A Practical Catalytic Method for the Preparation of Steroidal 1,4-Dien-3-ones by Oxygen Atom Transfer from Iodoxybenzene to Diphenyl Diselenide

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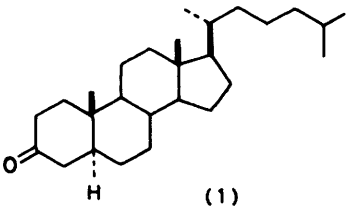
The dehydrogenation of steroidal 3-ketones can be accomplished in high yield using benzeneseleninic anhydride generated *in situ* by efficient oxygen atom transfer from iodoxybenzene to catalytic amounts of diphenyl diselenide. An experimentally convenient and economical development of this catalytic cycle is the use of *meta*-iodoxybenzoic acid which both avoids chromatography and allows recovery of *meta*-iodobenzoic acid and diphenyl diselenide. 12-Hydroxy- and 12-keto-steroids are also dehydrogenerated very efficiently using this catalytic process.

THE generation of the biologically important 1,4-dien-3-one unit by dehydrogenation of 3-oxo-steroids has been an area of intense research interest for many years. We have recently introduced benzeneseleninic anhydride [1] (BSA) as a convenient reagent for this purpose. It possesses certain advantages over the commonly used methods employing dicyanodichloroquinone (DDQ),[2] selenium dioxide,[3] or bromination–dehydrobromination.[4] Nevertheless, the formation of phenylselenic acid or other reduced forms of the anhydride generated in the elimination step may give rise to unwanted secondary reactions, particularly if reaction time is long.[1] The development of a catalytic cycle [1,5] based on rapid and efficient reoxidation of diphenyl diselenide would clearly obviate this problem. We now report, in some detail,[6] the development of such a system.

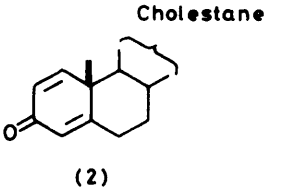
Initially we studied oxygen atom transfer to diphenyl diselenide from a variety of *N*-oxides. Pyridine *N*-oxide, 4-nitropyridine *N*-oxide, quinoxaline bis-*N*-oxide, 4-methylmorpholine *N*-oxide, and 2,4,4-trimethyl-Δ′-pyrroline *N*-oxide were unreactive. In the case of 3,5-diphenyl-1,2-diazacyclopenta-2,5-dien-4-one 1,2-dioxide oxygen atom transfer to diphenyl diselenide was observed, but reaction was too slow for the necessary rapid turnover in a catalytic system. We were, however, able to demonstrate that the product from dinitrogen trioxide and diphenyl diselenide did effect dehydrogenation of cholestanone (1) to the corresponding ring A dienone (2) (63%). The reactivity of dinitrogen trioxide, *per se*, would clearly preclude the application of this process to polyfunctional steroidal molecules. After reflection, we conceived the possibility of transfer reactions from the iodine–oxygen bond.

Preliminary experiments using iodosobenzene established that preparatively useful yields of cross-conjugated dienones could be obtained from cholestanone (65%) and androst-4-ene-3,17-dione (3) (55%), in the presence of only 0.15 catalytic equivalents of diphenyl diselenide. Nevertheless, reactions were sluggish even at 110 °C and required a four-fold excess of iodosobenzene. In view of the known disproportionation of iodosobenzene into iodobenzene and iodoxybenzene at this temperature [7] we reasoned that the latter reagent might be the real oxygen transfer reagent.

The results for a variety of steroidal substrates presented in Table 1 confirmed this idea. Typically,



(1)



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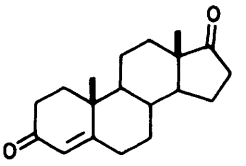

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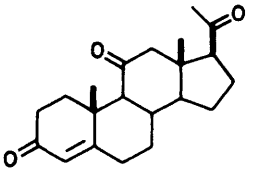

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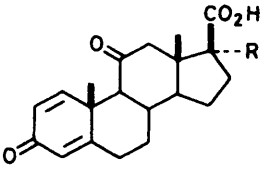
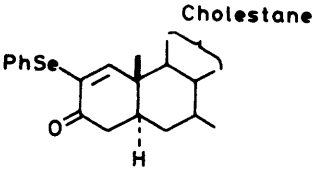


(5) R = H
(6) R = OH



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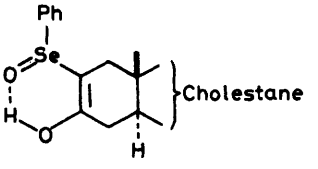

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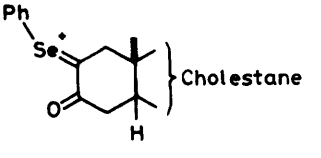


(9)

benzeneselenenic anhydride was used as the organoselenium catalyst, and reactions were carried out in refluxing benzene as solvent. Yields are generally equal or superior to those obtained by use of the anhydride in stoicheiometric amount.

trace amounts leads to a faster rate of reaction. Selenium dioxide can also be used in conjunction with iodoxybenzene to furnish cholesta-1,4-dien-3-one (58%) and hence this catalytic system should also be applicable to allylic oxidation of the carbon–carbon double bond.

