Reactions of Enol Acetates with Thallium(I) Acetate–Iodine

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The action of thallium(I) acetate and iodine on some enol acetates has been examined as a general method for the formation of α-iodo-ketones.

α-IODO-KETONES are usually prepared by treatment of a ketone with iodine in the presence of a strong base,[1] by a sodium iodide exchange reaction with a chloro- or bromo-ketone,[2] or by the use of *N*-iodosuccinimide [3,4] or iodine(I) chloride [3] on the enol acetate of the ketone. The first method suffers from the disadvantages that consistent results are sometimes difficult to obtain [5] and that subsequent cyclisation reactions can occur in the presence of a strong base.[6] The second method is subject to pronounced steric effects, neither 17-bromo-20-oxo-steroids [2] nor 4-bromo-3-oxo-5β-steroids,[7] for example, reacting to any appreciable extent. In the third method *N*-iodosuccinimide has an advantage over iodine(I) chloride in that it does not attack nuclear double bonds [3] but its formation involves the use of light-sensitive and relatively expensive silver oxide.

During a study of the utilization of thallium(I) salts in organic synthesis [8] we attempted to substitute the thallium(I) salt of succinimide for the silver salt in the preparation of *N*-iodosuccinimide (NIS).[3] Although *N*-thallio-succinimide could be readily prepared as a pale yellow precipitate by the reaction of thallium(I) ethoxide and succinimide, it was very unstable. This was not unexpected since most compounds which contain a thallium–nitrogen bond are very susceptible to hydrolysis.[9] However, while iodination of an enol acetate could be achieved using NIS prepared *in situ* by the above procedure, it was found more convenient to treat a solution of thallium(I) acetate and an enol acetate with a solution of the halogen in the same solvent.

Initial reactions were carried out on the enol acetates derived from heptan-2-one. Earlier workers [3,10] reported that this ketone afforded a single enol acetate (1) with isopropenyl acetate in the presence of an acid catalyst but more recently it has been shown that the equilibrium mixture of enol acetates prepared by this method contains a mixture of the compounds (1, *cis* and *trans*) and (2) in the ratio 94 : 6.[11] Treatment of the equilibrium mixture with thallium(I) acetate and iodine in chloroform gave an 81% yield of the iodo-ketone (3) and a 5% yield of the iodo-ketone (4). This result compares favourably with overall yields of 58 and 60% for comparable reactions with NIS and iodine(I) chloride [3] and, as the reaction with thallium(I) acetate–iodine could be performed on a small scale under mild conditions, the method appeared to offer an attractive alternative to the NIS procedure. A series of representative enol acetates was therefore treated with thallium(I) acetate–iodine giving results shown in the Table.

$CH_3\cdot[CH_2]_3\cdot CH{=}C(OAc)\cdot CH_3$

(1)

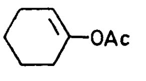
$CH_3\cdot[CH_2]_4\cdot C(OAc){=}CH_2$

(2)

$CH_3\cdot[CH_2]_3\cdot CHR^1\cdot CO\cdot CH_2R^2$

(3) $R^1 = I,\ R^2 = H$

(4) $R^1 = H,\ R^2 = I$



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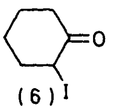

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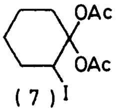

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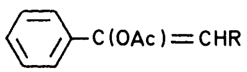
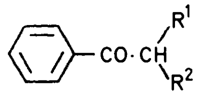


(8) R = H

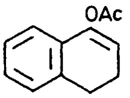
(9) R = Me



(10) $R^1 = H,\ R^2 = I$

(11) $R^1 = R^2 = H$

(12) $R^1 = Me,\ R^2 = I$



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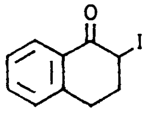

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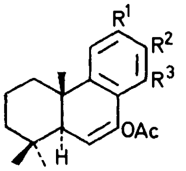

(15) $R^1 = H,\ R^2 = OMe,\ R^3 = CHMe_2$

(16) $R^1 = OAc,\ R^2 = CHMe_2,\ R^3 = H$

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[1] H. J. Ringold and G. Stork, *J. Amer. Chem. Soc.*, 1958, **80**, 250.

[2] P. L. Julian and W. J. Karpel, *J. Amer. Chem. Soc.*, 1950, **72**, 362.

[3] C. Djerassi and C. T. Lenk, *J. Amer. Chem. Soc.*, 1653, **75**, 3493.

