622. *Sesquiterpenoids. Part III.* The Stereochemistry of Caryophyllene.*

By A. Aebi, D. H. R. Barton, and A. S. Lindsey.

Mild acid-catalysed hydration of caryophyllene oxide affords a disecondary glycol formulated as 4 : 4 : 8-trimethyl*tricyclo*[6 : 3 : 1 : $0^{1,5}$]dodecane-2 : 9-diol. Similar hydration of *iso*caryophyllene oxide † furnishes a glycol stereoisomeric at $C_{(9)}$. These experiments prove that caryophyllene and *iso*caryophyllene are geometrical isomers about the endocyclic ethylenic linkage. On the basis of relative reactivities towards electrophilic reagents and by consideration of the course of isomerisation induced by nitrous acid, caryophyllene is regarded as the *trans*-isomer (I), and *iso*caryophyllene as the *cis*-isomer (X)

On palladium-catalysed hemihydrogenation both caryophyllene and *iso*caryophyllene give the same (*cis*-)dihydro-compound.

In recent communications (Šorm, Dolejš, and Pliva, *Coll. Czech. Chem. Comm.*, 1950, **15**, 186; Barton and Lindsey, *Chem. and Ind.*, 1951, **313**; *J.*, 1951, 2988; Dawson, Ramage, and Wilson, *Chem. and Ind.*, 1951, **464**; Barton, Bruun, and Lindsey, *ibid.*, 1951, 910; 1952, 691; *J.*, 1952, 2210; Dawson and Ramage, *J.*, 1951, 3382; Monteath Robertson and Todd, *Chem. and Ind.*, 1953, 437) the constitution (I) has been established for caryophyllene.† The *trans*-configuration for the ring fusion (cf. Rydon, *J.*, 1937, 1340) is demonstrated by the elegant *X*-ray studies of Robertson and Todd (*loc. cit.*). We now turn to two of the remaining problems of caryophyllene chemistry: the nature of *iso*caryophyllene and the configuration of the endocyclic ethylenic linkage.

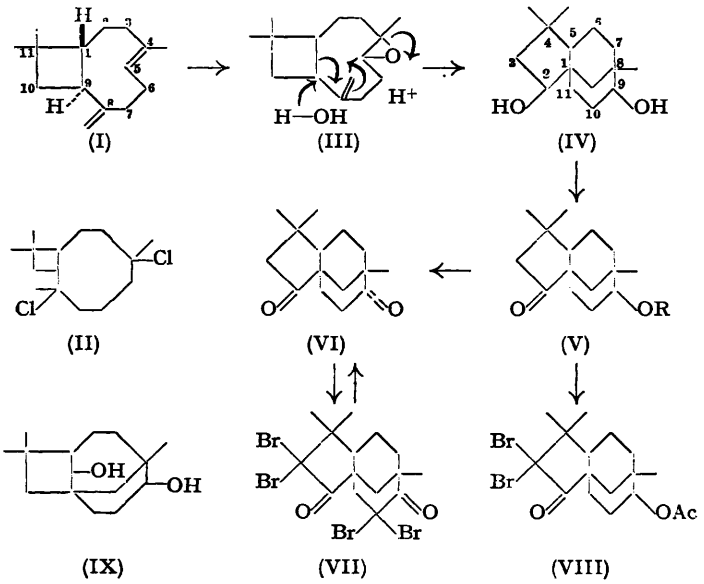
A close relation between caryophyllene and *iso*caryophyllene is indicated by the fact (see Simonsen and Barton, *op. cit.*) that both afford the same dihydrochloride (II). Caryophyllene and *iso*caryophyllene nitrosochlorides, on treatment with benzylamine, give the *same* nitrolbenzylamine. This would be best explained (see Barton, Bruun, and Lindsey, *Chem. and Ind.*, 1952, 691) if the two nitrosochlorides were stereoisomers, *not* structural isomers. The same conclusion can be reached from the important work of Ramage and Simonsen (*J.*, 1938, 1208; see Barton, Bruun, and Lindsey, *loc. cit.*). In addition Ramage and Simonsen have demonstrated that the exocyclic methylene grouping ($>C{=}CH_2$) is retained in *iso*caryophyllene. The infra-red spectrum of *iso*caryophyllene shows bands at 3100, 1630, and 880 $cm.^{-1}$, confirming the retention of this structural feature. Bands at 1666, 828, and 834 $cm.^{-1}$, indicative of $-CH{=}CMe-$, are also present as in the spectrum of caryophyllene. On these grounds we advanced the view (Barton, Bruun, and Lindsey, *loc. cit.*) that caryophyllene and *iso*caryophyllene must have the same constitution and that, as described in the literature, *iso*caryophyllene must be either impure caryophyllene or a geometrical isomer of caryophyllene about the endocyclic ethylenic linkage. The first objective then was to establish the purity of *iso*caryophyllene. In agreement with previous workers (see Simonsen and Barton, *op. cit.*) we find that the rotation of *iso*caryophyllene (α_D −24°) is significantly different from that of caryophyllene (α_D −8 to −9°) and that *iso*caryophyllene does not afford a nitrosite. With perphthalic acid *iso*caryophyllene gave a crystalline oxide different from ordinary caryophyllene oxide (Treibs, *Chem. Ber.*, 1947, **80**, 56). Hydrogenation of this oxide furnished an oily dihydro-derivative which

