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Reaction of 5 α -Cholest-2-ene with Iodine-Copper(II) Acetate

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Abstract

Reaction of 5 α -cholest-2-ene (1) with iodine (2.0mol equiv) and copper(II) acetate (2.0mol equiv) in acetic acid under refluxing yielded 5 α -cholestane-2 β , 3 β -diol 2-acetate (4) (13%), 2-iodoacetate (5) (55%), 3-iodoacetate (6) (10%), and 2-iodoacetate 3-acetate (7) (13%). Then the hydrolysis of these reaction mixtures afforded the more hindered 2 β , 3 β -diol (13) in good yield. In the case of cyclohexene (2), the similar compounds were obtained. In order to clarify the reaction pathway of the unexpected hydroxy iodoacetate, the reaction of *cis*-hydroxy acetate with iodine-copper(II) acetate was carried out. It was found that copper is coordinated to the oxygen of the hydroxyl group and the carbonyl group of the acetate so that the methyl group of the acetate may be activated, and then iodination occurs at the acetoxy group.

Much works have been reported on the *cis*-hydroxylation of olefins using the Prevost reaction and its Woodward modification.¹ These reactions are important methods for the formation of *vic*-diols on the more hindered β -face for 5 α -steroid.² Cambie *et al.*³ reported that the reaction of olefin with iodine-thallium(I) carboxylate gave the *cis*-hydroxy acetate; and Mangoni *et al.*⁴ described a convenient method for the preparation of 5 α -cholestane-2 β , 3 β -diol diacetate using potassium iodate. Also, Glotter and Schwartz⁵ reported that the reaction of 5 α -cholest-2-ene with thallium(III) acetate in acetic acid gave 5 α -cholestane-2 β , 3 β -diol diacetate and 3-acetate. Moreover, Corey and Das⁶ reported a new method involving the reaction of *trans*-2-bromocyclohexanol with cyanoacetic acid.

We have been investigating a novel iodination using iodine-copper(II) acetate or iodine-ammonium cerium(IV) nitrate (CAN); and as early steps in this research project, we have

already reported the α -iodination of ketones;⁷ the regioselective iodination of estradiol, estriol, and estrone;⁸ a convenient procedure for the iodination of electron-rich aromatic compounds;⁹ the α -iodination of carboxylic acid,¹⁰ and synthesis of hydroxy 1,4-benzoquinone.¹¹ Previously, we described the syntheses of steroidal *trans*-iodo acetate and more hindered *cis*-diol; 5 α -steroidal 2 β , 3 β -diol using iodine-copper(II) acetate in acetic acid.¹² More recently, we reported¹³ that the reaction mixtures of 5 α -cholest-2-ene with iodine-ammonium cerium(IV) nitrate (CAN(IV)) were converted with potassium hydroxide in methanol-water to give the more hindered 2 β , 3 β -diol.

Now, in the present paper, we would like to report that the reaction of 5 α -cholest-2-ene (1) with iodine and copper(I) acetate gave 5 α -cholestane-2 β , 3 β -diol 2-iodoacetate (5) as major product. The reaction of 5 α -cholest-2-ene (1) with iodine (2.0mol equiv) and copper(II) acetate (2.0mol equiv) in acetic acid under refluxing for 3 h yielded Compounds A (mp 134.5-135.5°C) (55%), B (mp 140-141°C) (10%), C (mp 88.0-88.5°C) (13%), and 5 α -cholestane-2 β , 3 β -diol 2-acetate (4) (13%). Compounds A and B showed absorption of hydroxyl group (3450cm⁻¹) and acetoxy group (1730 and 1275cm⁻¹ for A) (1710 and 1285 cm⁻¹ for B) peaks in the IR spectra. Elemental analysis and the high resolution mass spectrum of the Compounds A and B gave a molecular formula of C₂₈H₄₈O₃I. The NMR spectra of Compounds A, B, and C showed a singlet at 3.70 ppm due to the CH₂ICOO-. Treatment of these compounds with sodium borohydride gave 5 α -cholestane-2 β , 3 β -diol 2-acetate (4), 3-acetate (8), and diacetate (9), respectively. In the case of the reaction of 5 α -cholest-2-ene (1) with iodine-copper(II) acetate in propionic acid gave Compound D (mp 100-102 °C) (21%) and Compound E (8%) (mp 124-126°C). Compound D showed absorption at 3425 (OH), 1730 (C=O), and 1190 cm⁻¹ (C-O) in its IR spectrum. The NMR spectrum showed a multiplet (W/2=6 Hz) at δ 5.35 (C₂ α -H), a multiplet (W/2=21 Hz) at δ 4.82 (C₃ α -H), and quartet at δ 2.52 (CH₂CH₂COO-). Therefore, Compound D was presumed to be 5 α -cholestane-2 β , 3 β -diol 2-propionate (10). The IR spectrum of Compound E showed absorption at 3350 (OH), 1715 (C=O), and 1220 (C-O) cm⁻¹. The NMR spectrum showed a doublet at δ 2.0 due to the CH₃CH(I)- and a quartet at δ 4.50 due to the CH₂CH(I)-. This product was transformed by treating with sodium borohydride to 10. Therefore, Compound E was presumed to be 5 α -cholestane-2 β , 3 β -diol 2-(2-iodopropionate) (11).

