Dissolving Metal Reduction of Esters to Alkanes. A Method for the Deoxygenation of Alcohols

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Diverse carboxylic esters have been reduced with dissolving Group 1A metals. Using lithium in ethylamine, sterically hindered esters (RCO_2R') were deoxygenated giving the alkane (R'H) whereas non-hindered esters regenerated the parent alcohol (R'OH). This permitted the selective deoxygenation of diesters. Conversely, potassium–sodium eutectic solubilised with 18-crown-6 in t-butylamine and tetrahydrofuran (THF) efficiently deoxygenated both hindered and non-hindered esters. In the absence of nucleophiles at ambient temperature the principal reaction of carboxylic ester radical anions was deoxygenation.

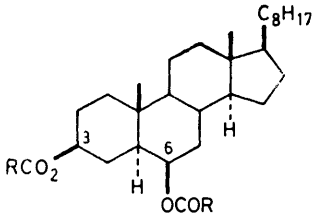
THE selective replacement of a hydroxy-group by hydrogen (deoxygenation) is an important synthetic transformation. Normally, prior conversion of the alcohol into a suitable derivative is required. Although a number of good methods [1,2] are now available, alternative processes are always of interest. We now report the

TABLE 1

Dissolving metal reductions

Entry	Ester (mmol)	Solvents (ml)	Metal (mmol)	Crown ether (mmol)	Products
1	(1a), 0.16	$EtNH_2$, 3; THF, 1	Li, 14		(2a) 75%
2	(1a), 0.16	Bu^tNH_2, 4	K, 2.56	0.29	(2a) 86%
3	(1b), 0.1	$EtNH_2$, 13	Li, 21		(2a) 40%; (2b) 32%
4	(1b), 0.14	Bu^tNH_2, 3; THF, 1	K, 2.5	1.8	(2b) 62%; (2a) 29%
5	(1b), 0.20	Bu^tNH_2, 3	K, 2.5	0.4	(2b) 56%; (2a) 27%
6	(1b), 1.49	DME, 20; THF, 3	K, 51	5.3	(2b) 51%; (2a) 23%; (2d) 11%; (2c) 0.7%
7	(1b), 0.17	Bu^tNH_2, 5; THF, 0.3	Rb, 2.3	2.3	(2a) 45%; (2b) 30%
8	(1c), 0.13	$EtNH_2$, 4	Li, 14		(2a) 61%; (2b) 15%
9	(1d), 0.20	$EtNH_2$, 3	Li, 14		(2a) 55%; (2b) 16%
10	(1d), 0.80	Bu^tNH_2, 10; THF, 10	K, 20	3.3	(2b) 65%; (2a) 9%; (2d) 7%; (2c) 4%
11	(1d), 0.19	DME, 5; THF, 0.5	K, 5	0.38	(2b) 37%; (2a) 30%
12	(1d), 0.20	Bu^tNH_2, 4; THF, 0.5	K, 2.5	0.38	(2b) 71%; (2a) 19%
13	(1e), 0.97	Bu^tNH_2, 30; THF, 4	K, 20	8.3	(2b) 37%; (2d) 30%; (2c) 10%; (2a) 7%
14	(1e), 0.13	Bu^tNH_2, 4; THF, 0.5	K, 7.7	0.76	(2b) 79%; (2a) 9%
15	(1f), 0.46	Bu^tNH_2, 8; THF, 12	K, 3.8	1.7	(2d) 45%; (2b) 27%; (2a) 8%; (2c) 6%; (13a) 92%
16	(1g), 0.14	$EtNH_2$, 3	Li, 14		(2a) 78%
17	(1g), 0.35	DME, 15; THF, 5	K 46	9.4	(2b) 45%; (2a) 36%; (2d) 5%
18	(3a), 0.65	Bu^tNH_2, 20; THF, 3	K, 33	5.3	(4d) 27%; (4c) 39%
19	(3b), 0.31	Bu^tNH_2, 10; THF, 3	K, 16	1.7	(2b) 57%; (4c) 18%; (2d) 4%
20	(3b), 0.12	$EtNH_2$, 12	Li, 29		(2b) 66%; (4c) 8%
21	(4a), 1.51	Bu^tNH_2, 25; THF, 10	K, 41	15	(4c) 55%; (4d) 29%
22	(4b), 0.18	$EtNH_2$, 25	Li, 43		(5a) 81%; (4e) 8%
23	(4b), 1.86	Bu^tNH_2, 20; THF, 10	K, 51	13	(5a) 24%; (4d) 23%; (5c) 12%
24	(4b), 0.62	$EtNH_2$, 5	Li, 36		(5a) 34%; (2a) 17%; (5c) 14%; (4e) 5%
25	(5b), 2.45	Bu^tNH_2, 15; THF, 12	K, 38	14	(5a) 76%; (5c) 20%
26	(6a), 0.78	Bu^tNH_2, 20; THF, 4	K, 20	4.9	(2b) 50%; (2d) 30%
27 [a]	(6a), 0.95	Bu^tNH_2, 10, Et_2O, 2	K, 15	3.8	(2b) 73%; (2d) 6%; (6d) 2%
28 [b]	(6b), 1.04	Bu^tNH_2, 10; THF, 2	K, 8.8; Na, 2.6	2.5	(2d) 73%; (2b) 15%
29	(6b), 1.03	Bu^tNH_2, 12; THF, 10	K, 22; Na, 8.7	5.3	(2d) 78%; (2b) 15%
30 [c]	(7a), 0.70	$EtNH_2$, 22	Li, 43		(5c) 38%; (7c) 30%; (7b) 7%
31 [d]	(8a), 0.38	$EtNH_2$, 25	Li, 43		(8c) 75%; (8b) 10%
32	(9a), 0.11	$EtNH_2$, 13	Li, 11		(9b) 85%
33	(10), 0.96	Bu^tNH_2, 12; THF, 17	K, 20; Na, 11	1.4	(11) 87%; (12) 9%
34	(13e), 3.06	Bu^tNH_2, 10; Et_2O, 3	K, 36	5.87	(13a) 95%
35	(13f), 1.65	Bu^tNH_2, 10; Et_2O, 5	K, 33	9.5	(13a) 90%; $n\text{-}C_{18}H_{37}OH$ 53%; $n\text{-}C_{18}H_{38}$ 40%
36 [b]	(13f), 0.40	Bu^tNH_2, 12	K, 8.8; Na, 3.7	0.98	$n\text{-}C_{18}H_{38}$ 74%; $n\text{-}C_{18}H_{37}OH$ 24%
37	(13h), 1.22	Bu^tNH_2, 12; Et_2O, 2	K, 10	2.35	(13c) 78%
38	$n\text{-}C_{18}H_{37}OAc$, 2.0	Bu^tNH_2, 10; Et_2O, 10	K, 13	4.06	$n\text{-}C_{18}H_{37}OH$ 78%
39 [b]	$n\text{-}C_{18}H_{37}OAc$, 0.40	Bu^tNH_2, 10; THF, 2	K, 8.6; Na, 2.8	0.97	$n\text{-}C_{18}H_{37}OH$ 61%; $n\text{-}C_{18}H_{38}$ 33%
40 [b,e]	$n\text{-}C_{18}H_{37}OAc$, 0.40	Bu^tNH_2, 12	K, 8.2; Na, 2.8	0.99	$n\text{-}C_{18}H_{38}$ 49%; $n\text{-}C_{18}H_{37}OH$ 34%

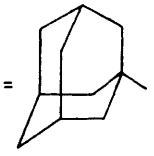
[a] Reaction carried out at −60 °C. [b] Crown ether refers to aza-crown (15b) otherwise 18-crown-6. [c] Ester added in ethylamine (10 ml), tabulated volume is total. Hydrocarbons separated by p.l.c. on silver nitrate-impregnated silica. [d] Ester added in ethylamine (15 ml), tabulated volume is total. [e] Ester added in Bu^tNH_2 (2 ml), tabulated volume is total.