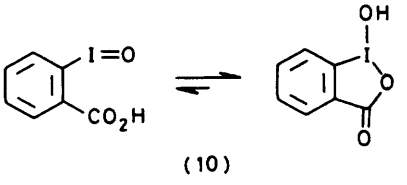
TABLE 1

Dehydrogenation of steroidal-3-ketones and alcohols using iodoxybenzene and BSA as catalyst in refluxing benzene

	Reaction conditions				
Substrate	Time (h)	BSA (equiv.)	Iodoxybenzene (equiv.)	Ring A 1,4-dien-3-one	Yield (%)
Cholestan-3-one	24	0.2	3.3	(2)	84
Cholestan-3β-ol	24	0.2	3.3	(2)	81
	12	0.2 + TsOH (trace)	3.3	(2)	77
Androst-4-ene-3,17-dione (3)	12	0.16	3.6		72
11-Oxoprogesterone (4)	12	0.18	3.3		51

The corresponding alcohol is also a suitable substrate for cyclohexadienone formation.[8] In the absence of BSA, dehydrogenation does not occur and only slow oxidation of cholestan-3β-ol to the ketone by iodoxybenzene is observed. The relatively poor yield in oxidation of compound (4) results from a secondary competitive oxidation to give compound (5) and the hydroxy-acid (6). The conversion of cholestan-3β-ol into the

During the course of preliminary studies on acid catalysis we discovered a new stoicheiometric reaction of BSA. Thus, treatment of cholestan-3-one with this reagent in acetic acid at room temperature gave the known[9] α-phenylseleno-enone (7) (51%). This was smoothly dehydrogenated to the corresponding 1,4-dien-3-one with BSA in chlorobenzene at 110 °C. It seems reasonable to postulate that under these conditions



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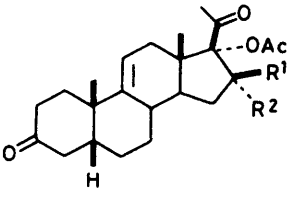
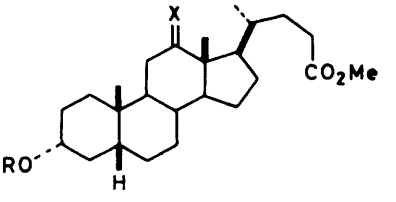
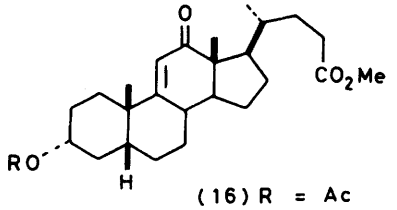


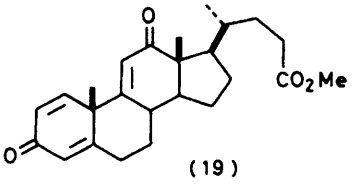
(11) R^1 = Me, R^2 = H
(12) R^1 = H, R^2 = Me



(13) R = H, X = H_2
(14) R = Ac, X = O
(15) R = CHO, X = O
(18) R = H, X = H, α-OH



(16) R = Ac
(17) R = CHO



(19)

(20) n = 3
(21) n = 2

1,4-dien-3-one involves, in fact, six separate chemical reactions. These are esterification (to the phenylselenite ester), elimination, phenylselenoxidation at C-2, elimination, similar substitution at C-4, and final elimination. Yields of 80—90% (Tables 1 and 2) demand that the average yield at each step be 97—98%! If enolisation is also regarded as a chemical reaction then there are 8 steps and the average yield is even higher. We also noted that the addition of toluene-*p*-sulphonic acid in

enolisation of the initially formed β-keto-selenoxide is faster than *syn*-elimination. The resulting intermediate (8), which may well be stabilised by intramolecular hydrogen bonding, cannot therefore adopt the required geometry for olefin formation and accordingly undergoes dehydration to give compound (9) and subsequent proton loss.