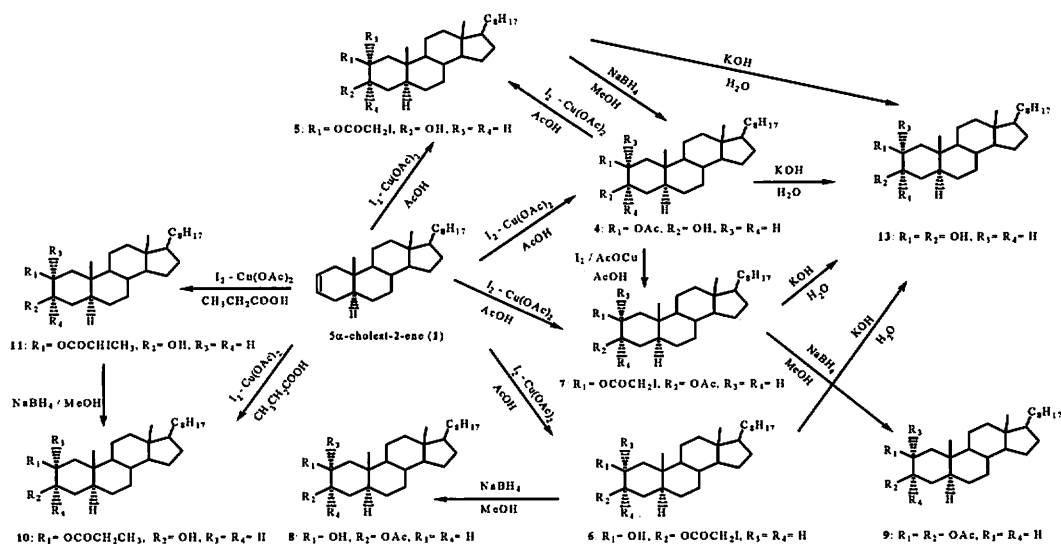
In the case of cyclohexene (2), Compounds F, and G, and *cis*-cyclohexane-1,2-diol (20) were obtained. Compound F showed a singlet due to the CH₂ICOO- group at δ 3.77 in the NMR spectrum, while Compound G showed two singlets due to the CH₂ICOO- and CH₃COO- groups at δ 3.76 and δ 2.13 in the NMR spectrum, respectively. From these data, both compounds were confirmed to be *cis*-cyclohexane-1,2-diol iodoacetate (15) and iodoacetate acetate (16) (50%). Also, in the case of cycloheptene (3), *cis*-cycloheptane-1,2-diol acetate (21) (50%), *cis*-diol diacetate (24) (14%), and *cis*-diol iodoacetate acetate (23) (38%) were obtained. Similarly, cyclohexene (2) in propionic acid gave the *cis*-1,2-diol

propionate (18) (34%). In the case of cycloheptene (3), the *cis*-1,2-diol propionate (25) (28%), the *cis*-1,2-diol 2-iodopropionate (26) (10%), and *trans*-iodo propionate (27) (10%) were also obtained.