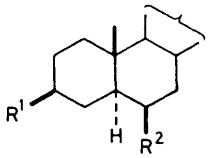


(1)

a; R = H
b; R = Me
c; R = Et
d; R = Pr^i
e; R = Bu^t
f; R = Ad
g; R = Ph

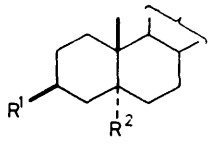
Ad =





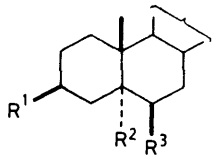
(2)

a; $R^1 = R^2 = OH$
b; $R^1 = OH$, $R^2 = H$
c; $R^1 = H$, $R^2 = OH$
d; $R^1 = R^2 = H$
e; $R^1 = Bu^tCO_2$; $R^2 = OH$
f; $R^1 = AdCO_2$; $R^2 = OH$



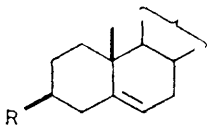
(3)

a; $R^1 = OAc$, $R^2 = OH$
b; $R^1 = R^2 = OAc$



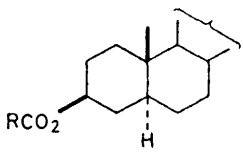
(4)

a; $R^1 = R^3 = OAc$, $R^2 = OH$
b; $R^1 = R^2 = R^3 = OAc$
c; $R^1 = R^3 = OH$, $R^2 = H$
d; $R^1 = R^3 = H$, $R^2 = OH$
e; $R^1 = R^2 = R^3 = OH$



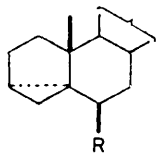
(5)

a; R = OH
b; R = OAc
c; R = H



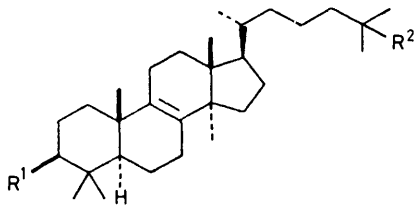
(6)

a; R = Me
b; R = Bu^t
c; R = Ad
d; R = AcCH$_2$



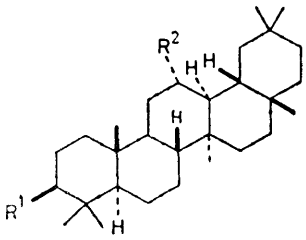
(7)

a; R = OAc
b; R = H
c; R = OH



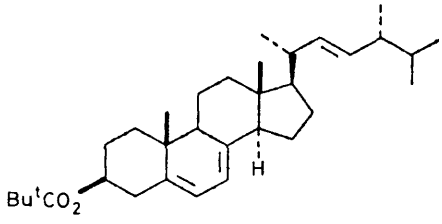
(8)

a; $R^1 = R^2 = OAc$
b; $R^1 = R^2 = OH$
c; $R^1 = OH$, $R^2 = H$

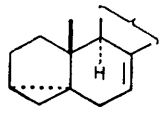


(9)

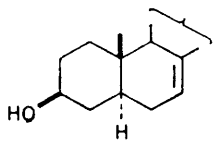
a; $R^1 = R^2 = OAc$
b; $R^1 = OH$, $R^2 = H$



(10)



(11)



(12)

Ad-X
(13)

a; X = CO_2H
b; X = CHO
c; X = CH_2OH
d; X = CONHEt
e; X = CO_2Et
f; X = $CO_2C_{17}H_{35}$-n
g; X = COCl
h; X = CH_2OAc

details of our work in which deoxygenation was achieved *via* reduction of a carboxylic ester derivative with a dissolving metal system,[3,4] as well as additional experiments.

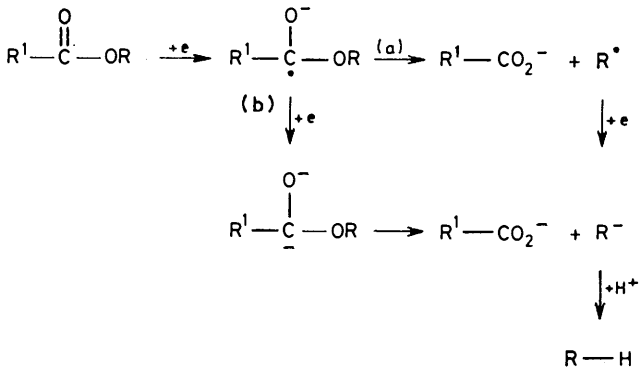
Both the classical Bouveault–Blanc [5] and acyloin [6] reduction of esters proceed *via* acyl oxygen fragmentation subsequent to electron transfer. In contrast to these well established procedures, we now consider that at ambient temperature *the principal pathway on the dissolving metal reduction of alkyl carboxylic esters is the formation of alkane and carboxylic acid anion.* These are formed *via* exclusive alkyl–oxygen cleavage of the ester radical-anion. Alternative products are derived *via* ester transacylation (see below).

The results obtained on the reductions of diesters of 5α-cholestane-3β,6β-diol (1a—g) are summarised in Table 1. Either lithium in ethylamine or potassium and 18-crown-6 in t-butylamine or 1,2-dimethoxyethane were used as reductants. The use of t-butylamine or 1,2-dimethoxyethane was prompted by the need for a less nucleophilic medium (see below). Particular attention is drawn to the use of 18-crown-6 to solubilise potassium giving royal-blue reducing solutions.[7] In all cases (Table 1), where deoxygenation was observed, this was greater at the more sterically hindered 6β-position. There was also a trend for increased deoxygenation as the bulk of the acyl substituent increased (compare experiments 4, 10, 13, and 15).

Reductions of selected ester derivatives of other alcohols are also summarized in Table 1. An attraction of

the present method of deoxygenation, and one not shared by alternative procedures,[1] is the useful selectivity that was observed when a molecule contains two (or more) ester groups in sterically different environments. The preparation of the acetate ester of a hindered alcohol is not normally difficult. For preparative purposes, the selective deoxygenation of these acetates by lithium in ethylamine would be the method of choice. The diesters (8a) and (9a) illustrate this point admirably (entries 31 and 32, Table 1). Effective yields were particularly good since the only side-reaction was the regeneration of the starting alcohol.

Possible mechanisms for the deoxygenation reaction are depicted in Scheme 1. In pathway (a) the initially



SCHEME 1

formed radical anion fragments to give an alkyl radical and carboxylate anion. Alternatively, in pathway (b), the radical anion is further reduced to the dianion which then collapses to yield a carbanion plus carboxylate anion. Under the reaction conditions reduction of an alkyl radical to the corresponding carbanion would be rapid. Thus, the formation of cholesterol (5a) in the reduction of cholestane-3β,5α,6β-triyl triacetate (4b) was presumably the result of displacement of the acetoxy-group from C-6 by a carbanion at C-5 (or *vice versa*) (Table 1, entries 22—24).

