), 3.6—3.9 (1H, m), 3.96 (3H, s), 6.23 (1H, t, J=3 Hz), 7.1—8.1 (5H, m). MS *m/e* (%): 292 (M^+, 100), 264 (95), 249 (91), 234 (38).

Reduction of **22**——A EtOH solution (10 ml) of **22** (10 mg) was hydrogenated in the presence of 5% Pd–C (5 mg). The product was chromatographed on a silica gel column to yield 5 mg of **19** and 2 mg of **20**.