Moreover, the reaction is applicable to the synthesis of the more hindered *cis*-diols. The reaction mixtures of 5 α -cholest-2-ene (1) with iodine (2.0mol equiv) and copper(II) acetate (2.0mol equiv) were converted with potassium hydroxide in methanol-water to give the 2 β , 3 β -diols (13) (91%). There results are summarized in Table 1 (Scheme 1).

Table 1. Products and Isolated Yields in the *cis*-Hydroxylation of Olefin with Iodine Copper(II) acetate

Materials	Acid	Temperature	Time	Product	Isolated Yield (%)
1	AcOH	reflux	3	13	91
1	EtCOOH	95	50	13	52
2	AcOH	reflux	10	20	83
2	EtCOOH	reflux	25	20	43
3	AcOH	reflux	15	28	80
3	EtCOOH	25	30	28	40



Scheme 1

It is noteworthy that this reaction may provide us with a new synthetic method for the more hindered *cis*-diols, more convenient than the method used heretofore.

From these results, it was found that unexpected *cis*-diol monoiodoacetate and *cis*-diol monoacetate were given in high yield. In order to clarify the reaction pathway of the unexpected iodoacetate, the following experiment was attempted. It was assumed that this unexpected compound was formed by iodination of *cis*-diol monoacetate produced as an intermediate. The reaction of *cis*-diol monoacetate with iodine-copper(II) acetate in acetic acid under refluxing yielded the corresponding hydroxy iodoacetate (Scheme 3). In the case of a *cis*-diol monopropionate, the corresponding hydroxy 2-iodopropionate was obtained. These results are summarized in Table 2. Cambie *et al.*¹ reported that treatment of 1-methyl-4-*t*-butylcyclohexene with thallium(I) acetate-iodine in wet acetic acid at 90 °C gave the *cis*-diol monoacetate (35%) and the α , β -unsaturated ketone (10%) together with the hydroxy iodoacetate (12%). They stated the formation of the *cis*-diol monoiodoacetate arises from the 1,3-dioxolan-2-ylum cation *via* a ketene acetate. In order to clarify this novel reaction pathway, we attempted the reaction of *cis*-cyclohexane-1, 2-diol diacetate (17) or cyclohexyl acetate (29) each with iodine-copper(II) acetate in acetic acid. However, the reaction of both Compounds 17 and 29 under refluxing for 40-50 h

Table 2. Products and Isolated Yields in the Iodination of *cis*-Hydroxy acylate

Materials	Time	Product	Isolated Yield (%)
4	3	5	55
		7	15
10	1	11	50
14	5	15	10
		16	50
		17	10
		19**	30
21	5	22***	60
25	30 (40°C) *	26	55

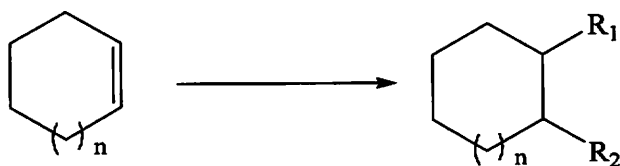
*The reaction of both compounds (18 and 25) under refluxing yielded l-iodopropionic acid (33) in good yield instead of *cis*-hydroxy 2-iodopropionates (19 and 26).

**Bp 132°C (7mmHg); IR (NaCl): 3460, 1740, and 1190cm⁻¹; ¹H NMR (CCl₄): δ = 2.32 (3H, d, C₁-OCOCHICH₂), 3.6-3.9 (1H, m), 4.21 (2H, q, C₁-OCOCHICH₂).

Found: *m/z* 298.0082. Calcd for C₇H₁₃O₃I; M, 298.0067.

***Bp (dec) 121°C (7mmHg); IR (NaCl): 3450, 1730, and 1260cm⁻¹; ¹H NMR (CCl₄): δ = 3.74 (2H, s, -OCOCH₂I), 3.8-4.1 (1H, m), and 4.8-5.0 (1H, m).

Found: *m/z* 298.0082. Calcd for C₇H₁₃O₃I; M, 298.0067.