[4] C. Djerassi and C. T. Lenk, *J. Amer. Chem. Soc.*, 1954, **76**, 1722; C. Djerassi, J. Grossman, and G. H. Thomas, *ibid.*, 1955, **77**, 3826.

[5] O. Halpern and C. Djerassi, *J. Amer. Chem. Soc.*, 1959, **81**, 439; E. S. Rothman, T. Perlstein, and M. E. Wall, *J. Org. Chem.*, 1960, **25**, 1966.

[6] M. Fieser and L. F. Fieser, ' Reagents for Organic Synthesis,' vol. 3, Wiley–Interscience, 1972, p. 159.

[7] G. Rosenkranz, O. Mancera, J. Gatica, and C. Djerassi, *J. Amer. Chem. Soc.*, 1950, **72**, 4077.

[8] R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J.C.S. Perkin I*, 1974, 1858, 1864; R. C. Cambie, Diana M. Gash, P. S. Rutledge, and P. D. Woodgate, *ibid.*, 1977, 1157.

[9] A. G. Lee, in ' Topics in Inorganic and General Chemistry: Monograph 14; The Chemistry of Thallium,' ed. P. L. Robinson, Elsevier, London, 1971, p. 258.

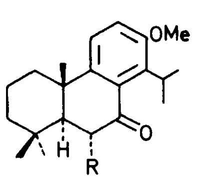
[10] F. G. Young, F. C. Frostick, J. J. Sanderson, and C. R. Hauser, *J. Amer. Chem. Soc.*, 1950, **72**, 3635.

[11] H. O. House and V. Kramar, *J. Org. Chem.*, 1963, **28**, 3362.

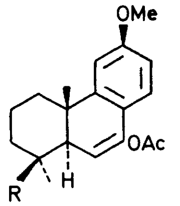
In those cases where the iodo-substituent could adopt α- or β-configurations, the stereochemistry of the product was determined from the ^1H n.m.r. spectrum. The C-6 iodine atom in the iodo-ketone (17) was shown to be α from spectral data and by comparison with the corresponding 6α-bromo-derivative (18).[12] Thus, the iodo-ketone (17) showed strong carbonyl i.r. absorption at 1 680 cm^{-1}, a shift of *ca* 15 cm^{-1} to higher frequency relative to that of the parent ketone, indicating an equatorial iodine atom and hence an α-configuration.[13] This was consistent with the appearance in the ^1H n.m.r. spectrum of the C-6 proton signal as a doublet, $J_{5,6}$ 8.0 Hz, and with downfield shifts of the C-4 *gem*-dimethyl and C-10 methyl signals relative to those of the parent ketone.[12] The magnitude of $J_{5,6}$ suggests that there is a larger H(5α)-C(5)-C(6)-H(6β) torsion angle in the iodo-ketone (17) than in the 6α-bromo-ketone (18), indicating that ring B in the former attains a full boat conformation.

Iodination reaction

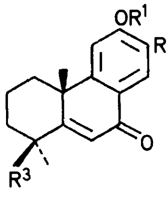
Enol acetate	Solvent	Products	Yields (%)
(1) (2)	$CHCl_3$	(3)	81
		(4)	5
(5)	CH_2Cl_2	(6)	32
		(7)	4
(5)	HOAc	(6)	46
		(7)	11
(8)	HOAc	(10)	39
		(11)	61
(9)	HOAc	(12)	59
(13)	CH_2Cl_2	(14)	75
(15)	$CHCl_3$	(17)	76
(16)	PhH	(22)	74
(20)	$CHCl_3$	(25)	37
		(23)	63
(21)	$CHCl_3$	(24)	88
(27)	CH_2Cl_2	(28), (29)	45
(30)	$CHCl_3$	(31)	93
(33)	$CHCl_3$ or HOAc	(34)	0



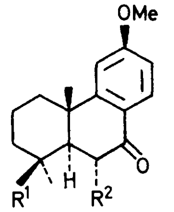
(17) R = I
(18) R = Br
(19) R = H



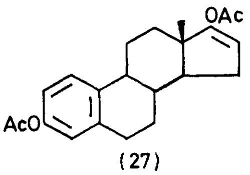
(20) R = CH_2OAc
(21) R = CO_2Me



(22) R^1 = Ac, R^2 = $CHMe_2$, R^3 = Me
(23) R^1 = Me, R^2 = H, R^3 = CH_2OAc
(24) R^1 = Me, R^2 = H, R^3 = CO_2Me



