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THE TRITERPENES OF *COMMIPHORA*—III

THE STRUCTURE OF COMMIC ACID E

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Abstract—Evidence is presented to show that commic acid E is best represented by (VI), namely 1β,2β,3β-trihydroxyurs-12-ene-23-oic acid. Several unusual reactions of this system are discussed.

The acid components of *Commiphora pyracanthoides* Engl. (= *C. glandulosa* Schinz) resin consist of small amounts of a monohydroxy acid (commic acid B), together with two dihydroxy acids (commic acids C and D) and a trihydroxy acid designated commic acid E.[2] In Part II,[3] the structures of the dihydroxy acids were discussed; in particular, acid D was linked with β-boswellic acid[4], thus fixing the carbon skeleton. From its reactions, commic acid D was shown to be a 2,3-dihydroxy-urs-12-ene-23(or 24)-oic acid, the 2β, 3β orientation being preferred for the hydroxyl groups, and the 23 position for the carboxyl group.

The present communication concerns the structure of commic acid E. Of the three hydroxyl groups present in the methyl ester, two are readily esterified.[2] Chlorination of the diacetate with phosphorus oxychloride resulted in a chlorodiacetate which, on reduction in the presence of alkaline Raney nickel, yielded a dihydroxy ester that proved to be identical with methyl commate D. Commic acid E was thus shown to be an urs-12-ene derivative (a fact already suspected when it was found that the chlorodiacetate was inert to selenium dioxide), and to have a 2,3-dihydroxy 23(or 24)-carboxylic acid group as D, with the same stereochemistry about at least the 3 and 4 positions. This reaction does not permit a definite stereochemical assignment about C-2, nor does it supply information about the position of the third hydroxyl group. Indeed, the two hydroxyl groups in the chlorodiol (obtained on hydrolysis of the acetate) are not the same as those of methyl commate D, since the latter is definitely a *cis*-1,2-glycol,[3] whilst the former did not react with either periodic acid or lead tetraacetate. The reductive dehalogenation must therefore be associated with a rearrangement of the oxygen atom.

Information concerning the whereabouts of the third hydroxyl group and the stereochemical relationship between the 3-hydroxyl and the carboxyl groups was provided by periodic acid oxidation of commic acid E and its methyl ester. The oxidation product from the acid was neutral, and its infra-red spectrum showed a strong

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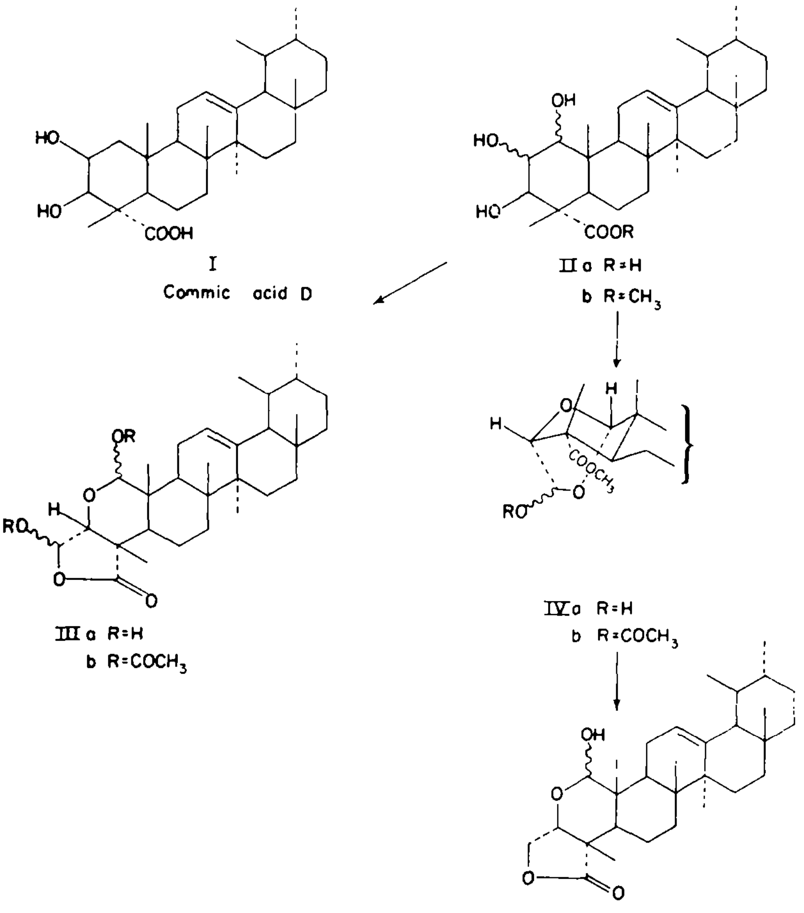
[2] A. F. Thomas and J. M. Müller, *Experientia* **16**, 62 (1960).