2: $n=1$, **3:** $n=2$

15: $n=1$, $R_1 = \text{OCOCH}_2\text{I}$, $R_2 = \text{OH}$

16: $n=1$, $R_1 = \text{OCOCH}_2\text{I}$, $R_2 = \text{OAc}$

17: $n=1$, $R_1 = R_2 = \text{OAc}$

18: $n=1$, $R_1 = \text{OCOCH}_2\text{CH}_3$, $R_2 = \text{OH}$

21: $n=2$, $R_1 = \text{OAc}$, $R_2 = \text{OH}$

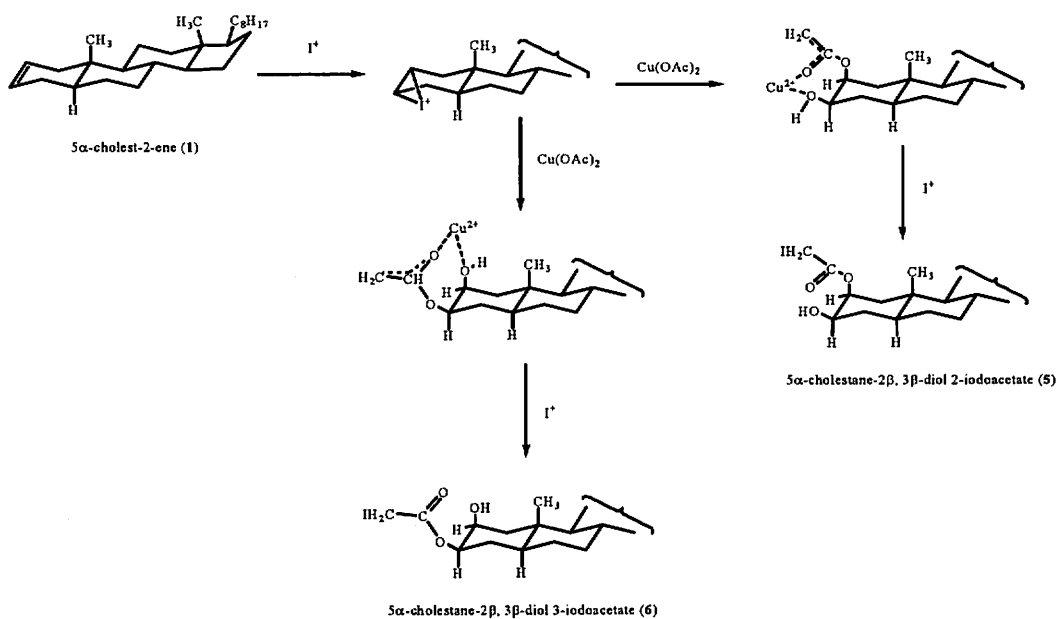
23: $n=2$, $R_1 = \text{OCOCH}_2\text{I}$, $R_2 = \text{OAc}$

24: $n=2$, $R_1 = R_2 = \text{OAc}$

25: $n=2$, $R_1 = \text{OCOCH}_2\text{CH}_3$, $R_2 = \text{OH}$

26: $n=2$, $R_1 = \text{OCOCHICH}_3$, $R_2 = \text{OH}$

Scheme 2



Scheme 3

yielded iodoacetic acid (**32**)¹⁰ in good yield (80%) instead of iodoacetate. The treatment of *cis*-hydroxy acetates **4** and **14** with iodoacetic acid in the presence of copper(II) acetate in acetic acid, resulted in the recovery of the starting materials, and *cis*-diacetoxy derivatives **9** and **17** were obtained. The reaction of *trans*-hydroxy acetate **30** gave *trans*-diacetate **31**. And as could be expected, no *cis*-hydroxy iodoacetate was formed in the iodination of *cis*-hydroxy acetate using copper(I) acetate or thallium(I) acetate (Scheme 2).

On the basis of the foregoing results, it is assumed that the copper is coordinated to the oxygen of the hydroxyl group and the carbonyl group of the acetate, or the methylene group of the propionate may be activated, and then iodination occurs at the acetoxy or propionyloxy group. This is the first time that α -iodination of *cis*-hydroxy acetates has been successfully accomplished.