Reduction of 3β,5α-cyclocholestan-6β-yl acetate (7a) afforded a hydrocarbon fraction (45%) which on separation using silver nitrate-impregnated Kieselgel GF_{254} gave cholest-5-ene (5c) (85%) and 3β,5α-cyclocholestane (7b) (15%) (Table 1, entry 30). This result is consistent with the occurrence of pathway (a), since the rapid rearrangement of the 3α,5α-cyclocholestan-6-yl radical into the more stable cholest-5-en-3-yl radical is a well established process.[8] Conversely the reduction of ergosteryl pivaloate (10) gave 3α,5α-cycloergosta-7,22-diene (11) (87%) and ergosta-7,22-dien-3β-ol (12) (9%) (Table 1, entry 33). Both these reactions support our belief that deoxygenation occurs predominantly, if not exclusively, *via* fragmentation of the radical anion [Scheme 1, pathway (a)]. The reduction of carboxylic esters to alkanes by photolysis in hexamethylphosphoric triamide and water has been shown to occur by a similar mechanism.[9]

Both pathways in Scheme 1 require that the acyl component of the ester is released at the carboxylate oxidation level. To test this point experimentally, the reduction of esters of adamantane-1-carboxylic acid (13a) was studied. A control experiment established that adamantane-1-carboxylic acid (13a) was stable to treatment with potassium and 18-crown-6 in t-butylamine under our standard conditions. Prolonged reaction with a large excess of lithium in ethylamine, however, gave adamantane-1-carbaldehyde (13b) (51%) and adamantan-1-ylmethanol (13c) (9%), in addition to recovered acid (13a) (10%). The reductions of 5α-cholestane-3β,6β-diyl bis(adamantane-1-carboxylate) (1f) and octadecyl adamantane-1-carboxylate (13f) (Table 1, experiments 15 and 35) gave adamantane-1-carboxylic acid (13a) in yields of 92% and 90% respectively. In each case the yield of the acid was substantially higher than that of the deoxygenation products. Competitive hydrolysis of the ester by adventitious water could have accounted for this fact, but seemed improbable in view of the precautions taken to ensure anhydrous conditions. Furthermore, reduction of the ester (6c) with the prior addition of iodomethane to scavenge any hydroxide ion present, did not lead to an increase in the ratio of 5α-cholestane (2d) to adamantane-1-carboxylic acid (13a).

The process which competes with deoxygenation and in which the starting alcohol is regenerated must therefore involve deacylation of the ester by some other nucleophile, Nu^- (Scheme 2). In the event that the nucleophile is oxygen-centred, subsequent reduction of the newly formed ester (16) would then generate the carboxylate anion. Convincing proof for the correctness of the above postulate followed from the isolation of 5α-cholestane (2d) (15% and 32% respectively) when a mixture of ethyl adamantane-1-carboxylate (13e) or ethyl acetate and 5a-cholestan-3β-ol (2b) was reduced. Table 2 summarises the reduction of 5α-cholestan-3β-yl adamantane-1-carboxylate (6c) under various conditions. With lithium in ethylamine there was little deoxygenation or formation of adamantane-1-carboxylic acid (13a). That this was due to the occurrence of transacylation is evident from the isolation of major amounts of the ethylamide (13d) in experiments 6 and 7 (Table 2). This problem was overcome by the use of t-butylamine as solvent. At lower temperatures transacylation was suppressed (experiment 9), as was radical-anion fragmentation (deoxygenation) (experiments 4 and 5).

The source of the nucleophile implicated in Scheme 2 thus remained to be established. It is known that tetrahydrofuran is fragmented by strong bases.[10] We have now found that 18-crown-6 is broken down by treatment with potassium in t-butylamine. Acylation of the decomposition products with 1-naphthoyl chloride gave a complex mixture from which *N*-t-butylnaphthalene-1-carboxamide and three oily esters tentatively assigned as (14a, b, and c) were isolated by chromatography. Thus, deoxygenation by dissolving metal reduction of carboxylic esters was limited by competitive deacyclation by solvent or crown ether-derived nucleo-

TABLE 2

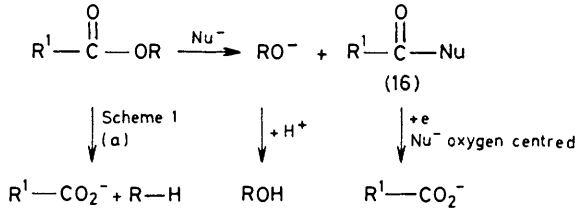
Dissolving-metal reduction of 5α-cholestan-3β-yl adamantane-1-carboxylate (6c)

Entry	Metal (mmol)	Solvents (ml)	Temp. (°C)	Ester (6c) (mmol)	Crown ether (mmol)	Products (2d)	(2b)	(13a)	(13c)	(13d)
1	K, 38	Bu^tNH_2, 30; THF, 10	46	1.04	11	43	57	96	2	
2	K, 20	Bu^tNH_2, 10; THF, 18	20	1.11	5	53	43	86		
3 [a]	K, 27	DME, 55; MeI, 2	20	1.20	7	30	57	92		
4	K, 36	Bu^tNH_2, 30; THF, 20	−45	1.09	6	27	66	77	5	
5 [b]	K, 36	Bu^tNH_2, 30; THF, 20	−53	1.04	6	15	81	71		
6	Li, 22	$EtNH_2$, 20; THF, 20	17	1.15	0	7	85	4	4	92
7 [c]	Li, 65	$EtNH_2$, 40; THF, 33; Bu^tOAc, 0.22	17	1.03	0	5	92	2	29	51
8 [d]	Li, 274	$EtNH_2$, 80	17	1.17	0	4	94	4	65	
9	Li, 29	$EtNH_2$, 20; THF, 10	−73	1.17	0	1	93		69	0.5
10 [e]	Na, 108	PhMe, 3; EtOH, 1	60	0.45	0		58		66	
11 [f]	K, 8.6; Na, 2.9	Bu^tNH_2, 10; THF, 2	25	0.40	1.09	90	6			
12	K, 28; Na, 8.7	Bu^tNH_2, 10; THF, 3	46	0.36	5.3	78	20	95	0	
13 [g]	K, 28; Na, 8.7	Bu^tNH_2, 10; THF, 3	25	0.36	5.3	57	26	81	13	
14 [g]	K, 28; Na, 8.7	Bu^tNH_2, 10; THF, 3	3	0.36	5.3	59	33	78	13	
15 [g]	K, 28; Na, 8.7	Bu^tNH_2, 10; THF, 3	−48	0.36	5.3	51	46	61	23	

[a] Iodomethane was added prior to the ester. A precipitate immediately formed. The ester was added in DME (40 ml) after the addition of more crown ether (25 mmol) (total quantities of DME and crown ether given in the Table). [b] The reaction required 4 h to go to completion. A minor component (10 mg), m.p. 80—86 °C, $\nu_{max.}$(CHCl$_3$) 1 090, 980, and 960 cm^{-1} (Found: C, 80.2; H, 11.65%) was also isolated. [c] A solution of t-butyl acetate in THF (3 ml) was added prior to the ester. The volume of THF in the Table is total. [d] The ester was added last as a solid. [e] Standard Bouveault–Blanc reduction. [f] Acid (13a) not isolated. Reaction carried out using crown–amine (15b). Otherwise crown ether refers to 18-crown-6. [g] Alcohols (2b) and (13c) were isolated together from chromatography. Ratios determined by n.m.r. spectroscopy.

philes. The selective deoxygenation of sterically hindered esters was a result of the suppression of this competitive deacylation.

Since 18-crown-6 was unstable under the reaction conditions we sought an alternative non-nucleophilic reduction system. Eschweiler–Clarke methylation of 1,4,7,10,13,16-hexa-azacyclo-octadecane (15a) gave the

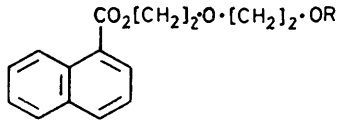


SCHEME 2

crown amine (15b) (92%). In t-butylamine the aza-crown (15b) failed to solubilise potassium metal. However with potassium–sodium eutectic [11] an intense royal-blue solution was obtained. This was stable under argon for several days at room temperature. As anticipated, the deoxygenation of esters (6b), (6c), and (13f) proceeded in excellent yields (Table 1, entries 28 and 36; Table 2, entry 11). Even the non-hindered primary ester octadecyl acetate was deoxygenated (49%). These results emphasise that deoxygenation is the principle reaction of ester radical-anions.