[3] A. F. Thomas, *Tetrahedron* To be published.

J. L. Beton, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.* 2904 (1956).

hydroxyl absorption, and most surprisingly, a single carbonyl peak at 5·62 μ, corresponding to a 5-membered ring lactone. Since commic acid E itself shows no tendency to lactonize, the lactonization must occur with an oxygen function at C-2, transformed by the periodate oxidation from a sterically unfavourable to a favourable orientation. Furthermore, the third hydroxyl group must be at C-1, since the formation of a 5-membered ring lactone requires an unbroken chain of four carbon atoms C-23-4-3-2) so that the cleavage must have occurred between C-1 and C-2. To account for the disappearance of both aldehyde groups during the periodate oxidation, acetalization must have occurred not only by the lactonization of the C-2 aldehyde, but also in some way at the C-1 aldehyde. Of the possible structures for the periodate oxidation product of commic acid E (IIa), we prefer IIIa, in which the ring containing the oxygen takes up the chair conformation with the lactone in the stable *cis*-form.[5] From structure IIIa it may be seen that the carboxyl and the 3-hydroxy group in acid IIa are *trans*-oriented. On account of the relatively easy hydrolysis of the ester, we chose



I
Commic acid D

IIa R=H
b R=CH$_3$

IIIa R=H
b R=COCH$_3$

IVa R=H
b R=COCH$_3$

V

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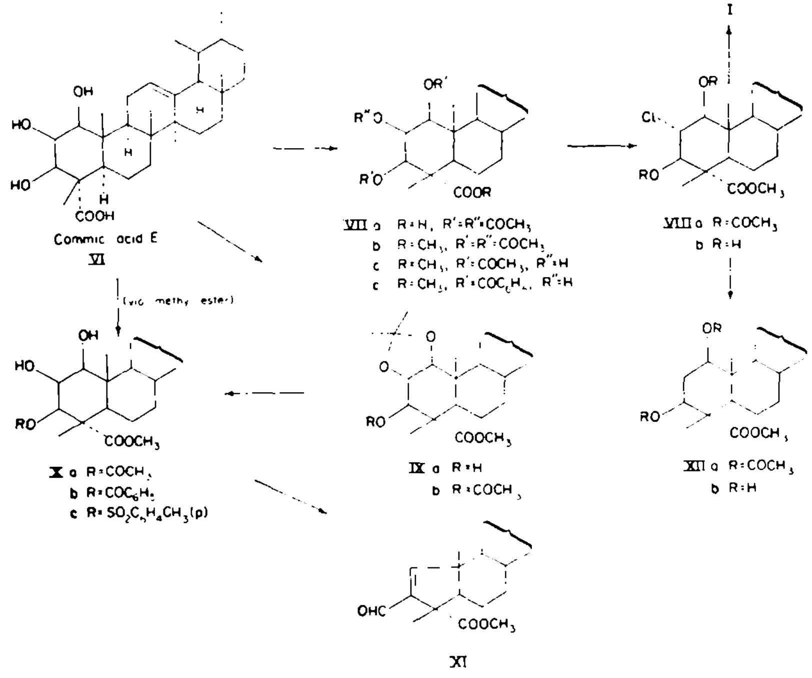
[5] The spontaneous lactonization and hemiacetalization implies that the product possesses the most stable possible structure; moreover the hemiacetal formation must occur very rapidly, otherwise an additional cleavage between C-2 and C-3 would take place. Epimerization at C-3 under the mild reaction conditions seems very unlikely.

the equatorial 4α-configuration for the carboxyl group (as in I[3]), resulting in the β-configuration for the 3-hydroxy group, allocations that were confirmed by subsequent reactions to be described.