Experimental

All the melting points are uncorrected. The IR spectra were measured using a Hitachi Model 215 grating infrared spectrometer. The NMR spectra were measured using a Hitachi-Perkin Elmer R-20A Model Spectrometer in deuteriochloroform or carbon tetrachloride with TMS as an internal standard. The high-resolution mass spectra were recorded at 75 eV on a JEOL JMS-01SG-2 instrument with a direct inlet.

Reaction of 5 α -Cholest-2-ene (1) with Iodine-Copper(II) Acetate in acetic acid. 5 α -Cholest-2-ene (**1**) (500mg) in acetic acid (50ml) was treated with iodine (690mg) and copper (II) acetate (542mg) under refluxing for 3 h. The reaction mixture was turned to brown, and then it was filtered to remove copper(I) iodide produced. The filtrate was taken up in ether, and the ether extracts were washed with sodium hydrogencarbonate solution and with water, and then dried and evaporated. The resultant oil was chromatographed on silica gel (30g). Elution with benzene-ether (10:1) (80ml) gave 5 α -cholestane-2 β , 3 β -diol 2-iodoacetate 3-acetate (**7**) (133mg) as plates from ethanol. Mp 88.0-88.5°C; IR (KBr): 1740, 1720, 1280, and 1240 cm⁻¹; ¹H NMR (CCl₄) δ = 2.02 (3H, s, C₁ β -OAc), 3.70 (2H, s, C₂ β -OCOCH₂I), 4.85 (1H, m, W/2 = 15.0 Hz, C₃ α -H), and 5.32 (1H, m, W/2 = 6.0 Hz, C₂ α -H).

Found: C, 60.65; H, 8.51%; HRMS: m/z 614.2789. Calcd for C₃₁H₅₀O₂I; C, 60.58; H, 8.36 %; M, 614.2829.

The second fraction, eluted by the same solvent (40ml) gave 5 α -cholestane-2 β , 3 β -diol 3-iodoacetate (**6**) (77mg) from ethanol, mp 140-141°C; IR (KBr): 3450, 1710, and 1285 cm⁻¹; ¹H NMR (CCl₄) δ = 3.70 (2H, s, C₃ β -OCOCH₂I), 4.13 (1H, m, W/2 = 6.0 Hz, C₂ α -H), and 4.80 (1H, m, W/2 = 24.0 Hz, C₃ α -H).

Found: C, 61.01; H, 8.23%; HRMS: m/z 572.2669. Calcd for C₂₉H₄₈O₂I; C, 60.83; H, 8.63%; M, 572.2724.

The third fraction, eluted by the same solvent (40ml) gave 5 α -cholestane-2 β , 3 β -diol

2-iodoacetate (5) (506mg) from ethanol, mp 134.5-135°C; IR (KBr): 3458, 1730, and 1275 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 3.73$ (2H, s), ca 3.5-4.0 (1H, m, C_3 α -H), and 5.20 (1H, W/2 = 6.0 Hz, C_2 α -H).

Found: C, 60.85; H, 8.17%; HRMS: m/z 572.2741. Calcd for $\text{C}_{29}\text{H}_{49}\text{O}_3\text{I}$; C, 60.83; H, 8.63%; M, 572.2724.

The fourth fraction, eluted by the same solvent (50ml) gave 5 α -cholestane-2 β , 3 β -diol 2-acetate (4) (78mg) from ethanol, mp 135-137°C (136-138 $^{\circ}\text{C}^{\circ}$); IR (KBr): 3430, 1740, and 1245 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 2.10$ (3H, s, C_2 - OCOCH_3), 3.70 (1H, m, W/2 = 18.0 Hz, C_3 α -H), and 5.15 (1H, m, W/2 = 6.0 Hz, C_2 α -H).

Found: C, 78.33; H, 10.95%; HRMS: m/z 446.3774. Calcd for $\text{C}_{29}\text{H}_{50}\text{O}_3$; C, 77.97; H, 11.28%; M, 446.3757.