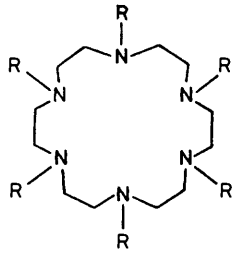
In a series of blank experiments the reduction of esters by potassium–sodium eutectic solubilised by 18-crown-6 in t-butylamine was examined. The eutectic system, presumably containing K^+Na^- [7] was superior to potassium, being more stable and more intensely coloured. This permitted rapid substrate addition without intermittent discharge of colour. Pivaloates (6b) and (10) and adamantane-1-carboxylate (6c) were deoxygenated in high yield (Tables 1 and 2).

The potassium–sodium eutectic and 18-crown system was used to examine the effects of temperature on the



(14)

a; R = H
b; R = CH_2CH_2OEt
c; R = $(CH_2CH_2O)_2Et$



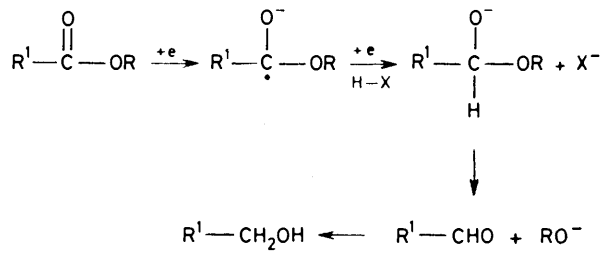
(15)

a; R = H
b; R = Me

reduction of 5α-cholestan-3β-yl adamantane-1-carboxylate (6c) (Table 2, entries 12—15). With a decrease in temperature, deoxygenation and formation of adamantane-1-carboxylic acid (13a) were suppressed. The two-electron Bouveault–Blanc product (13c) was formed in

increased yield at low temperature; this, presumably resulted from an increase in the lifetime of the ester radical-anion.

The conclusion that the radical anions derived from non-phenolic esters normally fragment to give the carboxylate anion and radical (Scheme 1, pathway a) makes the Bouleault–Blanc and acyloin reactions curiosities. We explain the Bouveault–Blanc reaction by a protonation of the ester radical-anion concerted with the second electron-transfer. This (Scheme 3) allows the



SCHEME 3

acyl-oxygen fission to take place with formation of the alkoxide and the aldehyde. Further reduction and protonation of the latter then affords the primary alcohol ($R'CH_2OH$). Protonation of the radical anion by ethanol prior to the transfer of the second electron is considered as excluded by pK_a considerations.[12a] The reason why the radical anion does not fragment immediately in ethanol solution is thought to result from solvation of the anion by the solvent. Clearly ester radical-anions are sensitive to solvation and to temperature (see further below).

The acyloin condensation is more difficult to rationalise. Two different types of experimental conditions are used.[5] At elevated temperatures in benzene or toluene in the presence of finely divided droplets of metal the reaction must be surface reaction in which the ester radical-anion remains bonded to the metal before coupling. The homogeneous conditions use liquid ammonia under reflux (−33 °C).[12b] Here we consider that the radical anion of the ester is formed and indeed, it has been trapped by alkylation.[13] It does not fragment quickly, however, because of the low temperature.

EXPERIMENTAL

M.p.s were determined on a Kofler hot stage and are uncorrected. Optical rotations were recorded as chloroform solutions. Chromatography was carried out on Merck Kieselgel 60 or H or B.D.H. M.F.C. grade materials. Compounds were eluted with petroleum–dichloromethane–diethyl ether–ethyl acetate gradients. P.l.c. was carried out on Merck Kieselgel GF_{254}; developing solvents are given in parentheses. Solvents and reagents were purified [14] before use. Light petroleum and petroleum refer to the reagents with respective boiling ranges 40—60 and 60—80 °C. DME refers to 1,2-dimethoxyethane. 18-Crown-6 was purified *via* the acetonitrile complex and double distillation;[15] the commercial reagent is unsatisfactory unless purified. Reductions were carried out using rigorously dried reagents [14] and with the apparatus under argon or oxygen-free nitrogen. Work-up refers to dilution with water and extraction into diethyl ether, drying (over anhydrous sodium or magnesium sulphate), and rotary evaporation (≤ 60 °C). The following products (Tables 1 and 2) were identified by spectral data and by comparisons with authentic samples:

(2a), m.p. 190—192 °C, $[\alpha]_D^{25}$ +12.2° (*c* 1.143) (lit.,[16] 192 °C, +13°); (2b), m.p. 141—142 °C, $[\alpha]_D^{23}$ +24.1° (*c* 0.236) (lit.,[17] 142 °C, +24°); (2c), m.p. 80—81 °C, $[\alpha]_D^{23}$ +7.5° (*c* 0.376) (lit.,[18] 81 °C, +8°); (2d), m.p. 79—80 °C, $[\alpha]_D^{23}$ +23.9° (*c* 1.252) (lit.,[17] 80 °C, +24°); (4c), m.p. 225—226 °C, $[\alpha]_D^{23}$ +19.6° (*c* 0.135) (lit.,[16] 225 °C, +20°); (4d), m.p. 106—107 °C, $[\alpha]_D^{23}$ +14.4° (*c* 1.268) (lit.,[19] 102—103 °C, +13.6°); (4e), m.p. 238—239 °C (lit.,[20] 237—239°); (5c), m.p. 90—91 °C, $[\alpha]_D^{23}$ −58.9° (*c* 1.128) (lit.,[18,21] 91—92 °C, −52.9°); (6d), m.p. 96—97 °C (lit.,[22] 97 °C); (7b), m.p. 78—79 °C, $[\alpha]_D^{23}$ +78.5° (*c* 0.11) (lit.,[23] 78.4—79.1 °C, +78.5°); (7c), m.p. 80—81 °C, $[\alpha]_D^{23}$ +26° (*c* 0.17) (lit.,[24] 74—75 °C, +23.9°); (8b), m.p. 176—178 °C, $[\alpha]_D^{23}$ +61° (*c* 0.15) (lit.,[25] 172—180 °C, +60°); (8c), m.p. 147—148 °C (lit.,[26] 146 °C); (9b) acetate derivative, m.p. 239—240 °C, $[\alpha]_D^{23}$ +20.7° (*c* 0.479) (lit.,[27] 284.5—285 °C, 239—240 °C, +21°); (11), m.p. 98—101 °C, $[\alpha]_D^{23}$ +40.8° (*c* 1.383) (lit.,[28] 103—105 °C, +43°); (12), m.p. 175—177 °C, $[\alpha]_D^{24}$ −19.8° (*c* 1.383) (lit.,[29] 178—180 °C, −19°); (13a), m.p. 175—176 °C (lit.,[30] 181°); (13c), m.p. 117—118 °C (lit.,[31] 115—116 °C); (13d), m.p. 128—133 °C sublimes (lit.,[32] 138 °C); (13 g), m.p. 54—56 °C (lit.,[31] 54—56 °C); octadecan-1-ol, m.p. 57—59 °C (lit.,[33] 59.4—59.8 °C); and octadecane, m.p. 27—28 °C (lit.,[33] 28.18 °C).