The periodic acid cleavage product of the ester (IIb) also exhibits only one carbonyl absorption band in its infra-red spectrum, namely that associated with the ester group, and we consider its structure to be best represented by IVa. In accord with structures IIIa and IVa, the oxidation cleavage products yielded a di- and monoacetate respectively (IIIb and IVb), neither acetate exhibiting hydroxyl absorption in the infrared. The assumption that the periodic acid cleavage of the ester also involved 1,2-bond rupture (and not 2,3-) was supported by the sodium borohydride reduction of the C-2 aldehyde in IVa (present here as a hemiacetal) which gave a 5-membered ring lactone (V).

Confirmation of the 1,2,3-trihydroxy group in methyl commate E (IIb) was provided by the results of oxidations using lead tetraacetate. Using glacial acetic acid as solvent, 1·7–1·8 equivalents were consumed, but the only product that was isolated was a small amount of compound IVa. In glacial acetic acid-chloroform (1:1), 2 equivalents of lead tetraacetate were consumed, although no crystalline product was isolated.

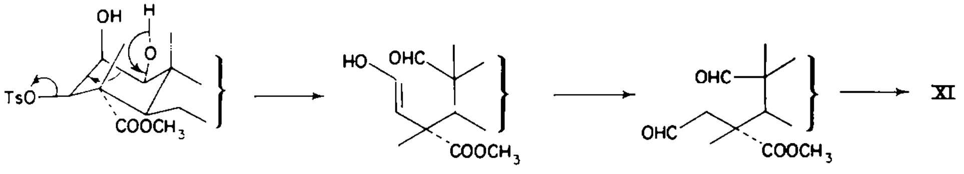
We now wished to obtain further information about the steric relationship between the other hydroxyl groups in ring A. In addition to the two easily esterified hydroxyl groups, characterised by a diacetate[2] and a dibenzoate, the third hydroxyl group can be esterified under more vigorous conditions, and a triacetate can be obtained from both acid (IIa) and ester (IIb). Since chlorination of the free hydroxyl in the ester diacetate and subsequent hydrolysis yields a 1,3-diol (see above), the hindered hydroxyl must be placed at C-2 in the axial 2β-configuration. The carboxyl group does not



lactonise with this hydroxyl, so the carboxyl must be equatorial (4α) (as we had suspected from the relatively easy ester hydrolysis). The ease of the periodic acid cleavage implies that the 1- and 2-hydroxy groups are *cis*-orientated, so that the remaining hydroxyl must have the 1β-configuration. The steric formula for commic acid E is therefore VI, and the various di- and triacylates obtained by direct acylation of the acid or its ester have formulae VIIa–d. Methyl commate E yields a single isopropylidene compound with acetone[2] in which the free hydroxyl group is readily acetylated. We assumed this to be a 1,2-isopropylidene derivative (IX) in anology with the fact that the periodic acid attack occurs exclusively at the 1,2-positions. The monoesters Xa and Xb were available from IX by acid hydrolysis, and reacted with periodic acid.

Since the 1β-hydroxyl group might be expected to be somewhat hindered by the 11α-hydrogen, it seemed likely that a direct monoesterification in the 3-position would be possible. In fact methyl commate E and *p*-toluenesulphonyl chloride gave only a monotosylate, which must be allotted structure Xc. Treatment of this tosylate with collidine gave rise to an unsaturated carbonyl compound containing no hydroxyl group (I.R.), to which we assign structure XI on the following mechanistic grounds. The high degree of substitution in ring A inhibits the formation of the intermediate boat conformation required for a 1,2-*trans*-elimination[6] of the tosyl group with the 2α-hydrogen atom.