With the establishment of an efficient catalytic system in hand, we examined an experimentally convenient

procedure which would permit recovery of diphenyl diselenide and the iodobenzene-derived reagent without chromatography. Initial experiments using *ortho*-iodosobenzoic acid (10) were unsuccessful in effecting oxygen atom transfer to diphenyl diselenide. However, the activity of the catalytic system was completely restored by use of *meta*-iodoxybenzoic acid.[10] The results (Table 2) confirm that efficient dehydrogenation can be achieved. The oxidation of cholestan-3β-ol on a one gram scale using only 0.03 equivalent of diphenyl diselenide is noteworthy. We have found that protection of the 17α-hydroxy-group as the acetate in the progesterone derivatives (11) and (12) is necessary to ensure a high yield of ring A dienone. The catalytic dehydrogenation reaction can also be applied to the introduction of the 9(11)-double bond in the *trans*-A/B series [1] or in the *cis*-A/B series. Dehydrogenation of the 12-keto-ester (14) gave the enone (16) in good (90%) yield. Similar dehydrogenation of the formate (15) afforded the enone (17), but the yield was less satisfactory, no doubt due to slow attack on the formate function.

The catalytic dehydrogenation of methyl deoxycholate (18) furnished a spectacular example of consecutive reactions, because the triene-dione (19) was obtained in 64% yield. Allowing for enolisation 13 distinct consecutive steps are involved with an average yield of *ca.* 97% for each. The dehydrogenation of spirocyclic ketones without rearrangement is also an important problem. Although BSA is claimed to be unreactive for this reaction,[11] we find, on the contrary that excellent yields of dienones (20) and (21) are obtained, either in the stoicheiometric reaction or by use of the catalytic system.

From the experimental viewpoint, purification of the product, and reagent recovery are very simple. Thus, extraction of the reaction mixture with aqueous sodium hydrogencarbonate leads to direct isolation of the desired organic product. Subsequent reduction of the aqueous phase with sodium dithionite followed by aerial oxidation regenerates diphenyl diselenide which can then be recovered. Finally, *meta*-iodobenzoic acid is precipitated on acidification.

Iodoxybenzene is normally prepared in two steps *via* the corresponding dichloride.[12a] We have found, however, that commercial hypochlorite oxidation (Stevens [12b] reagent) of *meta*-iodobenzoic acid in acetic acid solution leads directly to the desired reagent. Consequently, since the only consumable oxidant in the overall process is commercial hypochlorite, this method represents an attractive economic proposition. Preliminary experiments have shown that *meta*-iodoxybenzoic acid and its congeners are *per se* interesting selective oxidants in organic chemistry.[13]

Iodoxy-compounds are frequently reported to be explosive.[12a] Iodoxy-compounds undergo deflagration at *ca.* 230 °C, more than 100 °C above the temperature used in the dehydrogenation reactions. Their decomposition is similar to that of per acids introduced into a bath at a comparable (230 °C) temperature.

TABLE 2

Dehydrogenation using *meta*-iodoxybenzoic acid and BSA or diphenyl diselenide as catalyst

	Reaction conditions *					
Substrate	Time (h)	Solvent	Catalyst (equiv.)	*meta*-Iodoxybenzoic (equiv.)	Enone or dienone	Yield (%)
Cholestan-3β-ol	20	A	D (0.2)	3.3		74
	3	B	E (0.2)	3.3		88
	2	C	E (0.2)	3.3		79
	16	B	E (0.03)	4.16		73
(11)	2.5	B	E (0.2)	3.2		86
(12)	2.5	B	D (0.14)	3.0		75
Methyl lithocholate (13)	3	B	E (0.2)	3.3		84
(14)	96	B	E (0.1)	5.0		89
(15)	95	B	E (0.2)	5.0		87
(18)	71	B	E (0.1)	7.5		64
Spiro[5.5]undec-1-en-3-one	3	B	D (0.1)	2.0	(20)	85
	36	B	E (0.02)	3.0	(20)	87
Spiro[4.5]dec-6-en-8-one	3	B	D (0.1)	2.0	(21)	70

* Reagents and solvents: A, benzene at reflux; B, toluene at reflux; C, chlorobenzene at reflux; D, benzeneseleninic anhydride; E, diphenyl diselenide.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were taken on a Varian T-60 instrument in deuteriochloroform with tetramethylsilane as internal standard. I.r. spectra were recorded on a Perkin-Elmer 257 instrument. Optical rotations were measured on a Perkin-Elmer 141 polarimeter in chloroform solution (unless stated to the contrary). Mass spectra were recorded with an AEI MS9 instrument. All solvents and reagents were purified and dried by standard techniques.