The Preparation of Esters.—The following esters were prepared by standard procedures: (1b), m.p. 138—139 °C, $[\alpha]_D^{23}$ −23.0° (*c* 2.133) (lit.,[16] 139 °C, −23°); (3a), m.p. 185—186 °C, $[\alpha]_D^{23}$ +9.6 (*c* 1.859) (lit.,[16] 185 °C, +12°); (3b), m.p. 139.5—140 °C, $[\alpha]_D^{23}$ + 31.4°(*c* 0.223) (lit.,[16] 141 °C, +31.5°); (4a), m.p. 165—167 °C, (lit.,[34] 165 °C); (4b), m.p. 148.5—149 °C, $[\alpha]_D^{23}$ −30.9° (*c* 0.23) (lit.,[35] 149—150 °C, −34.6°); (5b), m.p. 115—116 °C, $[\alpha]_D^{23}$ −47° (*c* 0.217) (lit.,[17] 116 °C, −47°); (6a), m.p. 110—111 °C, $[\alpha]_D^{23}$ +12.6° (*c* 1.378) (lit.,[17] 111 °C, +13°); (7a), m.p. 74—75 °C, $[\alpha]_D^{23}$ +47° (*c* 0.21) (lit.,[36] 73 °C, +48.1°); (8a), m.p. 136—138°, $[\alpha]_D^{23}$ +52° (*c* 0.23) (Found: C, 77.3; H, 10.65. $C_{34}H_{56}O_4$ requires C, 77.2; H, 10.7%), from diol (8b), acetic anhydride and 4-dimethylaminopyridine;[37] (9a);[38] (13e), b.p. 99 °C at 0.3 mmHg (lit.,[39] 122—123 °C at 0.9 mmHg); (13h) as an oil (lit.,[39] b.p. 110—113 °C at 2.5 mmHg); octadecyl acetate, m.p. 33—34 °C (lit.,[33] 32 °C).

5α-Cholestane-3β,6β-diyl Diformate (1a).—To a solution of the diol (2a) (100 mg) in pyridine (2 ml) formic acetic anhydride (2 ml) was added with cooling and shaking. Work-up and crystallisation gave the *diformate* (1a) as white needles (98 mg, 86%), m.p. 92.5—94.5 °C (from diethyl ether–methanol), $[\alpha]_D^{23}$ −28.3° (*c* 0.29), $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 170 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.03 (3 H, s, 10-Me), 4.9 (1H, m, W_H 20 Hz, 3α-H), 5.1 (1 H, m, W_H 8 Hz, 6α-H), 8.03 and 8.1 (2 H, 2s, HCO_2); *m/e* 460 ($M^{+\cdot}$), 414, 368, and 260 (Found: C, 75.55; H, 10.5. $C_{29}H_{48}O_4$ requires C, 75.6; H, 10.5%).

5α-Cholestane-3β,6β-diyl Dipropionate (1c).—To a solution of diol (2a) (142 mg) in pyridine (2 ml) propionic anhydride (2 ml) was added and the mixture allowed to stand for 17 h. Work-up and crystallisation gave the *dipropionate* (1c) (152 mg, 83%) as white needles, m.p. 125—127.5 °C (from

dichloromethane–methanol), $[\alpha]_D^{23}$ −26.4° (*c* 0.125), $\nu_{max.}$ (Nujol) 1 742 and 1 185 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.03 (3 H, s, 10-Me), 1.17 and 1.25 (6 H, 2t, *J* 7 Hz, $CH_3CH_2CO_2$), 2.3 (4 H, 2q, *J* 7 Hz, $CH_3CH_2CO_2$), 4.7 (1 H, m, W_H 20 Hz, 3α-H), and 4.97 (1 H, m, W_H 8 Hz, 6α-H); *m/e* 516 ($M^{+\cdot}$), 442, 368, 255, 228, 213, and 57 (Found: C, 76.55; H, 10.95. $C_{33}H_{56}O_4$ requires C, 76.7; H, 10.9%).

5α-*Cholestane*-3β,6β-*diyl Di-isobutyrate* (1d).—To a solution of the diol (2a) (802 mg) in toluene (25 ml) and pyridine (10 ml), a solution of freshly distilled isobutyryl chloride (2.3 g) in toluene (10 ml) was added and the mixture was stirred overnight. Work-up and crystallisation gave the *di-isobutyrate* (1d) as white prisms (830 mg, 77%), m.p. 119.5—120.5 °C (from dichloromethane–methanol), $[\alpha]_D^{23}$ −22.2° (*c* 1.325), $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 160 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.05 (3 H, s, 10-Me), 1.14 and 1.17 (12 H, 2d, *J* 7 Hz, Me_2CH), 2.5 (2 H, m, Me_2CH), 4.6 (1 H, m, W_H 18 Hz, 3α-H), and 4.9 (1 H, m, W_H 8 Hz, 6α-H); *m/e* 544 ($M^{+\cdot}$), 456, 368, 353, 255, 213, and 71 (Found: C, 77.25; H, 11.2. $C_{35}H_{60}O_4$ requires C, 77.15; H, 11.1%).

5α-*Cholestane*-3β,6β-*diyl Bis*-(2,2-*dimethylpropanoate*) (1e).—The diol (2a) (1.21 g) and imidazole (20 mg) in THF (50 ml) were added to sodium hydride (80%, 1.5 g) in THF (10 ml) under nitrogen. After a period of 2 h under reflux 2,2-dimethylpropanoyl chloride (4 ml) was added and the mixture refluxed for 0.5 h. Excess of sodium hydride was quenched with acetic acid. Work-up and chromatography on Kieselgel H (14 g) gave [eluant diethyl ether–petroleum (1 : 19)] the 3β,6β-*diester* (1e) (257 mg, 15%), first m.p. 123—125 °C with resolidification, second m.p. 150—152 °C (from chloroform–methanol), $[\alpha]_D^{23}$ −25.4° (*c* 0.761), $\nu_{max.}$ (Nujol) 1 730, 1 275, and 1 150 cm^{-1}; δ (CCl_4) 1.13 and 1.17 (18 H, 2s, Bu^t), and 4.7 (2 H, m, 3α-H, 6α-H), *m/e* $M^{+\cdot}$ absent, 470, 455, 385, 368, 353, 58, and 57 (Found: C, 77.55; H, 11.4. $C_{37}H_{64}O_4$ requires C, 77.55; H, 11.25%); [eluant diethyl ether–petroleum (3 : 17)] the 3β-*mono-ester* (2e) (292 mg, 20%), m.p. 181—183 °C (from dichloromethane–methanol), $[\alpha]_D^{23}$ −5.4° (*c* 0.652), $\nu_{max.}$ (Nujol) 3 540, 1 705, 1 290, 1 185, and 1 115 cm^{-1}; δ ($CDCl_3$) 1.18 (9 H, s, Bu^t), 3.7 (1 H, m, W_H 8 Hz, 6α-H), and 4.7 (1 H, m, W_H 18 Hz, 3α-H); *m/e* 488 ($M^{+\cdot}$), 470, 386, 368, 353, 228, 213, and 57 (Found: C, 78.4; H, 11.7. $C_{32}H_{56}O_3$ requires C, 78.65; H, 11.55%); and (eluant ethyl acetate) diol (2a) (663 mg, 55%).