(25) R^1 = CH_2OAc, R^2 = H
(26) R^1 = CO_2Me, R^2 = I



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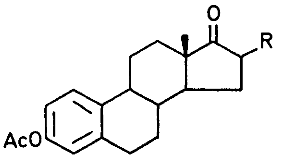

(28) R = α—I
(29) R = β—I

Unexpectedly, iodination of the diterpenoid enol acetates (16), (20), and (21) which each possess oxygenated substituents at C-12, did not yield the corresponding 6-iodo-ketones but afforded the αβ-unsaturated ketones (22)—(24). The enol acetate (20) also afforded the ketone (25) in 37% yield. Formation of compounds analogous to (22)—(24) has hitherto been achieved from the C-7 ketone by bromination and dehydrobromination,[13,14] by dehydrogenation with selenium dioxide,[15] or by photosensitized oxidation of a 6,7-didehydro-diterpenoid.[16] The present reaction offers a moderate yield (65—88%) two-step route to C-12 oxygenated 5,6-didehydro-7-oxo-diterpenoids from the C-7 ketones.

In an attempt to prepare the iodo-ketone (26) the enol acetate (21) was treated with mercury(II) acetate and iodine in acetic acid but this also yielded the αβ-unsaturated ketone (24). Similar treatment of the enol acetate (20) afforded the ketone (25) as the sole product. The latter product may arise by hydrolysis of the parent enol acetate or by reduction of an initially formed iodo-ketone by iodide ion (*cf.* refs. 17 and 18). Further treatment of the only ring C aromatic iodo-ketone which was isolated, *viz.* (17), with thallium(I) acetate in acetic acid gave only very low yields of the ketones (36) and (19). However, treatment with silver acetate in acetic acid gave the same ketones in 75 and 23% yield, respectively.

The enol acetate (27) of estrone acetate gave a mixture of the C-16 epimeric iodides (28) and (29) similar to that obtained[17] with NIS, but distinct from the single isomer (28) which we obtained using mercury(II) acetate and iodine in acetic acid (*cf.* ref. 19). On the other hand, iodination of the enol acetate (30) of the tetracyclic diterpenoid 17-norphyllocladan-16-one with thallium(I) acetate–iodine occurred with a high degree of stereo-selectivity to yield the 15α-iodo-ketone (31) as a result of the blocking effect of the C-10 methyl group on the

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[12] R. C. Cambie, D. R. Crump, W. A. Denny, and T. J. Fullerton, *Austral. J. Chem.*, 1971, **24**, 1237.

[13] E. Wenkert, P. Beak, R. W. J. Carney, J. W. Chamberlin, D. B. R. Johnston, C. D. Roth, and A. Tahara, *Canad. J. Chem.*, 1963, **41**, 1924.

[14] D. H. Miles and E. J. Parish, *Tetrahedron Letters*, 1972, 3987; Y-L. Chow and H. Erdtman, *Acta Chem. Scand.*, 1962, **16**, 1305.

[15] J. A. Hill, A. W. Johnson, T. J. King, S. Natori, and S. W. Tam, *J. Chem. Soc.*, 1965, 361.

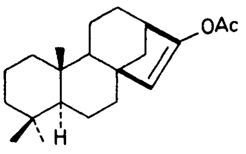
[16] R. C. Cambie and R. C. Hayward, *Austral. J. Chem.*, 1974, **27**, 2001.

[17] G. P. Mueller and W. F. Johns, *J. Org. Chem.*, 1961, **26**, 2403.

[18] H. O. House, V. Paragamian, R. S. Ro, and D. J. Wulka, *J. Amer. Chem. Soc.*, 1960, **82**, 1457.

[19] C. Georgoulis and J. M. Valery, *Bull. Soc. chim. France*, 1975, 1431.

β-face.[20] Substitution of bromine for iodine in the reaction with the enol acetate (3) resulted in a high (88%) yield of the 15α-bromoketone (32), but in this case a similar yield of the bromo-ketone (32) was also obtained in the absence of thallium(I) acetate. No reaction occurred when the enol acetate (33) of 5α-cholestan-3-one was treated with thallium(I) acetate–iodine in either dichloromethane or acetic acid but it is not clear why this was so since the enol acetate (33) reacted with iodine(I) chloride to give the iodo-ketone (34) (25%) and the parent ketone (35) (22%*).