Reaction of 5 α -Cholest-2-ene (1) with Iodine-Copper(II) Acetate in Propionic Acid. 5 α -cholest-2-ene (1) (500mg) in propionic acid (50ml) was treated with iodine (690mg) and copper(II) acetate (542mg) at 95°C for 50 h. The precipitated copper(I) iodide was removed by filtration, and the filtrate was poured into water and extracted with ether. After a similar work-up, the resulting oil was chromatographed on silica gel (20g). Elution with hexane (120ml) gave 5 α -cholest-2-ene (1) (170mg) as needles from acetone. The next fraction, eluted by benzene (350ml) gave 5 α -cholestane-2 β , 3 β -diol 2-propionate (10) (131mg) from methanol, mp 99-102°C; IR (KBr): 3425, 1730, and 1190 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 2.52$ (2H, q, C_2 β - $\text{OCOCH}_2\text{CH}_3$), 4.82 (1H, m, W/2 = 21.0 Hz, C_3 α -H), and 5.35 (1H, m, W/2 = 6.0 Hz, C_2 α -H).

Found: m/z 460.3826. Calcd for $\text{C}_{30}\text{H}_{52}\text{O}_3$; M, 460.3919.

The third fraction, eluted by benzene (50ml) gave 5 α -cholestane-2 β , 3 β -diol 2-(2-iodopropionate) (11) (65mg) as plates from methanol, mp 122-125°C; IR (KBr): 3350, 1715, and 1220 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 2.0$ (3H, d, C_2 β - OCOCHICH_3), 3.75 (1H, m, W/2 = 24.0 Hz, C_3 α -H), 4.50 (1H, q, C_2 β - OCOCHICH_3) and 5.18 (1H, m, W/2 = 6.0 Hz, C_2 α -H).

Found: m/z 586.2834. Calcd for $\text{C}_{30}\text{H}_{51}\text{O}_3\text{I}$; M, 586.2883.

Reaction of Cyclohexene (2) with Iodine-Copper(II) acetate in Acetic acid. Cyclohexene (2) (1.0g) in acetic acid (50ml) was treated with iodine (2.317g) and the usual work-up, the resulting oil was chromatographed on silica gel (50g). Elution with benzene-ether (10:1) (210ml) gave *cis*-1-iodoacetoxy-2-acetoxycyclohexane (16) (660mg) bp 139°C (6mmHg); IR (NaCl): 1738, 1270, and 1240 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 2.13$ (3H, s, C_2 - OCOCH_3), and 3.76 (2H, s, C_1 - OCOCH_2I).

Found: C, 36.81; H, 4.65%; HRMS: m/z 326.0036. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_4\text{I}$; C, 36.83; H, 4.64%; M, 326.0015.

The next fraction, eluted by benzene-ether (5:1) (50ml) gave *cis*-1,2-diacetoxycyclohexane (17) (238mg), bp 101-101.5°C (6mmHg) (118 $^{\circ}\text{C}^{15}$) (13mmHg); IR (NaCl): 1750

and 1240 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 1.98$ (6H, s, OCOCH_3).

The third fraction, eluted by benzene-methanol (20:1) (75ml) gave *cis*-1-iodoacetoxy-2-hydroxycyclohexane (**15**) (371mg), bp 148°C (7mmHg); IR (NaCl) 3430, 1725, 1270, and 1190 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 3.77$ (2H, s, C_1 - OCOCH_2I).

Found: C, 33.55; H, 4.60%; HRMS: m/z 284.0954. Calcd for $\text{C}_6\text{H}_{13}\text{O}_3\text{I}$: C, 33.82; H, 4.61%; M, 283.9910.

Reaction of Cyclohexene (2) with Iodine-Copper(II) Acetate in Propionic Acid.

Cyclohexene (**2**) (1.0g) in propionic acid (50ml) was treated with iodine (2.317g) and copper(II) acetate (1.077g) under refluxing for 25 h. After the usual work-up, the resulting oil was chromatographed on silica gel (16g). Elution with benzene-ether (5:1) (240ml) gave *cis*-1-propionyloxy-2-hydroxycyclohexane (**18**) (721mg), bp 119°C (22mmHg); IR (NaCl): 3460, 1730, and 1195 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 1.13$ (3H, t, C_1 - $\text{OCOCH}_2\text{CH}_3$), 2.28 (2H, q, C_1 - $\text{OCOCH}_2\text{CH}_3$), 3.40-3.70 (1H, m) and 4.82-5.12 (1H, m).