A concerted reaction therefore takes place where p-toluene-sulphonic acid is lost and cleavage between C-1 and C-2 occurs as follows:[7]



Xc

XIII

The dialdehyde initially formed (XIII) subsequently cyclizes under the reaction conditions to the αβ-unsaturated aldehyde (XI).[8]

There finally remains to be discussed the conversion of the chlorodiacetate, now believed to have structure VIIIa, to methyl commate D (I) by means of Raney nickel and hydrogen in alkaline solution, a reaction that was mentioned at the outset. Alkali alone gives only the chlorodiol (VIIIb) from the acetate (VIIIa). With so many substituents in ring A, it is almost impossible to attain coplanarity of the Cl-C-C-OH chain required for formation of an epoxide. To account for the simultaneous dechlorination and oxygen shift under the influence of alkali and Raney

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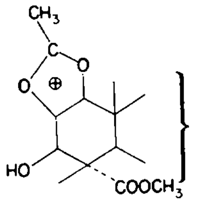
[6] *cf.* In this connection the rearrangement of a 2β-hydroxy-3β-*p*-toluenesulphonyloxysteroid in J. C. Sheehan and W. F. Erman, *J. Amer. Chem. Soc.* **79**, 6050 (1957).

[7] On account of the 1β-hydroxyl group, the steric requirements for this reaction are probably even better fulfilled than for the reaction reported to occur in the presence of alcoholates with a 1α-hydroxy-3β-tosyloxysteroid [R. B. Clayton, H. B. Henbest and M. Smith, *J. Chem. Soc.* 1982 (1957)]. For the mechanism, see also F. V. Brutcher and H. J. Cenci, *Chem. & Ind.* 1625 (1957). The observed shift of the 4,5-bond in 5,6-unsaturated 4,4-dimethyl-3β-tosylates [*cf.* R. M. Moriarty and E. S. Wallis, *J. Org. Chem.* **24**, 1274 (1959)] does not occur here because the methoxycarbonyl group renders the intermediate generation of a positive charge at C-4 more difficult.

[8] The observed U.V. maximum of XI (E^{EtOH}_{237} = 13,050) accords well with that of cyclopentene aldehydes in the steroid series [see e.g. P. Wieland, K. Heusler and A. Wettstein, *Helv. Chim. Acta* **41**, 416 (1958)]; in the I.R. spectrum of IX the absorption band of the C—H bond of the aldehyde is clearly visible at 3.67 μ.

nickel,[9] it therefore appears as if a transition state is involved that is less exacting in its stereoelectronic requirements than is the formation of an epoxide by means of alkali. Besides methyl commate D (I), a second dihydroxyester could be isolated from the reaction, and since this ester did not react with periodic acid, we propose to ascribe to it structure XIIb. It is conceivable that the C-Cl bond is broken under the influence of the nickel, and that in the alkaline solution, before the more difficult hydrolysis of the 1β-acetate occurs, an intermediate of the type XIV is formed, which can then give both diols (I and XIIb) by elimination of a proton from either C-1 or C-2 followed by hydrogenation and hydrolysis of the resulting enol acetates.



XIV

The commic acids are unusual in having all their oxygen functions around ring A, without the commonly accompanying C-28 carboxyl group; the only other similar triterpene acids being the boswellic acids occurring in a plant related to *Commiphora*.[4,10] Commic acid E is, indeed, unique, for whilst other natural products with an oxygenated function at C-1 are known,[11] and recently, even some 1,2,3-trihydroxy-compounds have been described,[12] none had been positively identified until now in the triterpene or related 5α-steroid series.

EXPERIMENTAL

M.p.s are corrected. Rotations were measured at concentrations of 1% in chloroform unless otherwise stated. Alumina for chromatography was Woelm, neutral, grade III unless otherwise stated.