5α-*Cholestane*-3β,6β-*diyl Bis*-(*adamantane*-1-*carboxylate*) (1f).—n-Butyl-lithium in petroleum (1.49 M; 5 ml) was added to the diol (2a) (1.46 g) in THF (15 ml) at 0 °C under nitrogen. At 23°C adamantane-1-carbonyl chloride (13g) (1.76 g) in benzene (3 ml) was added. After 24 h at 23 °C acetic acid (2 ml) was added. Work-up and chromatography twice on Kieselgel H (20, 12 g) gave [eluant diethyl ether–petroleum (1 : 49)] the *bis-adamantane*-1-*carboxylate* (1f) (460 mg, 17%), m.p. 294—300 °C (decomp.) (from dichloromethane–methanol), $[\alpha]_D^{23}$ −20.4° (*c* 1.419), $\nu_{max.}$ (Nujol) 1 728, 1 235, and 1 070 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.03 (3 H, s, 10-Me), 4.6 (1 H, m, W_H 20 Hz, 3α-H), and 4.8 (1 H, m, W_H 8 Hz, 6α-H); *m/e* 728 at 12 eV, 290° ($M^{+\cdot}$), 548, 368, 353, and 135 (Found: C, 80.5; H, 10.6. $C_{49}H_{76}O_4$ requires C, 80.7; H, 10.5%); [eluant diethyl ether–petroleum (1 : 9)] the 3β-*monoadamantane*-1-*carboxylate* (2f) (199 mg, 10%), m.p. 249—250 °C (from ethyl acetate), $[\alpha]_D^{23}$ −0.51 (*c* 0.976), $\nu_{max.}$ ($CHCl_3$) 3 500, 1 710, 1 330, 1 270, 1 105, and 1 075 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.07 (3 H, s, 10-Me), 3.7 (1 H, m, W_H 9 Hz, 6α-H), and 4.7 (1 H, br, W_H 18 Hz, 3α-H); *m/e* $M^{+\cdot}$ absent, 548, 383, 368, 253, 135 (Found: C, 80.65; H, 10.95 $C_{38}H_{62}O_3$ requires C, 80.5; H, 11.0%); and (eluant ethyl acetate) unchanged diol (2a) (871 mg, 60%).

5α-*Cholestane*-3β,6β-*diyl Dibenzoate* (1g).—Benzoyl chloride (4 ml) in benzene (4 ml) was added to the diol (2a) (686 mg) in triethylamine (25 ml) and chloroform (25 ml). Work-up after 2 h and crystallisation from dichloromethane gave the *dibenzoate* (1g) (916 mg, 88%), m.p. 187—189.5 °C, $[\alpha]_D^{23}$ −39.0° (*c* 0.20), $\nu_{max.}$ (Nujol) 1 715, 1 600, 1 490, 1 310, 1 275, 1 175, 1 100, 1 070, 1 025, and 710 cm^{-1}; δ ($CDCl_3$) 0.67 (3 H, s, 13-Me), 1.23 (3 H, s, 10-Me), 4.9 (1 H, m, W_H 18 Hz, 3α-H), 5.1 (1 H, m, W_H 8 Hz, 6α-H), 7.3—7.5, and 7.8—8.1 (10 H, m, aryl-H); *m/e* 612 ($M^{+\cdot}$), 490, 368, 353, and 255 (Found: C, 80.35; H, 9.45. $C_{41}H_{56}O_4$ requires C, 80.35; H, 9.2%).

5α-*Cholestan*-3β-*yl* 2,2-*Dimethylpropanoate* (6b).—2,2-Dimethylpropanoyl chloride (10 ml) in dichloromethane (20 ml) was added to 5α-cholestan-3β-ol (2b) (10 g) in pyridine (30 ml). After 17 h at 50 °C work-up and crystallisation from diethyl ether–methanol, then chloroform–methanol gave the 2,2-*dimethylpropanoate* (6b) (11.1 g, 91%) as white needles, m.p. 164—166 °C, $[\alpha]_D^{23}$ +14.5° (*c* 0.50) identical with an authentic sample.[40]

5α-*Cholestan*-3β-*yl Adamantane*-1-*carboxylate* (6c).—5α-Cholestan-3β-ol (2b) (4.0 g) and imidazole (40 mg) in THF (25 ml) were added to sodium hydride (50%, 1.5 g) in THF (8 ml) and the mixture was refluxed under nitrogen for 3 h. Adamantane-1-carbonyl chloride (13g) (2.45 g) in THF (10 ml) was added and the period of reflux continued for 24 h. Work-up, chromatography on neutral grade III alumina (50 g) [eluant chloroform–petroleum (1 : 19)], and crystallisation from dichloromethane gave the *adamantane*-1-*carboxylate* (6c) (1.7 g, 30%), m.p. 218—222 °C, $[\alpha]_D^{23}$ +14.1 (*c* 2.594); $\nu_{max.}$ (Nujol) 1 728, 1 235, and 1 080 cm^{-1}; δ (CCl_4) 0.67 (3 H, s, 13-Me) and 4.55 (2 H, m, 3α-H); *m/e* 550 ($M^{+\cdot}$), 370, 355, 193, 181, 159, 158, and 135 (Found: C, 83.0; H, 11.45. $C_{38}H_{62}O_2$ requires C, 82.85; H, 11.35%). 5α-Cholestan-3β-ol (2b) (10 g) and 18-crown-6 (686 mg) in THF (75 ml) were added to potassium hydride (50%, 4.6 g) in THF (20 ml) under nitrogen and the mixture was refluxed for 3 h. Adamantane-1-carbonyl chloride (13g) (8 g) in benzene (15 ml) was added at 20 °C. After 24 h at 20 °C acetic acid (1 ml) was added. Work-up and chromatography on MFC silica (200 g) gave [eluant diethyl ether–petroleum (1 : 19)] ester (6c) (8.5 g, 60%) after recrystallisation from dichloromethane. A solution of 5α-cholestan-3β-ol (2b) (4.66 g), 4-(*NN*-dimethylamino)pyridine (200 mg), and adamantane-1-carbonyl chloride (13g) (2.5 g) in pyridine (300 ml) and benzene (10 ml) was allowed to stand at 20 °C for 60 h, heated to reflux for 50 h, and stirred for 3 weeks at 20 °C. No ester (6c) was detected by t.l.c.

Preparation of Ergosta-5,7,22-*trien*-3β-*yl* 2,2-*Dimethylpropanoate* (10).—2,2-Dimethylpropanoyl chloride (1.0 ml) was added to ergosterol (1.0 g) in dry toluene (20 ml) and pyridine (2 ml). After 3 days the mixture in light petroleum was washed with water, 0.1M-hydrochloric acid (×2), saturated aqueous sodium hydrogencarbonate (×2), and water, dried, and evaporated. The residue on crystallisation from dichloromethane and methanol gave the *pivaloate* (10) (0.843 g). Chromatography of the mother liquor on Kieselgel H (eluant dichloromethane) and recrystallisation from dichloromethane gave additional ester (10) (0.113 g, total 79%), m.p. 165—169 °C, $[\alpha]_D^{24}$ −81° (*c* 0.564), $\nu_{max.}$ 1 728, 1 288, and 1 160 cm^{-1}; $\lambda_{max.}$ (EtOH) 262 (ε 10 100), 271 (14 500), 282 (15 300), and 193 nm (8 600); δ 0.62 (3 H,

s, 13-Me), 1.18 (9 H, s, Bu^t), 4.7 (1 H, m, 3α-H), 5.25 (2 H, m, 22-H, 23-H), 5.4 and 5.6 (2 H, m, 6-H, 7-H); *m/e* 480 ($M^{+\bullet}$), 378, and 253 (Found: C, 82.6; H, 11.05. $C_{33}H_{52}O_2$ requires C, 82.45; H, 10.9%).

Octadecyl Adamantane-1-carboxylate (13f).—Octadecan-1-ol (6.7 g) in THF (75 ml) was added to sodium hydride (50%, 2.0 g) and imidazole (100 mg) in THF (10 ml) under nitrogen. After reflux for 3 h adamantane-1-carbonyl chloride (13g) (5.5 g) in toluene (20 ml) was added and the mixture refluxed for 20 h. Work-up and chromatography on MFC silica (130 g) gave [eluant diethyl ether–petroleum (1 : 19)] the *adamantane-1-carboxylate* (13f) (9.55 g, 89%) as white needles, m.p. 37—38 °C (from petroleum–ethanol), $\nu_{max.}$ (Nujol) 1 730, 1 230, and 1 075 cm^{-1}; δ (CCl_4) 3.9 (2 H, t, *J* 6 Hz, OCH_2); *m/e* 432 ($M^{+\bullet}$), 297, 252, 181, and 135 (Found: C, 80.6; H, 12.4. $C_{29}H_{52}O_2$ requires C, 80.5; H, 12.1%).