Found: m/z 173.1156. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_3$: [MH], 173.1178.

Reaction of Cycloheptene (3) with Iodine-Copper(II) Acetate in Acetic Acid.

Cycloheptene (**3**) (1.171g) in acetic acid was treated with iodine-copper(II) acetate for 15 h. After the usual work-up, the resulting oil was chromatographed on silica gel (20g). Elution with benzene-ether (10:1) (25ml) gave *cis*-cycloheptene-1,2-diol iodoacetate acetate (**23**) (1.654g), bp 143°C (1mmHg); IR (NaCl): 1738, 1270 and 1240 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) $\delta = 2.02$ (3H, s, C_2 - OCOCH_3), 3.66 (2H, s, C_1 - OCOCH_2I), and 4.90-5.30 (2H, m).

Found: m/z 340.0182. Calcd for $\text{C}_{11}\text{H}_{17}\text{O}_4\text{I}$: M, 340.0172.

The second fraction, eluted by the same solvent (25ml) gave *cis*-cycloheptane-1,2-diol diacetate (**24**) (373mg) bp 96°C (1mmHg); IR (NaCl): 1740, 1252 and 1242 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) $\delta = 2.03$ (6H, s), 5.03 (1H, m), and 5.16 (1H, m).

Found: m/z 214.120. Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_4$: M, 214.121.

The third fraction, eluted by the same solvent (105ml) gave *cis*-cycloheptane-1,2-diol acetate (**21**) (1.041g) bp 122°C (1mmHg); IR (NaCl): 3480, 1738, 1250 and 1028 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) $\delta = 2.07$ (3H, s, OCOCH_3), 3.77-4.20 (1H, m), and 4.77-5.30 (1H, m).

Found: m/z 172.1110. Calcd for $\text{C}_9\text{H}_{16}\text{O}_3$: M, 172.1100.

Reaction of Cycloheptene (3) with Iodine-Copper(II) Acetate in Propionic Acid.

A mixture of cycloheptene (**3**) (2.0g), iodine (5.403g), and copper(II) acetate (4.152g) in propionic acid (50ml) was stirred at room temperature for 30 h. After a similar work-up, the resultant oil was chromatographed on silica gel (25g). Elution with benzene (50ml) gave *trans*-1-iodo-2-propionyloxycycloheptane (**27**) (607mg), IR (NaCl): 1740 and 1170 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) $\delta = 1.16$ (3H, t, $\text{OCOCH}_2\text{CH}_3$), 4.05-4.50 (1H, m), and 4.70-5.35 (1H, m).

The second fraction, eluted by the same solvent (80ml) gave *cis*-1-(iodopropionyloxy)-2-hydroxycycloheptane (**26**) (721mg), bp 157°C (7mmHg); IR (NaCl): 3450, 1720, and 1200 cm^{-1} ; ^1H NMR (CCl_4) δ = 1.98 (3H, d, OCOCHICH_3), 3.75-4.13 (1H, m), 4.54 (1H, q, C_1 - OCOCHICH_3), and 4.78-5.10 (1H, m).

Found: m/z 321.0258. Calcd for $\text{C}_{10}\text{H}_{17}\text{O}_3$ I; M, 312.0223.

The third fraction, eluted by the same solvent (75ml) gave *cis*-1-propionyloxy-2-hydroxycycloheptane (**25**) (1.101g), bp 121°C (6mmHg); IR (NaCl): 3450, 1720 and 1190, cm^{-1} ; ^1H NMR (CCl_4) δ = 1.18 (3H, t, C_1 - $\text{OCOCH}_2\text{CH}_3$), 2.25 (2H, q, C_2 - $\text{OCOCH}_2\text{CH}_3$), 3.75-4.13 (1H, m), and 4.70-5.28 (1H, m).

Found: m/z 186.1264. Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_3$; M, 186.1256.

Reaction of Cyclohexene (**2**) with Iodine-Copper(II) Acetate in Propionic Acid at Room Temperature.