Commic acid E. Methyl commate E[2] (0·5 g) was heated under reflux with potassium hydroxide (5 g) in methanol (50 ml). After 40 min the potassium salt of the acid began to crystallize, and after 6 hr this was removed, washed with methanol and ether and converted to *commic acid E* with methanol–conc. hydrochloric acid; after crystallization from methanol this had m.p. 328–330° (decomp., evac. tube), $[\alpha]_D^{81°}$ - 104° (*c* = 1% in pyridine), pK_a 7·42 (80% cellosolve). (Found on substance dried at 140°/0·1 mm for 24 hr: C, 72·5, 72·5, 72·7; H, 10·2, 9·7, 9·8. $C_{30}H_{48}O_5 \cdot \frac{1}{2}CH_3OH$ requires: C, 72·6; H, 9·8%). Methylation of this acid with diazomethane in ether resulted in methyl commate E, identical with previously described material.[2] The acid was recovered unchanged after treatment with conc. sulphuric acid-dioxan.

Triacetylcommic acid E (VIIa). Commic acid E (0·15 g) was heated for 2 hr at 60° with acetic anhydride (5 ml) and conc sulphuric acid (5 drops). The solution was poured into ice water (75 ml)

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[9] Raney nickel and hydroxide appear to be essential for this reaction; it did not occur when sodium acetate was used as the base, nor when nickel was replaced by palladium on charcoal.

[10] A. Vogel, O. Jeger and L. Ruzicka, *Helv. Chim. Acta* **34**, 2321 (1951).

[11] These are rare, but examples of remotely related compounds are ouabagenin [R. B. Turner and J. A. Meschino, *J. Amer. Chem. Soc.* **80**, 4862 (1958); G. Volpp and Ch. Tamm, *Helv. Chim. Acta* **40**, 1860 (1957)], limonin and some other bitter principles [D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger, L. Caglioti, Sukh Dev, P. G. Ferrini, E. R. Glazier, A. Melera, S. K. Pradhan, K. Schaffner, S. Sternhill, J. F. Templeton and S. Tobinaga. *Experientia* **16**, 41 (1960)].

[12] Kogagenin [T. Kubota, *Chem. Pharm. Bull. Japan* **7**, 898 (1959); K. Takeda, T. Kubota (*Tetrahedron* **10**, 1 (1960)], and Tokorogenin [K. Morita, *Bull. Chem. Soc. Japan* **32**, 476, 791, 796 (1959)].

and ethanol (25 ml), and the resulting solid crystallized from methanol, m.p. 329–331° (decomp.), $[\alpha]_D^{27°}$ +63° (Found: C, 70·3; H, 8·7. $C_{36}H_{54}O_8$ requires: C, 70·3; H, 8·9%). $\lambda_{max}^{CH_2Cl_2}$ 2·87, 5·70 (vs), 5·85 μ.

Triacetal methyl commate E (VIIb). This was prepared in the same way from methyl commate E and purified by filtration in benzene through a column of aluminia, then crystallized from methanol, m.p. 225–228°, $[\alpha]_D^{20°}$ +56° (Found: C, 70·7; H, 9·1, $C_{37}H_{56}O_8$ requires: C, 70·7; H, 9·0%). $\lambda_{max}^{CH_2Cl_2}$ 5·69 (vs), 5·73 μ (shoulder), no band at 2·5–3·0 μ.

Dibenzoyl methyl commate E (VIId). This was prepared from methyl commate E with benzoyl chloride in pyridine and crystallized from methanol, m.p. 193–194°, $[\alpha]_D^{27°}$ −4° (Found: C, 75·8; H, 8·1. $C_{45}H_{58}O_7$ requires: C, 76·0; H, 8·2%). $\lambda_{max}^{CH_2Cl_2}$ 2·77, 5·76, 6·22 μ.