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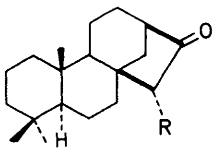
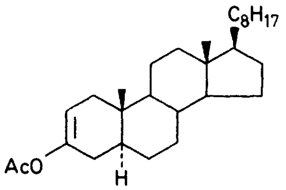


(31) R = I
(32) R = Br



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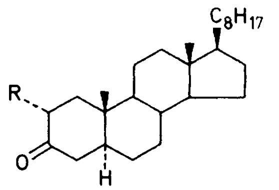
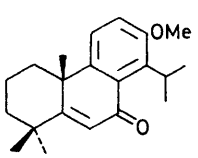


(34) R = α-I
(35) R = H



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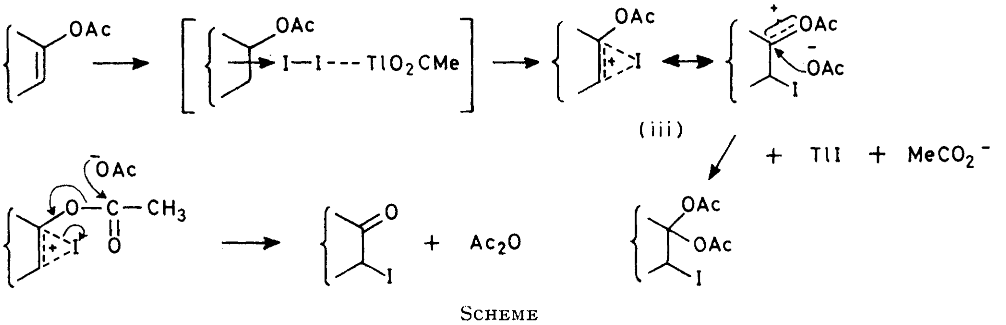

SCHEME

The iodo-ketones above are probably formed *via* an acetoxy-iodonium ion which is opened by acetate ion as indicated (Scheme). Such a pathway is similar to that proposed for the reaction of thallium(I) acetate–iodine with alkenes [8] and to a mechanism proposed by Djerassi and Lenk for the corresponding NIS reaction with enol acetates.[3] In addition to the iodo-ketone (6), a geminal diacetate was produced in the case of iodination of the enol acetate (5). The diacetate was unstable but its structure (7) was assigned from its spectral parameters (see Experimental section). It presumably arises from the intermediate (iii) as indicated (Scheme).

In earlier work significant differences were observed between the behaviour of thallium(I) carboxylates and silver carboxylates towards some alkenes in the presence of iodine.[8] Reaction of the enol acetates (1) and (2) with silver acetate and iodine in dichloromethane was also examined in the present study. Although this resulted in conversion into the iodo-ketones (3) and (4), the yield was only 38%.

EXPERIMENTAL

General experimental details have been described previously.[8, 21]

General Procedure for Iodination of Enol Acetates.—Unless otherwise indicated, a solution of iodine (1 equiv.) in dry dichloromethane or dry chloroform (5—10 ml) was added dropwise to a stirred suspension of thallium(I) acetate (1 equiv.) and the enol acetate (1 equiv.) in the same solvent at 20 °C. The mixture was stirred for 20—24 h, the precipitated thallium(I) iodide was removed, and the filtrate was concentrated *in vacuo* to yield the crude products. When an excess of thallium(I) acetate was used it was removed by extraction of the residue with ether, in which it is insoluble.

Iodination of Enol Acetates of Heptan-2-one.—Iodination of the equilibrated mixture [11] of the enol acetates (1) and (2) (0.50 g, 3.2 mmol) in chloroform gave a brown oil (0.59 g, 86%) containing 3-iodoheptan-2-one (3) (81%) [3] and 1-iodoheptan-2-one (4) (5%) (^{1}H n.m.r. analysis), $\nu_{max.}$ (film) 1 730 cm^{-1} (CO), $\delta(CCl_4)$ 2.38 [s, COMe of (3)], 2.72 [t, *J* 6 Hz, CH_2CO of (4)], 3.71 [s, CH_2I of (4)], and 4.38 [t, *J* 6 Hz, CHI of (3)].