General Procedure for Lithium–Ethylamine Reductions.—All glassware was oven-dried before use. Ethylamine (2—5 ml) was distilled from sodium hydroxide straight into the reaction vessel equipped with a solid CO_2–acetone condenser. Freshly cut, oil-free lithium (100 mg) was added to the amine and the mixture stirred under dry oxygen-free nitrogen until the dark blue colour appeared. A solution of the ester (100 mg) in THF (1 ml) was added dropwise to the blue solution until the colour was discharged. On reappearance of the blue colour more ester solution was added until the colour was discharged again and so on until all the ester was added. After the addition was complete the mixture was stirred until the blue colour persisted. The excess of lithium was quenched by the dropwise addition of methanol with cooling (exothermic reaction). When all the lithium had dissolved the solvents were removed under reduced pressure and the residue was diluted with water and extracted with ether. The organic layer was washed with aqueous hydrochloric acid (1 M), and water, dried, filtered, and the solvent removed under reduced pressure. The product was recrystallised or chromatographed. Reductions were carried out in refluxing ethylamine (+17 °C), unless otherwise stated. Alternatively, the ester was dissolved in ethylamine and lithium added last. The mixture was stirred until the permanent blue colour appeared and worked up as above (see Tables 1 and 2).

General Procedure for Potassium, 18-Crown-6, and t-Butylamine Reductions.—Small freshly cut pieces of oil-free potassium (20 mg-atom) were added to a solution of 18-crown-6 (5 mmol) in dry t-butylamine (20 ml; freshly distilled from potassium) under dry oxygen-free nitrogen and stirred for a short time until a dark-blue colour developed. A solution of ester (1 mmol) in THF (freshly distilled from potassium–benzophenone ketyl) (5 ml) was immediately added on appearance of the blue colour at such a rate that the colour did not disappear for long periods. After addition of all the substrate and reappearance of the blue colour, the reduction was complete and the excess potassium was destroyed with absolute ethanol. The solvents were removed under reduced pressure, water was added to the residue, and the products extracted into ether; the ethereal layer was washed with water, dried, filtered, evaporated to dryness, and the products chromatographed. The aqueous layer was acidified with aqueous hydrochloric acid (6M) to pH 1, extracted with ether, and the organic layer washed with water, dried, filtered, the solvent removed under reduced pressure, and the residue recrystallised to give the carboxylic acid (see Tables 1 and 2).

Preparation of 1,4,7,10,13,16-Hexamethyl-1,4,7,10,13,16-hexa-aza-cyclo-octadecane (15b).—To a solution of 1,4,7,10,-13,16-hexa-aza-cyclo-octadecane (15a) (1.00 g, 3.88 mmol) in formic acid (10 ml, 90%) at room temperature, was added paraformaldehyde (2.49 g, 5-fold excess) in one portion. The stirred suspension was heated to reflux under an atmosphere of nitrogen. After 72 h, the bulk of the excess of formic acid was distilled off at atmospheric pressure. The residue was diluted with water, and the resultant solution basified (potassium hydroxide solution) and extracted with dichloromethane (×3). The organic extracts were combined, dried, filtered, and evaporated under reduced pressure to give an oily residue. Bulb-to-bulb distillation at reduced pressure gave the *title compound* (15b) as a colourless oil which darkened on prolonged exposure to the atmosphere (1.22 g, 92%), b.p. bath temperature 140 °C at 2×10^{-2} mmHg; $\nu_{max.}$ (film) 2 950, 2 820, 2 790, 1 460, 1 305, 1 120, and 1 040 cm^{-1}; δ ($CDCl_3$) 2.30 (18 H, s, N*Me*), and 2.57 (24 H, s, N-CH_2-CH_2-N); *m/e* 343 ($M^{+\bullet}$ + 1), 298, 286, 272, 254, 241, 229, 215, 196, 184, 158, and 113 (100) (Found: C, 62.9, H, 12.65; N, 24.4. $C_{18}H_{42}N_6$ requires C, 63.1; H, 12.35; N, 24.55%).

General Procedure for Sodium–Potassium Eutectic Hexamethylhexa-aza-18-crown-6 (15b) *and t-Butylamine Reductions.*—To a solution of 1,4,7,10,13,16-hexamethyl-1,4,7,-10,13,16-hexa-aza-cyclo-octadecane (15b) (373 mg, 1.09 mmol) in dry t-butylamine (freshly distilled from 4Å molecular sieves) (10 ml) under an atmosphere of dry argon at 25 °C were added small pieces of freshly cut oil-free potassium (0.34 g) and sodium (67 mg); the mixture was stirred until formation of the sodium–potassium eutectic and a blue solution had occurred. A solution of ester substrate (0.4 mmol) in dry tetrahydrofuran (2 ml) (freshly distilled from molten potassium benzophenone ketyl) or dry t-butylamine was then added dropwise at such a rate as to maintain a blue solution. After the addition was complete, the dropping funnel was washed through with more solvent (1 ml), and the residue partitioned between water and diethyl ether. The aqueous phase was re-extracted with diethyl ether, and the combined organic layers dried, filtered, and evaporated to dryness. The residue was separated by chromatography on Kieselgel H (15 g) and the crystalline products recrystallised once. The aqueous phase was acidified to pH 1 with dilute hydrochloric acid, extracted with diethyl ether, and the combined organic layers dried, filtered, and evaporated to give the acid component (see Tables 1 and 2).

General Procedure for Sodium–Potassium Eutectic 18-Crown-6 and t-Butylamine Reductions.—To freshly distilled t-butylamine (10 ml) under an atmosphere of dry argon at 25 °C, were added small pieces of freshly cut, oil-free potassium (1.1 g, 28 mmol) and sodium (0.20 g, 8.7 mmol). The mixture was stirred until formation of the sodium–potassium eutectic was complete and then dry 18-crown-6 (1.4 g, 5.3 mmol) was added in one portion. The resultant blue solution was adjusted to the required (internal) temperature and then a solution of the ester in dry tetrahydrofuran (3 ml) was added dropwise at such a rate as to constantly maintain a blue solution (*ca.* 30 min). After addition was complete, the reaction was quenched by the careful addition of methanol (2 ml). The reaction mixture was worked up as before, and separated by chromatography (see Tables 1 and 2).

Reduction of Adamantane-1-carboxylic Acid (13a).—Potassium adamantane-1-carboxylate (332 mg) was added

to the blue partial solution of potassium (500 mg) and 18-crown-6 (460 mg) in t-butylamine (8 ml). Work-up of the blue solution gave adamantane-1-carboxylic acid (13a) (240 mg, 87%). To a solution of adamantane-1-carboxylic acid (13a) (397 mg) in ethylamine (20 ml) was added lithium (250 mg). After 6 h at 17 °C more lithium (3 × 100 mg) was added every 2 h. Saturated aqueous ammonium chloride (8 ml) was added after a final 2 h at 17 °C, after cooling to −78 °C. The mixture was extracted with diethyl ether and the organic phase washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate, and water, dried, and evaporated. Chromatography on Kieselgel H (10 g) gave (petroleum–diethyl ether gradient) adamantane-1-carbaldehyde (13b) (183 mg, 51%), $\nu_{max.}$ ($CHCl_3$) 2 700, 1 720, 1 150, 1 110, 990, and 910 cm^{-1}; δ 9.18 (1 H, s, CHO), 2,4-dinitrophenylhydrazone m.p. 230—231 °C (lit.,[41] 225 °C) and adamantan-1-ylmethanol (13c) (33 mg, 9%). Acidification and extraction of the aqueous phase gave starting material (13a) (41 mg, 10%).