Reaction of commic acid E with periodic acid (IIIa). Commic acid E (0·095 g) was dissolved in dioxan (20 ml) and periodic acid (1·0 ml, 0·5 M). After 24 hr excess standard sodium arsenite solution was added, and back-titration against standard iodine showed that exactly one equivalent of periodic acid had been consumed. Water (50 ml) was added, and the precipitate recrystallized from 90% methanol to m.p. 175–177°, $[\alpha]_D^{18°}$ +76° (Found: C, 74·3; H, 9·6. $C_{30}H_{46}O_5$ requires: C, 74·0; H, 9·5%). $\lambda_{max}^{CH_2Cl_2}$ 2·78, 5·62 μ, no absorption at 3·5–4·0 μ or 5·7–6·0 μ. The *diacetate* (IIIb) was made in pyridine with acetic anhydride and crystallized from methanol, m.p. 244–246°, $[\alpha]_D^{20°}$ +5° (Found: C, 71·6; H, 8·7. $C_{34}H_{50}O_7$ requires: C, 71·6; H, 8·8%). $\lambda_{max}^{CH_2Cl_2}$ 5·58, 5·64, 5·70 μ, no absorption 2·5–3·0 μ.

Reaction of methyl commate E with periodic acid (IVa). This was carried out in the same way as the corresponding experiment with commic acid E. One equivalent of periodic acid was consumed, and the *product*, (IVa) crystallized from 90% methanol, m.p. 185°, $[\alpha]_D^{28°}$ +94° (Found: C, 74·2; H, 9·7. $C_{31}H_{48}O_5$ requires: C, 74·4; H, 9·7%). $\lambda_{max}^{CH_2Cl_2}$ 2·77, 5·76 μ, no absorption at 3·6–4·0 μ. The *acetate* (IVb) was made in pyridine and recrystallized from 90% methanol, m.p. 198–199°, $[\alpha]_D^{18°}$ +89° (Found: C, 73·2; H, 9·4; (CO)CH_3, 2·9. $C_{33}H_{50}O_6$ requires: C, 73·0; H, 9·3; (CO)CH_3, 2·8%). $\lambda_{max}^{CH_2Cl_2}$ 5·75, 5·80 μ, no absorption at 2·5–3·0 μ or 3·6–4·0 μ.

Reaction of IVa *with sodium borohydride* (V). The compound (IVa) obtained in the previous experiment (0·15 g) was dissolved in methanol (20 ml) and excess sodium borohydride. After 24 hr the *product* was isolated from the solution by dilution with water and ether extraction, then crystallized from methanol to m.p. 235–239°, $[\alpha]_D^{18°}$ +85° (Found: C, 76·3; H, 9·8. $C_{30}H_{48}O_4$ requires: C, 76·5; H, 9·8%). $\lambda_{max}^{CH_2Cl_2}$ 2·77, 5·63, 9·71 μ.

Lead tetraacetate oxidations. These were carried out by allowing the compound to react at room temperature for 12 hr with 0·1 N $Pb(OCOCH_3)_4$ in acetic acid or acetic acid–chloroform (1:1). Excess standard sodium arsenite was then added and the solution titrated against standard iodine in the presence of Criegee's solution. On one occasion using methyl commate E (0·464 g) in glacial acetic acid, the product was isolated by diluting with water and extracting with ether. Repeated crystallization from aqueous methanol gave 0·25 g of a substance m.p. 181–4°, undepressed on admixture with IVa and of identical I.R. spectrum. Otler experiments with methyl commate E using acetic acid-chloroform mixtures did not give crystalline material.

Acetylisopropylidene methyl commate E (IXb). Isopropylidene methyl commate E (IXa)[3] (0·25 g) was treated with acetic anhydride in pyridine and the *product* purified by chromatography on alumina; it was eluted with benzene and crystallized from methanol, m.p. 195–196°, $[\alpha]_D^{29°}$ +37° (Found: C, 73·9; H, 9·8. $C_{36}H_{56}O_6$ requires: C, 73·9; H, 9·7%). $\lambda_{max}^{CH_2Cl_2}$ 5·71, 5·74 μ (no absorption at 2·5–3·0 μ).