Iodination of Cyclohex-1-enyl Acetate (5).—(i) *In dichloromethane.* Cyclohex-1-enyl acetate, b.p. 75—80° at 15 mmHg (lit.,[22] 84—85° at 25 mmHg) (0.25 g, 1.8 mmol) was

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* This may include material derived from the iodo-ketone (34) as a result of reductive replacement of iodine during work-up with sodium disulphite.[17]

[20] K. M. Baker, L. H. Briggs, J. G. St. C. Buchanan, R. C. Cambie, B. R. Davis, R. C. Hayward, G. A. S. Long, and P. S. Rutledge, *J.C.S. Perkin I*, 1972, 190; L. H. Briggs, R. C. Cambie, and P. S. Rutledge, *J. Chem. Soc.*, 1963, 5374; J. MacMillan and M. F. Barnes, *J. Chem. Soc.* (*C*), 1967, 361; J. MacMillan and E. R. H. Walker, *J.C.S. Perkin I*, 1972, 981.

[21] R. C. Cambie, R. C. Hayward, B. G. Lindsay, A. I. T. Phan, P. S. Rutledge, and P. D. Woodgate, *J.C.S. Perkin I*, 1976, 1961.

[22] N. J. Leonard and F. H. Owens, *J. Amer. Chem. Soc.*, 1958, **80**, 6039.

iodinated in dichloromethane using 2 equiv. of thallium(I) acetate to give a brown oil (0.23 g) containing products and starting material (t.l.c. and ^{1}H n.m.r. analysis). Multiple p.l.c. [hexane–ether (4 : 1) and hexane] gave 2-iodocyclohexanone (6) [21] (0.13 g, 32%) (correct i.r. and ^{1}H n.m.r. spectra [21]), and 2-iodocyclohexane-1,1-diyl diacetate (7) (22 mg, 4%) as an unstable oil, $\nu_{\max.}$ (film) 1 750 cm^{-1} (OAc), δ 1.37—1.80 (m, CH_2), 2.06 (s, 2 OAc), and 5.17 (t, *J* 5 Hz, CHI), *m*/*e* 326 ($M^{+\cdot}$), 267 ($M^{+\cdot}$–OAc), 266 ($M^{+\cdot}$–HOAc), 199 ($M^{+\cdot}$–I), and 139 ($M^{+\cdot}$–HOAc–I).

(ii) *In glacial acetic acid*. Cyclohex-1-enyl acetate (0.10 g, 0.71 mmol) was iodinated in glacial acetic acid (30 ml). Water (15 ml) was added to the mixture, which was then extracted with ether. Work-up gave a brown oil (0.10 g) containing 2-iodocyclohexanone and 2-iodocyclohexane-1,1-diyl diacetate in relative yields of 73 and 27%.

Iodination of 1-*Phenylethenyl Acetate*.—The enol acetate (8), b.p. 75° at 0.2 mmHg, n_D^{23} 1.530 2 (lit.,[23] 85° at 2 mmHg, n_D^{20} 1.533 0) (0.20 g, 1.23 mmol) was iodinated in glacial acetic acid to give an oil containing 2-iodoacetophenone (10) [21] and acetophenone (11) (4 : 3). P.l.c. (benzene) gave the 2-iodoacetophenone (0.12 g, 39%) (correct i.r. and ^{1}H n.m.r. spectra [21]).

1-*Phenylprop*-1-*enyl Acetate* (9).—Propiophenone (10.0 g, 0.75 mol) was enol acetylated with isopropenyl acetate (22.5 g, 2.25 mol) and concentrated sulphuric acid (0.1 ml) at 80 °C for 4 h. Copper(II) acetate (0.10 g) was added and the crude product was flash distilled at 0.2 mmHg. Fractional distillation gave 1-phenylprop-1-enyl acetate (2.4 g, 18%), b.p. 90° at 0.3 mmHg, δ 1.67 (d, *J* 7 Hz, $CHCH_3$), 2.20 (s, OAc), 5.78 (q, $CHCH_3$), and 7.28 (m, ArH).

Iodination of 1-*Phenylprop*-1-*enyl Acetate*.—The enol acetate (9) (57 mg, 0.32 mmol) was iodinated in glacial acetic acid to give an oil (50 mg, 59%) composed mainly of 2-iodopropiophenone (12) [21] (correct i.r. and ^{1}H n.m.r. spectra [21]).