Dehydrogenation of Cholestan-3-one by Dinitrogen Trioxide catalysed by Diphenyl Diselenide.—A slow stream of dinitrogen trioxide [generated as required by dropwise addition of concentrated sulphuric acid onto sodium nitrite (50 g)] was passed into a solution of cholestan-3-one (1) (1.16 g, 3 mmol) and diphenyl diselenide (312 mg, 1 mmol) in chlorobenzene (50 ml) heated at 110 °C until reaction was complete (t.l.c.) (4 d). The reaction mixture was cooled and crystalline benzeneseleninic anhydride (720 mg) was filtered off. Evaporation of solvent under reduced pressure and

chromatography on silica gel (70—230 mesh) gave cholesta-1,4-dien-3-one (2) (725 mg, 63%), m.p. and mixed m.p. 111—112 °C (from methanol) (lit.,[14] 111.5—112.5 °C), $[\alpha]_D^{22}$ +28° (lit.,[15] +28°), $\lambda_{max.}$ 242 nm [ε 14 800) (lit.,[14] $\lambda_{max.}$ 242 nm (ε 15 000)], $\nu_{max.}$ 1 660, 1 620, 1 600, 1 290, 1 240, 885, and 810 cm^{-1}; *m/e* 382 (M^+, 100%).

Dehydrogenation of Cholestan-3-one by Iodosobenzene catalysed by Diphenyl Diselenide.—Iodosobenzene (5.5 g, 25 mmol) was added portionwise during a 12 h period to a solution of cholestan-3-one (1) (1.16 g, 3 mmol) and diphenyl diselenide (312 mg, 1 mmol) in chlorobenzene (50 ml) at 110 °C. Removal of solvent and column chromatography gave cholesta-1,4-dien-3-one (2) (750 mg, 65%), m.p. 110—112 °C (from methanol) identical with the above sample.

Dehydrogenation of Androst-4-ene-3,17-dione (3) *by Iodosobenzene catalysed by Diphenyl Diselenide.*—Iodosobenzene (3.3 g, 15 mmol) was added portionwise during a 12 h period to a stirred solution of androst-4-ene-3,17-dione (3) (572 mg, 2 mmol) and diphenyl diselenide (208 mg, 0.6 mmol) in chlorobenzene (35 ml) at 110 °C. Removal of solvent and column chromatography on silica gel gave androsta-1,4-diene-3,17-dione (314 mg, 55%), m.p. 140 °C (from acetone–hexane) (lit.,[16] 140 °C); $[\alpha]_D$ +118° (lit.,[16] 118°).

Iodoxybenzene Improved One-step Procedure.—Acetic acid (5 ml) was added dropwise to a vigorously stirred suspension of iodobenzene (2 g) in sodium hypochlorite solution (25 ml; 'Eau de Javel') at room temperature. An exothermic reaction took place with the formulation of a yellow precipitate (10 min). The mixture was stirred overnight at room temperature and the resultant, white precipitate was filtered off, washed with water, acetone, and finally ether, and then dried *in vacuo* at room temperature (1.75 g, 76%), m.p. 250—253 °C [lit.,[12] 230 °C (decomp.)]. The above experiment was successfully repeated on a larger scale using acetic acid (75 ml), iodobenzene (25 g), and sodium hypochlorite solution (400 ml), the temperature being kept less than 40 °C during addition to give 21.5 g (74%) of the title compound. *meta*-Iodoxybenzoic acid[10] [m.p. 245 °C (decomp.)] was prepared in an analogous manner [lit.,[10] m.p. 243 °C (decomp.)].

General Procedure for Oxidations with Iodoxybenzene Catalysed by Diphenyl Diselenide or Benzeneseleninic Anhydride.—Iodoxybenzene (300 mg) and diphenyl diselenide (20 mg) were heated and stirred in the indicated solvent (5 ml) (Table 1) until all the yellow colour of the diselenide had disappeared (10 min). The steroidal alcohol or ketone (100 mg) was then added and the reaction mixture was heated with stirring until t.l.c. indicated complete reaction. Removal of solvent and chromatographic separation afforded the required dienone.

General Procedure for Dehydrogenation with meta-*Iodoxybenzoic Acid Catalysed by Diphenyl Diselenide or Benzeneseleninic Anhydride with Recovery of* meta-*Iodobenzoic Acid and Diphenyl Diselenide.*—*meta*-Iodoxybenzoic acid (720 mg) and diphenyl diselenide (50 mg) were heated with stirring in the indicated solvent (20 ml) (Table 2) until the yellow colour of the diselenide disappeared (15 min). The steroid (300 mg) was added and heating and stirring were continued until t.l.c. indicated complete reaction. After cooling the reaction mixture was thoroughly extracted with saturated aqueous sodium hydrogencarbonate and the organic phase was washed with water and dried (Na_2SO_4). Removal of solvent and recrystallisation gave the corresponding steroidal dienone. The combined aqueous extracts were reduced by treatment at room temperature with a saturated solution of sodium dithionite (excess) for 1 h. The aqueous phase was then oxidized by a stream of air for 1 h to destroy the excess of hydrosulphite and diphenyl diselenide was recovered by extraction with toluene. After acidification with dilute sulphuric acid the precipitated *m*-iodobenzoic acid was filtered off, washed with water, and dried.