Monoacetyl methyl commate E (Xa). The acetylisopropionylidene compound (IXb), prepared in the previous experiment, was dissolved in hot methanol (15 ml) and conc. hydrochloric acid (1 drop) and allowed to cool to room temperature. After 30 min water was added and the precipitate crystallized from 90% methanol, m.p. 214–215° (mixed with diacetyl methyl commate,[2] m.p. 200–204°), $[\alpha]_D^{18°}$ +71° (Found: C, 72·4; H, 9·3. $C_{33}H_{52}O_6$ requires: C, 72·7; H, 9·6%).

Monobenzoyl methyl commate E (Xb). This was made by treating isopropylidene methyl commate E[3] (IXa) with benzoyl chloride in pyridine. Dilution with water and crystallization of the precipitate from methanol gave the acetone-free *monobenzoate*, m.p. 151–153°, $[\alpha]_D^{18°}$ +95° (Found: C, 75·1; H, 8·9. $C_{38}H_{54}O_6$ requires: C, 75·2; H, 9·0%). $\lambda_{max}^{CH_2Cl_2}$ 2·78, 5·75, 6·22 μ. Treatment of this substance with methanol–conc. hydrochloric acid left it unchanged; it reacted with one equivalent of periodic acid in dioxan solution.

p-*Toluenesulphonyl methyl commate E* (Xc). This was made from methyl commate E and *p*-toluenesulphonyl chloride in pyridine and crystallized from 90% methanol, m.p. 191–192° (decomp.), (Found: C, 69·2; H, 8·6; S, 4·9. $C_{38}H_{56}O_7S$ requires: C, 69·5; H, 8·6; S, 4·9%). $\lambda_{max}^{CH_2Cl_2}$ 2·78, 5·75, 6·24, 8·42, 8·52 μ.

Collidine treatment of p-*toluenesulphonyl methyl commate E* (to give XI). The *p*-toluenesulphonate described in the previous experiment (0·15 g) was heated for 6 hr at 140° with collidine (10 ml). The mixture was made acid with 2 N hydrochloric acid and the product filtered and chromatographed on alumina (Merck, neutral, grade I–II). A *substance* (XI) (40 mg) was eluted with benzene and was crystallized from methanol, m.p. 164°, $[\alpha]_D^{25^\circ}$ +110° (Found: C, 79·5; H, 9·8. $C_{31}H_{46}O_3$ requires: C, 79·8; H 9·9%). ϵ_{max}^{EtOH} 237 mμ 13,050, $\lambda_{max}^{CHCl_2}$ 3·67, 5·76, 5·93, 6·26, $\lambda_{max}^{CS_2}$ 3·69, 5·74, 5,91, 13·53 μ.

Reaction of diacetyl methyl commate E (VIIc) *with phosphorus oxychloride, diacetyl methyl chlorocommate* (VIIIa). Diacetyl methyl commate E[2] (0·4 g) was dissolved in pyridine (15 ml), and phosphorus oxychloride (3 ml) was added. The solution was heated under reflux for 2 hr, cooled and added slowly to ice (about 200 g). *Diacetyl methyl chlorocommate* (VIIIa) was extracted with benzene, and, after washing the solution with hydrochloric acid and sodium bicarbonate and removing the solvent, was chromatographed on alumina. It was eluted with petroleum ether–benzene (1:1) and crystallized from methanol, m.p. 227°, $[\alpha]_D^{18^\circ}$ +35° (Found: C, 69·8; H, 8·9; Cl, 6·1. $C_{35}H_{53}O_6Cl$ requires: C, 69·5; H, 8·8; Cl, 5·9%). $\epsilon_{max}^{CH_2Cl_2}$ 5·73 (v broad), $\lambda_{max}^{CS_2}$ 5·74, 5·78 μ.