Iodination of 3,4-*Dihydro*-1-*naphthyl Acetate*.—The enol acetate (13), m.p. 58—59° (lit.,[24] 58—59.5°) (0.25 g, 1.33 mmol) was iodinated in chloroform to give 2-*iodo*-3,4-*dihydronaphthalen*-1(2H)-*one* (14) (0.27 g, 75%), which crystallized from 2-methylpentane as needles, m.p. 75—78° (Found: C, 44.25; H, 3.3; I, 46.0. $C_{10}H_9IO$ requires C, 44.1; H, 3.3; I, 46.6%), $\nu_{\max.}$ 1 650 cm^{-1} (aryl CO), δ 2.20 (m, 3-H_2), 2.93 (m, 4-H_2), 5.00 (t, *J* 6 Hz, 2-H), 7.27 (m, 5-, 6-, and 7-H), and 8.02 (d, *J* 7 Hz, 8-H), *m*/*e* 272 ($M^{+\cdot}$).

Iodination of 13-*Methoxytotara*-6,8,11,13-*tetraen*-7-*yl Acetate*.—(*a*) The enol acetate (15) [16] (0.16 g, 0.45 mmol) was iodinated in chloroform to give 6α-*iodo*-13-*methoxytotara*-8,11,13-*trien*-7-*one* (17) (0.15 g, 76%), which crystallized from aqueous methanol as pale yellow rods, m.p. 175—178° (decomp. below m.p.) (Found: C, 55.4; H, 6.35; I, 28.0. $C_{21}H_{29}IO_2,H_2O$ requires C, 55.0; H, 6.8; I, 27.7%), $\nu_{\max.}$ 1 680 cm^{-1} (aryl CO), δ 1.07 and 1.13 (2s, *gem*-Me_2), 1.33 (s, 10-Me), 1.39, 1.44 (2d, *J* 7 Hz, 15-Me_2), 3.43 (septet, *J* 7 Hz, 15-H), 4.80 (d, *J* 8 Hz, 6β-H), and 6.98 (AB_2, *J* 8 Hz, 11- and 12-H).

(*b*) A solution of the enol acetate (15) (0.10 g, 0.28 mmol) and mercury(II) acetate (89 mg, 0.28 mmol) in glacial acetic acid (5 ml) was treated with a solution of iodine (71 mg, 0.28 mmol) in the same solvent at 20 °C. After 15 min, water was added and the mixture was extracted with chloroform. The extract was washed with water and saturated aqueous sodium hydrogen carbonate and worked up to give the 6α-iodoketone (17) (90 mg, 73%).

Abieta-6,8,11,13-*tetraene*-7,12-*diyl Diacetate* (16).—Sugiyl acetate [25] (0.50 g, 1.46 mmol) was enol acetylated with isopropenyl acetate (23 g, 0.23 mol) and toluene-*p*-sulphonic acid (0.10 g) to give *abieta*-6,8,11,13-*tetraene*-7,12-*diyl diacetate* (0.49 g, 87%), which crystallized from aqueous methanol as needles, m.p. 130—132° (Found: C, 75.1; H, 8.3. $C_{24}H_{32}O_4$ requires C, 75.0; H, 8.4%), $\nu_{\max.}$ 1 760br (OAc) and 1 670 cm^{-1} (C=C), δ 0.97 and 1.06 (2s, *gem*-Me_2), 1.23 (s, 10-Me), 1.15 and 1.25 (2d, *J* 7 Hz, 15-Me_2), 2.33 (s, 2 OAc), 3.00 (septet, *J* 7 Hz, 15-H), 5.67 (d, $J_{5,6}$ 4 Hz, 6-H), 6.80 (s, 14-H), and 7.07 (s, 12-H).

Attempted Iodination of Abieta-6,8,11,13-*tetraene*-7,12-*diyl Diacetate*.—The enol acetate (16) (0.15 g, 0.39 mmol) was treated by the general iodination procedure using 1.5 equiv. of thallium(I) acetate in benzene. P.l.c. of the product gave starting material (39 mg, 26%), and 7-*oxoabieta*-5,8,11,13-*tetraen*-12-*yl acetate* (22) (0.10 g, 74%) which crystallized from aqueous methanol as needles, m.p. 167—170° (Found: C, 77.3; H, 8.2. $C_{22}H_{28}O_3$ requires C, 77.6; H, 8.3%), $\nu_{\max.}$ 1 750 (aryl OAc) and 1 650 cm^{-1} (aryl CO), δ 1.21 and 1.33 (2d, *J* 7 Hz, 15-Me_2), 1.37 and 1.40 (2s, *gem*-Me_2), 1.60 (s, 10-Me), 2.42 (s, OAc), 3.07 (septet, *J* 7 Hz, 15-H), 6.50 (s, 6-H), 7.20 (s, 11-H), and 8.13 (s, 14-H), *m*/*e* 340 ($M^{+\cdot}$).