Reduction of Ethyl Adamantane-1-carboxylate (13e) *in the Presence of 5α-Cholestan-3β-ol* (2b).—Potassium (800 mg) was added to 5α-cholestan-3β-ol (2b) (420 mg) and 18-crown-6 (1.20 g) in t-butylamine (20 ml). When the blue colour appeared ethyl adamantane-1-carboxylate (13e) (280 mg) in THF (1 ml) was added. The blue mixture was quenched with hydrochloric acid (1M; 10 ml). Work-up and chromatography on Kieselgel H (10 g) gave (eluant petroleum–diethyl ether gradient) 5α-cholestane (2d) (61 mg, 15%) and 5α-cholestan-3β-ol (2b) (290 mg, 69%). Acidification and extraction of the aqueous phase gave adamantane-1-carboxylic acid (13a) (206 mg, 85%). Similarly, reduction of 5α-cholestan-3β-ol (388 mg) using an excess of potassium–sodium eutectic and ethyl acetate in t-butylamine and THF gave 5α-cholestane (2d) (117 mg, 31%) and 5α-cholestan-3β-ol (2b) (184 mg, 47%).

Bouveault–Blanc Reduction of 5α-Cholestan-3β-yl Adamantane-1-carboxylate (6c).—The ester (6c) (250 mg) suspended in absolute ethanol (1 ml) was added with stirring to sodium sand (2.5 g) in toluene (3 ml) at 60 °C. Excess of sodium was destroyed with ethanol and the mixture evaporated. The residue in ether was washed with water (× 2), dried, and separated by p.l.c. [diethyl ether–light petroleum (3 : 7)] to give adamantan-1-ylmethanol (13c) (50 mg, 66%) and 5α-cholestan-3β-ol (2b) (103 mg, 58%).

Reduction of 18-Crown-6.—A partial solution of potassium (300 mg) and 18-crown-6 (900 mg) in t-butylamine (20 ml) was stirred under nitrogen at 23 °C for 18 h. All the potassium dissolved and the solution was no longer blue. The solution was acidified with 1M-hydrochloric acid and evaporated to dryness by azeotrope with benzene. The residue was dissolved in dichloromethane, dried (Na_2SO_4), and evaporated to give an oil, $\nu_{max.}$ (CH_2Cl_2) 3 350, 3 100, 1 600, 1 350, 1 240, 1 210, 1 110—1 060, 960, and 840 cm^{-1}; δ ($CDCl_3$) 1.4 (s), 3.6 (s), and 3.7 (s). To the oil in chloroform (5 ml) and triethylamine (5 ml) 1-naphthoyl chloride (from 1.5 g acid and thionyl chloride) was added. After 18 h at 20 °C the mixture was evaporated and the residue thoroughly leached with benzene–petroleum (1 : 1), filtered, and evaporated. The oil was chromatographed on Kieselgel H (12 g) to give (eluant diethyl ether–light petroleum gradient) 1-naphthoic anhydride (120 mg), m.p. 145—146 °C (lit.,[42] 145 °C); a mixture of 1-naphthoic acid and *N*-t-butylnaphthalene-1-carboxamide (259 mg), $\nu_{max.}$ ($CHCl_3$) 3 520, 3 430, 3 400—2 300, 1 725—1 650, 1 595, 1 575, 1 500, 1 300—1 170, 1 145, and 1 120; and (eluant ethyl acetate) a black tar and several u.v.-active components (412 mg); $\nu_{max.}$ ($CHCl_3$) 1 710, 1 130, and 910 cm^{-1}. The amide fraction in dichloromethane was washed with 5% aqueous sodium hydrogencarbonate and water, dried, separated by p.l.c. [diethyl ether–petroleum (1 : 1)], and crystallised from chloroform–diethyl ether to give *N-t-butylnaphthalene-1-carboxamide* as white needles, m.p. 151—152 °C, $\nu_{max.}$ (Nujol) 3 315, 1 640, 1 620, 1 590, 1 575, 1 525, 1 310, 800, and 775 cm^{-1}; δ ($CDCl_3$) 1.6 (9 H, s, Bu^t), and 7.3—8.6 (7 H, m, aryl-H); *m/e* 227 ($M^{+\cdot}$), 212, 171, 155, 127, and 57 (Found: C, 79.25; H, 7.6; N, 6.4. $C_{15}H_{17}NO$ requires C, 79.25; H, 7.55; N, 6.15%). The polar oil was rechromatographed on Kieselgel H (12 g) to give [eluant ethyl acetate–petroleum (3 : 17—3 : 2)] fractions (A) (184 mg) and (B) (158 mg). Fraction (A) was separated by p.l.c. [ethyl acetate–petroleum (1 : 1)] giving two fractions A_1 (88 mg); δ ($CDCl_3$) 1.0 (t, *J* 8 Hz), 1.4 (t, *J* 7 Hz), 3.1 (q, *J* 7 Hz), 3.8 (m), 4.5 (m), and 7.2—9.0 (m); and A_2 (65 mg); $\nu_{max.}$ (film) 3 370, 1 715, 1 595, 1 580, 1 510, 1 280, 1 245, 1 200, 1 150—1 120, 1 070, 1 045, and 785 cm^{-1}; δ ($CDCl_3$) 3.7 (m), 3.9 (t), 4.6 (t), 7.3—8.3 (m), and 8.8—9.1 (m); *m/e* 260 ($M^{+\cdot}$), 242 ($M^{+\cdot} - H_2O$), 199 ($C_{10}H_7CO_2CH_2CH_2$), 155 ($C_{10}H_7CO$), and 127 ($C_{10}H_7$) (Found: $M^{+\cdot}$ 260.1049. $C_{15}H_{16}O_4$ requires 260.1049). Fraction A_2 was tentatively identified as the ester (14a). A_1 was re-separated by p.l.c. [ethyl acetate–petroleum (2 : 3)] to give A_{11} (12 mg) which was still inhomogeneous, δ ($CDCl_3$) 1.0 (t, *J* 7 Hz), 1.3 (t, *J* 7 Hz), 3.4 (m), 4.5 (t), and 7.3—8.2 (m); *m/e* 255, 227, 212, 198, 155, and 127; and A_{12} (57 mg) as a mixture of ester (14a) and another component tentatively assigned as the ester (14b), δ ($CDCl_3$) 1.0 (t, *J* 8 Hz), 1.3 (t, 7 Hz), 3.1 (q, *J* 7 Hz), 3.6 (m), and 7.2—8.0 (m); *m/e* 332 ($M^{+\cdot}$), 260, 242, 212, 199, 155, and 127 (Found: $M^{+\cdot}$ 332.1625. $C_{19}H_{24}O_5$ requires $M^{+\cdot}$ 332.1624). Fraction B was separated by p.l.c. [ethyl acetate–petroleum (47 : 53)] to give a brown oil (131 mg) tentatively assigned as the ester (14c), $\nu_{max.}$ ($CHCl_3$) 1 715, 1 595, 1 580, 1 280, 1 260—1 190, 1 140—1 090, and 1 070 cm^{-1}; δ ($CDCl_3$) 1.2 (t, *J* 7 Hz), 3.6 and 3.65 (2m), 3.9 (t, *J* 7 Hz), 4.6 (t, *J* 7 Hz), 7.4—8.3 (m), and 8.8—9.0 (m); *m/e* 376 ($M^{+\cdot}$), 304 ($M^{+\cdot} - C_4H_8O$), 286, 274, 260, 221, 216, 199, 172, 155, and 127 (Found: $M^{+\cdot}$ 376.1890. $C_{21}H_{28}O_6$ requires $M^{+\cdot}$ 376.1886).

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