2-*Phenylselenocholest*-1-*en*-3-*one* (7).—A solution of cholestan-3-one (386 mg, 1 mmol), BSA (360 mg, 1 mmol), and toluene-*p*-sulphonic acid (5 mg) in glacial acetic acid (15 ml) was set aside at room temperature for 24 h. The reaction mixture was then poured into aqueous sodium hydrogencarbonate and thoroughly extracted with dichloromethane. The organic phase was dried and the solvent evaporated. Chromatography of the residue on a column of silica gel gave the title derivative (275 mg, 51%), m.p. and mixed m.p. 104—106 °C (from hexane) (lit.,[9] m.p. 104—107 °C; the m.p. 128—129 °C given is a misprint), $\nu_{max.}$ ($CHCl_3$) 1 666 cm^{-1}; δ 7.31 (5 H, m, ArH), 6.67 (1 H, s, 1-H), 0.93 (3 H, s, 10-Me), 0.64 (3 H, s, 18-Me); *m/e* 540 (M^+, 100%).

2-*Phenylselenocholesta*-1,4-*dien*-3-*one.*—2-Phenylselenocholest-1-en-3-one (540 mg, 1 mmol) and BSA (360 mg, 1 mmol) in chlorobenzene (25 ml) were stirred and heated at 110 °C for 4 h. Removal of solvent under reduced pressure and chromatography on silica gel (elution with benzene–ether, 9 : 1) afforded the title *dienone* (290 mg, 55%), m.p. 118—119 °C (from methanol), $\nu_{max.}$ ($CHCl_3$) 1 590, 1 617, and 1 640 cm^{-1}; δ 7.37 (5 H, m, ArH), 6.40 (1 H, s, 1-H), 6.06 (1 H, s, 4-H), 1.07 (3 H, s, 19-Me), and 0.66 (3 H, s, 18-Me) (Found: C, 73.65; H, 8.6. $C_{33}H_{46}OSe$ requires C, 73.72; H, 8.62%).

Dehydrogenation of Cholestan-3-one (1).—Cholestan-3-one (1) (100 mg, 0.26 mmol) with iodoxybenzene (200 mg) and BSA (18 mg) gave cholesta-1,4-dien-3-one (2) (83 mg, 84%), m.p. 110—112 °C (from methanol) (lit.,[14] 111.5—112.5 °C), $[\alpha]_D^{22}$ +28° (lit.,[7] +28°).

Oxidation and Dehydrogenation of Cholestan-3β-ol.—Cholestan-3β-ol (100 mg, 0.26 mmol) with iodoxybenzene (200 mg) and BSA (18 mg) gave cholesta-1,4-dien-3-one (2) (80 mg, 81%), m.p. 110—112 °C (from methanol) (lit.,[7] m.p. 111.5—112.5 °C) identical with the previous sample. Under identical conditions but in the presence of toluene-*p*-sulphonic acid (5 mg) the time for reaction was halved without diminishing the yield (77%). Replacement of iodoxybenzene by *m*-iodoxybenzoic acid (240 mg) in the above experiment gave the dienone (73 mg, 74%) after chromatographic separation. Diphenyl diselenide (16 mg) in conjunction with *m*-iodoxybenzoic acid (240 mg) also effected the above reaction to yield cholesta-1,4-dien-3-one (2) [88%, in toluene (5 ml) as solvent and 79%, in chlorobenzene as solvent]. Cholestan-3β-ol (1 g) with *meta*-iodoxybenzoic acid (3 g) and diphenyl diselenide (25 mg) in toluene (30 ml) gave, after 16 h, the above dienone (720 mg, 73%) and recovered *meta*-iodobenzoic acid (2.45 g, 92%).

Cholesta-1,4-*dien*-3-*one: use of Selenium Dioxide.*—Cholestan-3-one (386 mg, 1 mmol) with iodoxybenzene (1 g, 3 mmol) and selenium dioxide (55.5 mg, 0.5 mmol) in chlorobenzene (30 ml) gave, after column chromatography on silica gel, cholesta-1,4-dien-3-one (205 mg, 58%) identical with the above samples.

Dehydrogenation of Androst-4-ene-3,17-dione (3).—Androst-4-ene-3,17-dione (3) (100 mg) with iodoxybenzene (300 mg) and BSA (20 mg) gave androsta-1,4-diene-3,17-

dione (71 mg, 72%), m.p. 140 °C (from acetone–hexane) (lit.,[15] 140 °C); $[\alpha]_D$ +118° (lit.,[15] +118°).