Methyl chlorocommate (VIIIb). This was made by dissolving the diacetate (VIIIa), prepared as described above, in hot methanolic sodium hydroxide (2%) and allowing to cool. The precipitate was crystallized from methanol (in which it is sparingly soluble) to m.p. 282–284° (gas evolution), $[\alpha]_D^{26^\circ}$ +86° (Found: C, 71·17; H, 9·3; Cl, 6·7. $C_{31}H_{49}O_4Cl$ requires: C, 71·4; H, 9·5; Cl, 6·8%). λ_{max}^{Nujol} 2·88, 5·87 μ.

Reduction of diacetyl methyl chlorocommate (VIIIa). Diacetyl methyl chlorocommate (0·24 g) dissolved in alcohol was added to alcohol containing sodium hydroxide (0·4 g) and Raney nickel and shaken in hydrogen. Reduction was fairly slow, and it was difficult to measure exactly how much hydrogen was absorbed, but after 10 hr there was little further change, whereupon the catalyst was removed and the solution poured into water (300 ml). The solid was isolated with ether and acetylated in pyridine, and the crude acetate mixture chromatographed on alumina. Benzene eluted an *diacetate* (55 mg) that was crystallized from methanol to m.p. 179–181°, undepressed on admixture with diacetyl methyl commate D[2] (Found: C, 73·8; H, 9·6. Calc. $C_{35}H_{54}O_6$: C, 73·8; H, 9·5%). Its I.R. spectrum in $CHCl_3$ was identical with that of diacetyl methyl commate D, and hydrolysis with methanolic sodium hydroxide gave material that was identical in all respects with methyl commate D.[2,3] Further elution of the column with ether yielded a different *diacetate* (XIIa) (60 mg) (that was crystallized from petroleum ether to m.p. 210°, $[\alpha]_D^{18^\circ}$ +94° (Found: C, 73·6; H, 9·6. $C_{35}H_{54}O_6$ requires: C, 73·8; H, 9·5%). $\lambda_{max}^{CHCl_3}$ 5·78 μ, very slight absorption around 2·7 μ. On another occasion, instead of the Grade III alumina normally taken for this work, Woelm alumina, neutral, Grade I–II was used, and the acetates were allowed to stay on the column for 48 hr. Diacetyl methyl commate was eluted with benzene–ether (9:1), but instead of the diacetate (XIIa) described above, a *monoacetate* was eluted with chloroform and recrystallized from methanol, m.p. 235–237°, $[\alpha]_D^{24^\circ}$ +102° ($c = 0·5$) (Found: C, 74·9; H, 9·9. $C_{33}H_{52}O_5$ requires: C, 75·0; H, 9·9%). $\lambda_{max}^{CH_2Cl_2}$ 2·65, 5·78 μ, spectrum not identical with that of the diacetate. Reacetylation with pyridine acetic anhydride gave the diacetate XIIa.

Hydrolysis of monoacetate to substance XIIb. The monoacetate described in the previous experiment was dissolved in hot methanolic sodium hydroxide (2%) and the solution allowed to cool. The *product* was precipitated with water (unlike other diols in this series, XIIb is readily soluble in methanol) and crystallized from aqueous methanol to m.p. 204–206°, $[\alpha]_D^{22^\circ}$ +102° (Found: C, 76·2; H, 10·3. $C_{31}H_{50}O_4$ requires: C, 76·5; H, 10·4%). $\lambda_{max}^{CHCl_3}$ 2·76, 2·92, 5·85 μ. This compound was difficult to dry, indeed, on one occasion after drying for 6 hr at 80° and 0·05 mm (instead of 24 hr at 120°) it had m.p. 175–178°, and proved to be a hydrate (Found: C, 74·2; H, 10·3; $C_{31}H_{50}O_4{\cdot}H_2O$ requires: C, 73·8; H, 10·4%). It was identical in all other respects with the substance XIIb described above.

Acknowledgements—Among many helpful discussions with colleagues both in Leeds and Basle, we feel obliged to mention those with Dr. J. Kalvoda, who first suggested the possibility of a fragmentation reaction with the tosylate (Xc). One of the authors (A. F. T.) thanks Professor B. L. Lythgoe for his interest in the problem.