Cyclohexene (**2**) (2.0g) in propionic acid (100ml) was treated with iodine (4.364g) and copper(II) acetate (2.154g) at room temperature for 30 h. After the usual work-up, as mentioned above, the resultant oil gave *trans*-1-iodo-2-propionate **27** (5.513g), bp 113°C (6mmHg); IR (NaCl): 1730 and 1180, cm^{-1} ; ^1H NMR (CCl_4) δ = 1.18 (3H, t), 2.25 (2H, q), 3.75-4.35 (1H, m), and 4.65-5.10 (1H, m).

Found: m/z 282.0066. Calcd for $\text{C}_8\text{H}_{16}\text{O}_2\text{I}$; M, 282.0118.

Reaction of **27** with *m*-Chloroperbenzoic Acid.

The *trans*-1-iodo-2-propionate **27** (3.0g) in dichloromethane (50ml) was treated with *m*-chloroperbenzoic acid (1.835g) at room temperature for 1 h. After the work-up as mentioned above, the resultant oil gave *cis*-1-propionyloxy-2-hydroxycyclohexane (**18**) (1.96g), bp 119°C (22mg).

Reaction of 5 α -Cholestane-2 β , 3 β -diol 2-iodoacetate (**5**) with Sodium Borohydride.

The *cis*-diol iodoacetate **5** (40mg) in methanol (5ml) was treated with sodium borohydride (3mg). After the usual work-up, as mentioned above, the resultant oil on crystallization from methanol, yielded 2 β -acetoxy-5 α -cholestan-3 β -ol (**4**) (32mg), mp 13 5-137°C (136-138°C^b).

Reaction of 5 α -Cholestane-2 β , 3 β -diol 3-iodoacetate (**6**) with Sodium Borohydride.

By practically the same method as that in the case of **5** above, **6** (10mg) was converted to 5 α -cholestane-2 β , 3 β -diol 3-acetate (**8**) (6mg), mp 152-154°C (154-155°C^b).

Reaction of 5 α -Cholestane-2 β , 3 β -diol 2-iodoacetate 3-acetate (**7**) with Sodium Borohydride.

By practically the same method as that in the case of **5** above, **7** (11mg) was converted

to 5 α -cholestane-2 β , 3 β -diol diacetate (9) (7mg), mp 107-109°C (108-110°C⁵).

Reaction of 5 α -Cholestane-2 β , 3 β -diol 2-(2-iodopropionate) (11) with Sodium Borohydride.

By practically the same method as that in the case of 5 above, 11 (10mg) was converted to 2 β -propionyloxy- 5 α -cholestan-3 β -ol (10) (7mg), mp 99-102°C.

Hydrolysis of Reacton Mixtures of Olefin (1, 2, or 3) with Iodine-copper(II) Acetate in Acetic Acid or Propionic Acid. Typical Procedure.

A mixture of 5 α -cholest-2-ene (1) (500mg) iodine (690mg), copper(II) acetate (542mg), and acetic acid (50ml) was stirred under refluxing for 3 h. After the usual work-up, the resulting oil yielded reaction mixtures of 4, 5, 6, and 7. The reaction mixtures in methanol (50ml) were treated with potassium hydroxide (50mg) in water (2.5ml) under refluxing for 0.5 h. After evaporation of the reaction mixtures, the residue was dissolved in ether. The ethereal solution was washed with water, dried, and evaporated. Crystallization of the residue from methanol gave plates of 5 α -cholestane-2 β , 3 β -diol (13) (491mg), mp 174-177°C (175-176°C⁵).

Reaction of *cis*-1,2-Diol Monoacetate or Monopropionate with Iodine-Copper(II) Acetate. General Procedure.

A mixture of 2 β -acetoxy-5 α -cholestan-3 β -ol (4) (1.36mmol), iodine (1.36mmol), copper (II) acetate (1.36mmol), and acetic acid (50ml) was stirred under refluxing for 1 h. The reaction mixture turned to brown; and then it was filtered to remove copper(I) iodine produced. The filtrate was taken up in ether, and the ether extracts were washed with sodium hydrogencarbonate solution and with water, and then dried and evaporated. Crystallization of the residue from ethanol gave 5 α -cholestane-2 β , 3 β -diol 2-iodoacetate (5) (55%) and 2-iodoacetate 3-acetate (7) (15%).

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