Dehydrogenation of 11-*Oxoprogesterone: Catalytic Method.*—11-Oxoprogesterone (4) (100 mg) with iodoxybenzene (300 mg) and BSA (200 mg) gave 1-dehydro-11-oxoprogesterone (50 mg, 51%), m.p. 169—173 °C (from ether) (lit.,[16] 170—172 °C); $[\alpha]_D$[17] +195 (*c*, 0.9) [lit.,[16] +223° (*c*, 0.6)]; $\lambda_{max.}$ 240 nm (ε 13 100); $\nu_{max.}$ ($CHCl_3$) 1 595, 1 615, 1 653, and 1 695 cm^{-1}; *m/e* 326 (M^+, 72%). The acidic products formed in this reaction at longer reaction times were identified in separate experiments as follows. Dehydrogenation of 11-oxoprogesterone (2 g) with BSA (1 g) and iodoxybenzene (6 g) in benzene (100 ml) was continued for 60 h with portionwise addition of a further quantity of iodoxybenzene (16 g) during this period. After cooling the reaction mixture was extracted thoroughly with aqueous sodium hydroxide (1M) and the alkaline extract was treated with an excess of aqueous sodium dithionite. The solution was acidified with concentrated sulphuric acid and extracted with dichloromethane. The extract was dried (Na_2SO_4), evaporated, and treated with an ethereal solution of diazomethane. Removal of solvent gave a crude product which was chromatographed on a silica gel column (70—230 mesh). Elution with toluene gave diphenyl diselenide (826 mg, 95%). Further elution with toluene–ether (3 : 7) afforded 17β-*methoxycarbonylandrosta*-1,4-*diene*-3,11-*dione* (5; Me ester) (340 mg, 17%), m.p. 179—181 °C (from acetone–hexane), $[\alpha]_D$[21] +204.7° (*c*, 0.85); $\nu_{max.}$ ($CHCl_3$) 1 600, 1 618, 1 657, 1 701, and 1 623 cm^{-1}; δ 7.64 (d, 1 H, J_{12} 10 Hz, 1-H), 6.17 (dd, 1 H, J_{12} 10 Hz, J_{24} 2 Hz, 2-H), 6.07 (m, 1 H, 4-H), 3.65 (s, 3 H, OMe), 1.43 (s, 3 H, 19-Me), and 0.70 (s, 3 H, 18-Me); *m/e* 342 (M^+, 100%) (Found: C, 73.5; H, 7.65. $C_{21}H_{26}O_4$ requires C, 73.66; H, 7.65%).

In a second experiment, a solution of 11-oxoprogesterone (1 g) and BSA (4 g) in chlorobenzene (40 ml) was heated under reflux for 2.5 h. Work-up as described above gave 17β-methoxycarbonylandrosta-1,4-diene-3,11-dione (5; Me ester) (90 mg, 9%) identical with the above sample and a second product identified as 17β-methoxycarbonyl-17α-hydroxyandrosta-1,4-diene-3,11-dione (6; Me ester) (170 mg, 17%), m.p. 208—212 °C (from methanol) (lit.,[17] 206—209 °C); $[\alpha]_D$[21] +161.4° (*c*, 0.7); $\nu_{max.}$ ($CDCl_3$) 1 600, 1 619, 1 659, 1 706, 1 721, and 3 550 cm^{-1}; δ 7.35 (d, 1 H, $J_{1,2}$ 10 Hz, 1-H), 6.10 (dd, 1 H, $J_{1,2}$ 10 Hz, $J_{2,4}$ 2 Hz, 2-H), 6.01 (m, 1 H, 4-H), 3.72 (s, 3 H, OMe), 1.42 (s, 3 H, 19-Me), and 0.72 (s, 3 H, 18-Me); *m/e* 358 (M^+, 95%).

Dehydrogenation of Spiro[5.5]*undec*-1-*en*-3-*one.*—(*a*) Spiro[5.5]undec-1-en-3-one (1.64 mg, 10 mmol) with *meta*-iodoxybenzoic acid (5.6 g, 20 mmol) and BSA (0.36 g, 1 mmol) in toluene (40 ml) for 3 h gave after basification with aqueous sodium hydroxide (1M) and distillation spiro[5.5]-undeca-1,4-dien-3-one (20) (1.37 g, 85%) which crystallised on cooling, m.p. 85—88 °C (lit.,[11] m.p. 86—88 °C), δ 6.29 (2 H, C*H*=CH–CO) and 7.13 (2 H, CH=C*H*–CO). Treatment of the aqueous extract gave recovered diphenyl diselenide (311 mg, 100%) and *m*-iodobenzoic acid (4.4 g, 89%).

(*b*) Spiro[5.5]undec-1-en-3-one (1.64 g, 10 mmol) with *meta*-iodoxybenzoic acid (5.6 g, 20 mmol) and diphenyl diselenide (62.4 mg, 0.2 mmol) in toluene (40 ml) for 18 h followed by addition of further *meta*-iodoxybenzoic acid (2.8 g, 10 mmol) and a further period under reflux (18 h) gave spiro[5,5]undeca-1,4-dien-3-one (1.40 g, 87%) identical with the above sample, recovered diphenyl diselenide (13 mg, 21%), and *m*-iodobenzoic acid (5.3 g, 72%).