Attempted Iodination of Methyl 7-*Acetoxy*-12-*methoxypodocarpa*-6,8,11,13-*tetraen*-19-*oate*.—The enol acetate (21) [26] (0.10 g, 0.28 mmol) was treated by the general iodination procedure to give methyl 7-oxopodocarpa-5,8,11,13-tetraen-19-oate (24) [26] (77 mg, 88%), m.p. and mixed m.p. 172—174°.

Treatment of the enol acetate (21) with mercury(II) acetate and iodine in glacial acetic acid as for (15) gave the 7-oxo-ester (24) (79%).

Attempted Iodination of 12-*Methoxypodocarpa*-6,8,11,13-*tetraene*-7,19-*diyl Diacetate*.—The enol acetate (20) [12] (0.15 g, 0.40 mmol) was treated by the general iodination procedure using 1.5 equiv. of thallium(I) acetate in chloroform. P.l.c. (chloroform) of the product gave 12-methoxy-7-oxopodocarpa-8,11,13-trien-19-yl acetate (25) [12] (50 mg, 37%), m.p. and mixed m.p. 113—115° (correct i.r. and ^{1}H n.m.r. spectra [12]), and 12-*methoxy*-7-*oxopodocarpa*-5,8,11,13-*tetraen*-19-*yl acetate* (23) (83 mg, 63%), m.p. 111—112° (Found: C, 72.5; H, 7.2. $C_{20}H_{24}O_4$ requires C, 73.1; H, 7.4%), $\nu_{\max.}$ 1 650 cm^{-1} (conj. aryl CO), δ 1.33 (s, 4-Me), 1.50 (s, 10-Me), 2.06 (s, OAc), 3.90 (s, ArOMe), 4.38 (d, *J* 3 Hz, 19-H_2), 6.40 (s, 6-H), 6.80 (m, 11, 13-H), and 8.00 (d, $J_{13,14}$ 8 Hz, 14-H), *m*/*e* 328 ($M^{+\cdot}$).

Treatment of the enol acetate (20) with mercury(II) acetate and iodine in glacial acetic acid as above gave the 7-oxo-acetate (25) (72%) as the only product.

Iodination of Estra-1,3,5(10),16-*tetraene*-3,17-*diyl Diacetate*.—(*a*) Iodination of the enol acetate (27), m.p. 149—151° (lit.,[27] 149—150°) (0.10 g, 0.28 mmol) in dichloromethane using 2 equiv. of thallium(I) acetate gave a mixture of 16α- and 16β-iodo-17-oxoestra-1,3,5(10)-trien-3-yl acetates (28), and (29) (56 mg, 45%), which crystallized from aqueous methanol as a mixture of plates and needles, m.p.

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129—132.5°. The i.r. and ^{1}H n.m.r. spectra were identical with those of the 16α-iodo-epimer described below.

(*b*) A solution of the enol acetate (27) (0.15 g, 0.42 mmol) and mercury(II) acetate (0.13 g, 0.42 mmol) in glacial acetic acid (20 ml) was treated with a solution of iodine (0.11 g, 0.42 mmol) in the same solvent (5 ml) at 20 °C. Work up after 30 min and p.l.c. (hexane–ether, 3 : 2) of the product (0.17 g) gave 16α-iodo-17-oxoestra-1,3,5(10)-trien-3-yl acetate (28) (0.13 g, 70%), which crystallized from methanol as needles, m.p. 143—145° (lit.,[17] 142—143.6°), $\nu_{max.}$ 1 740 cm^{-1} (CO), δ(CCl_4) 0.88 (s, 18-H_3), 2.23 (s, OAc), 2.86 (m, $W_{1/2}$ 14 Hz, 6β-H), 4.75 (dd, $J_{a,e}$ 3, $J_{a,a}$ 6 Hz, 16β-H), and 7.00 (m, ArH).

A mixture of the 16α- and 16β-iodo-epimers (65%) was obtained using iodine–copper(II) acetate monohydrate [28] in glacial acetic acid.