Dehydrogenation of Spiro[4.5]*dec*-6-*en*-8-*one.*—(*a*) Spiro[4.5]dec-6-en-8-one (375 mg, 2.5 mmol) with BSA (900 mg, 2.5 mmol) in chlorobenzene (20 ml) at 100 °C for 1 h followed by a further addition of BSA (450 mg, 1.25 mmol) and heating for 1 h gave after chromatography spiro[4.5]-deca-6,9-dien-8-one (21) [11] (286 mg, 77%), m.p. 33—35 °C, δ 6.26 (2 H, C*H*=CH–CO), 6.91 (2 H, CH=C*H*–CO).

(*b*) Spiro [4.5]dec-6-en-8-one (750 mg, 5 mmol) with BSA (180 mg, 0.5 mmol) and *meta*-iodoxybenzoic acid (2.8 g, 10 mmol) gave spiro[4.5]deca-6,9-dien-8-one (520 mg, 70%) identical with the previous sample. Diphenyl diselenide (56 mg, 36%) and *meta*-iodobenzoic acid (2.1 g, 85%) were recovered.

17α-*Acetoxy*-16β-*methylpregna*-1,4,9-*triene*-3,20-*dione by Dehydrogenation of Compound* (11).—The ketone (11) (300 mg) with diphenyl diselenide (52 mg) and *meta*-iodoxybenzoic acid (720 mg) gave the title *dione* (255 mg, 86%), m.p. 230—233 °C (from acetone–hexane), $[\alpha]_D$[19] +10° (*c*, 0.9); $\nu_{max.}$ ($CHCl_3$) 1 598, 1 617, 1 658, 1 707, and 1 721 cm^{-1}; δ 7.11 (1 H, d, J_{12} 10 Hz, 1-H), 6.22 (1 H, dd, J_{12} 10 Hz, $J_{2,4}$ 1.5 Hz, 2-H), 6.04 (1 H, m, 4-H), 5.52 (1 H, d, broad, 11-H), 2.08 (3 H, s, COMe), 1.96 (3 H, s, OCOMe), 1.41 (3 H, s, 19-Me), 1.37 (3 H, d, *J* 7 Hz, 16-Me), and 0.69 (3 H, s, 18-Me); *m/e* 382 (M^+, 1%), 322 (M^+ − HOAc; 20%) and 273 (M^+ − HOAC − Ac, 100%) (Found: C, 75.25; H, 7.9. $C_{24}H_{30}O_4$ requires C, 75.35; H, 7.91%). Diphenyl diselenide (47 mg, 90%) and *meta*-iodobenzoic acid (550 mg, 86%) were also recovered.

17α-*Acetoxy*-16α-*methylpregna*-1,4,9-*triene*-3,20-*dione by Dehydrogenation of the Ketone* (12).—The ketone (12) (160 mg) with BSA (30 mg) and *meta*-iodoxybenzoic acid (360 mg) gave the title *dienone* (110 mg, 75%), m.p. 217—220 °C (from acetone–hexane), $[\alpha]_D$[19] +1.2° (*c*, 0.9); $\nu_{max.}$ ($CHCl_3$) 1 601, 1 619, 1 658, 1 704, and 1 728 cm^{-1}; δ 7.07 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.20 (1 H, dd, $J_{1,2}$ 10 Hz and $J_{2,4}$ 1.5 Hz, 2-H), 6.02 (1 H, m, 4-H), 5.49 (1 H, d, broad, H-11), 2.09 (3 H, s, COMe), 0.93 (3 H, d, *J* 7 Hz, 16-Me), 0.70 (3 H, s, 18-Me); *m/e* 382 (M^+, 15%), 322 (M^+ − HOAc, 35%) and 279 (M^+ − HOAc-Ac, 100%) (Found: C, 75.25; H, 7.9. $C_{24}H_{30}O_4$ requires C, 75.35; H, 7.91%). Diphenyl diselenide (23 mg, 89%) and *m*-iodobenzoic acid (265 mg, 80%) were also recovered.

Dehydrogenation of Lithocholic Acid Methyl Ester (13).—The ester (13) with diphenyl diselenide (16 mg) and *meta*-iodoxybenzoic acid (240 mg) gave the corresponding *dienone* (83 mg, 84%), m.p. 131—133 °C, $[\alpha]_D$[22] +25° (*c* 1.0) $\nu_{max.}$ ($CHCl_3$) 1 593, 1 609, 1 647, and 1 719 cm^{-1}; δ 6.98 (1 H, d, $J_{1,2}$ 9.5 Hz, 1-H), 6.15 (1 H, dd, $J_{1,2}$ 9.5 Hz, $J_{2,4}$ 1.5 Hz, 2-H), 6.04 (1 H, m, 4-H), 3.64 (3 H, s, OMe), 1.22 (3 H, s, 19-Me), and 0.77 (3 H, s, 18-Me); *m/e* 384 (M^+, 37%) and 122 (100%) (Found: C, 77.85; H, 9.35. $C_{25}H_{36}O_3$ requires C, 78.08; H, 9.44%). Diphenyl diselenide (14 mg, 87%) and *meta*-iodobenzoic acid (190 mg, 90%) were also recovered.

Dehydrogenation of Methyl 3α-*Acetyl*-12-*oxolithocholate* (14).—The ester (14) [18] (220 mg, 0.5 mmol) with diphenyl diselenide (31 mg, 0.1 mmol) and *meta*-iodoxybenzoic acid (750 mg) in toluene (20 ml) gave methyl 3α-acetyl-9(11)-dehydro-12-oxolithocholate (16) (197 mg, 89%), m.p. 147—148 °C (lit.,[19] 145—147 °C) $[\alpha]_D$[20] +110° (*c*, 1.0) (lit.,[19] +110.8°), $\lambda_{max.}$ (EtOH) 241 nm (log ε 3.96) [lit.,[19] 241 nm (log 4.06)].

Dehydrogenation of Methyl 3α-*Formyl*-12-*oxolithocholate* (15).—To a stirred solution of 3α-formyl-12-oxolithocholic acid (824 mg, 2 mmol), and *N*,*N*,*N*′,*N*′-tetramethyl-*N*″-t-butylguanidine [20] (350 mg) in dichloromethane

(20 ml) at 0 °C was added dropwise *via* a syringe methyl iodide (313 mg, 2.2 mmol). After 15 min, the solvent was removed under reduced pressure and the residue chromatographed directly on silica gel (eluant dichloromethane–diethyl ether mixtures) to afford the title *ester* (15) (743 mg, 87%), m.p. 172—173 °C (from dichloromethane–diethyl ether); $[\alpha]_D^{20}$ +112° (*c*, 1.0), $\nu_{max.}$ ($CHCl_3$) 1 740—1 680br cm^{-1}; δ 3.55 (3 H, s, OMe), 4.67 (1 H, m, 3βH), and 7.8 (1 H, s, CHO); *m/e* 432 (M^+) (Found: C, 72.35; H, 9.35. $C_{26}H_{40}O_5$ requires C, 72.19; H, 9.32%).

The ester (15) (214 mg, 0.5 mmol) with diphenyl diselenide (31 mg, 0.1 mmol) and *meta*-iodoxybenzoic acid (750 mg) in toluene (20 ml) for 96 h gave the *enone* (17) (133 mg, 62%), m.p. 147—149 °C (from dichloromethane–ether), $[\alpha]_D^{20}$ +114° (*c*, 1.0), $\lambda_{max.}$ 241 nm (log ε 4.0); $\nu_{max.}$ ($CHCl_3$) 1 710br, 1 675, 1 600, and 1 175 cm^{-1}; δ 7.85 (1 H, s, CHO), 5.67 (1 H, m, 11 H), 4.83 (1 H, m, 3βH), 3.63 (3 H, s, Me); *m/e* 430 (M^+) (Found: C, 72.25; H, 9.0. $C_{26}H_{38}O_5$ requires C, 72.53; H, 8.90%).

Dehydrogenation of Methyl Deoxycholate (18).—A mixture of the ester (18) (406 mg, 1 mmol), *meta*-iodoxybenzoic acid (1.4 g, 5 mmol), and diphenyl diselenide (31 mg, 0.1 mmol) in toluene (20 ml) was refluxed under a nitrogen atmosphere. After 32 h a further portion of *meta*-iodoxybenzoic acid (750 mg, 2.5 mmol) was added and heating was continued for a further 39 h. Normal work-up followed by medium-pressure column chromatography on silica gel (eluant dichloromethane–diethyl ether mixtures) gave the 1,4,9(11)-triene-3,12-dione (19) (254 mg, 64%), m.p. 137—139 °C (from dichloromethane–ether) (lit.,[21] 137—139 °C); $[\alpha]_D^{20}$ 72° (*c* 1.0); $\lambda_{max.}$ 237 nm (ε 28 300) [lit.,[21] $\lambda_{max.}$ 236 nm (ε 28 800)]; δ 0.95 (6 H, br, 18-, 21-Me), 1.50 (3 H, s, 19-Me), 3.59 (3 H, s, OMe), 5.66 (1 H, d, *J* 2 Hz, 4-H), 6.05 (1 H, br, 11-H), 6.23 (1 H, dd, *J* 10 Hz and *J* 2 Hz, 2-H), and 7.01 (1 H, d, *J* 10 Hz, 1-H); $\nu_{max.}$ (Nujol) 1 745, 1 680, 1 665, 1 625, 1 615, and 1 600 cm^{-1}.

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