Iodination of 17-*Nor*-13β-*kaur*-15-*en*-16-*yl Acetate*.—The enol acetate (30) [29] (0.16 g, 0.51 mmol) was iodinated in chloroform using 1.5 equiv. of thallium(I) acetate. Work up gave 15α-*iodo*-17-*nor*-13β-*kauran*-16-*one* (31) (0.19 g, 93%), which crystallized from methanol as needles, m.p. 166—168° (Found: C, 57.0; H, 7.2; I, 31.5. $C_{19}H_{29}IO$ requires C, 57.0; H, 7.3; I, 31.7%), $\nu_{max.}$ 1 730 cm^{-1} (OAc), δ 0.84 (s, 10-Me), 0.88 (s, *gem*-Me_2), 2.39 (m, $W_{1/2}$ 10 Hz, 13-H), and 4.95 (d, *J* 2 Hz, 15β-H), o.r.d. (*c* 6.9 in CH_2Cl_2) $[\phi]_{589}$ − 284°, $[\phi]_{500}$ − 444°, $[\phi]_{400}$ − 1 744°, $[\phi]_{368}$ − 3 368°, $[\phi]_{350}$ − 2 108°.

Iodination of 5α-*Cholest*-2-*en*-3-*yl Acetate*.—The enol acetate (33) (0.10 g, 0.23 mmol), m.p. 91—92° (lit.,[30] 90—90.5°), in dichloromethane (10 ml) was stirred with iodine(I) chloride (40 mg, 0.23 mmol) in dichloromethane (5 ml) at 20 °C for 4 h. The mixture was washed with 5N-sodium disulphite and water and the solvent was removed to give an oil (0.16 g). P.l.c. (hexane–ether, 5 : 1) yielded (i) starting material (trace); (ii) 2α-iodocholestan-3-one (34) (30 mg, 25%), m.p. 126—130° [lit.,[7] 125—127° (decomp.)], δ(CCl_4) 0.67 (s, 18-H_3), 1.23 (s, 19-H_3), and 4.85 (dd, $J_{a,e}$ 6, $J_{a,a}$ 12 Hz, *eq*-2-H); and (iii) 5α-cholestan-3-one [31] (20 mg, 22%), m.p. and mixed m.p. 126—127°.

Attempts to form the iodo-ketone (34) by the general procedure using 1 or 2 equiv. of thallium(I) acetate in either dichloromethane or glacial acetic acid were unsuccessful.

Bromination of 17-*Nor*-13β-*kaur*-15-*en*-16-*yl Acetate*.—A solution of bromine (80 mg, 0.5 mmol) in glacial acetic acid (10 ml) was added dropwise to a stirred solution of the enol acetate (30) (0.16 g, 0.51 mmol) and thallium(I) acetate (0.13 g, 0.5 mmol) at 20 °C. The mixture was stirred for 1 h, thallium salts were removed, and the filtrate was poured into water. Extraction with ether and work-up in the normal manner gave 15α-*bromo*-17-*nor*-13β-*kauran*-16-*one* (32) (0.16 g, 88%), which crystallized from methanol as needles, m.p. 147—148° (Found: C, 64.6; H, 8.2; Br, 22.8. $C_{19}H_{29}BrO$ requires C, 64.6; H, 8.3; Br, 22.6%), $\nu_{max.}$ 1 745 cm^{-1} (CO), δ 0.80 (s, 10-Me), 0.87, 0.90 (2s, *gem*-Me_2), 2.48 (m, 13-H), and 4.51 (d, *J* 3 Hz, 15α-H), o.r.d. (*c* 3.0 in CH_2Cl_2) $[\phi]_{600}$ − 13°, $[\phi]_{500}$ 0°, $[\phi]_{300}$ − 33°, $[\phi]_{275}$ + 13°, $[\phi]_{268}$ − 20°, $[\phi]_{220}$ + 480°.

A similar reaction in the absence of thallium(I) acetate gave an 83% yield of the bromo-ketone (32).

Solvolysis of 6α-*Iodo*-13-*methoxytotara*-8,11,13-*trien*-7-*one*.—A solution of the iodo-ketone (17) (30 mg, 0.07 mmol) in glacial acetic acid (5 ml) was heated under reflux with silver acetate (25 mg, 0.13 mmol) for 8 h. Work up and p.l.c. (benzene) gave 13-methoxytotara-5,8,11,13-tetraen-7-one (36) [32] (16 mg, 76%) and 13-methoxytotara-8,11,13-trien-7-one (19) [33] (5 mg, 23%), each identical (i.r. and ^{1}H n.m.r. spectra) with an authentic sample.

Similar treatment of the iodo-ketone (17) with thallium(I) acetate for 24 h gave only a low yield of the ketones (36) and (19).

[7/1060 *Received*, 20*th June*, 1977]

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