* Part II, *J.*, 1952, 2210. The majority of the work reported in Part III has been summarised elsewhere (Aebi, Barton, and Lindsey, *Chem. and Ind.*, 1953, 487).

† We have used the name caryophyllene consistently for the naturally occurring hydrocarbon. Previous nomenclature (see Simonsen and Barton, "The Terpenes," Vol. III, Cambridge Univ. Press, 1952) distinguishes three (α-, β-, and γ-)caryophyllenes. The name α-caryophyllene has been replaced by humulene (see Simonsen and Barton, *op. cit.*). Since in the α- and β-caryophyllene alcohols the prefixes are not related to the prefixes used to name the hydrocarbons, it seems to us that a clarification of nomenclature results if the name "β-caryophyllene" is replaced by caryophyllene and the name "γ-caryophyllene" by *iso*caryophyllene. This is in fact, a reversion to the earlier nomenclature of Deussen and Lewinsohn (*Annalen*, 1907, **356**, 20). The work described in our present paper removes the main basis for doubts previously expressed as to the homogeneity of naturally occurring caryophyllene, in that it establishes a mechanism for the ready isomerisation of the latter to *iso*caryophyllene.

on acid-catalysed hydration gave a nicely crystalline α-glycol. Caryophyllene oxide, treated in the same way, afforded the known crystalline dihydro-derivative (Treibs, *loc. cit.*), which under the same hydration conditions gave only oils. Caryophyllene and *iso*caryophyllene are, therefore, different chemical individuals.

The nature of *iso*caryophyllene was decisively confirmed in the following way. Mild acid-catalysed hydration of ordinary caryophyllene oxide (III) (Barton and Lindsey, *J.*, 1951, 2988; Barton, Bruun, and Lindsey, *J.*, 1952, 2210) afforded in good yield a crystalline disecondary glycol, characterised as the diacetate. On the basis of the established structure of (III) and of reactions summarised in the sequel this glycol must be formulated as (IV). Oxidation by chromic acid proceeded in two stages. First, a keto-alcohol (V; R = H), characterised as the crystalline acetate (V; R = Ac) and as the 2 : 4-dinitrophenylhydrazone, was obtained. Secondly, a diketone (VI), characterised as the bis-2 : 4-dinitrophenylhydrazone, resulted. In the infra-red, (V; R = H) showed a band at 1730 cm.$^{-1}$ (five-ring ketone), and (VI) showed bands at 1732 (five-ring ketone) and 1702 cm.$^{-1}$ (six-ring ketone), in agreement with the structures assigned. Bromination of (VI) to completion gave a tetrabromo-diketone (VII), which regenerated (VI) on reduction with zinc dust and acetic acid. This shows that the two keto-groups of (VI) are flanked by

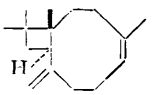
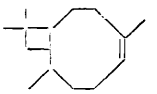


carbon atoms bearing at least four (replaceable) hydrogen atons. Bromination of (V; R = Ac) to completion gave a dibromo-acetate (VIII); therefore *both* keto-groups have two replaceable α-hydrogen atoms. A variant structure (IX) for the disecondary glycol is thus excluded. In agreement with the assigned structure, refluxing (VIII) with collidine provoked, not the elimination of hydrogen bromide, but reductive removal of one bromine atom. Wolff–Kishner reduction of the keto-alcohol (V; R = H) gave an oily alcohol oxidised by chromic acid to a ketone characterised as its 2 : 4-dinitrophenylhydrazone.

Similar hydration of *iso*caryophyllene oxide also afforded a crystalline disecondary glycol, shown to be a stereoisomer of (IV). Oxidation by chromic acid gave successively a keto-alcohol stereoisomeric with (V; R = H) and then the diketone (VI), already obtained from the glycol from ordinary caryophyllene oxide. The stereoisomer of (V; R = H) showed a band at 1730 cm.$^{-1}$ (five-ring ketone), thus confirming the assigned structure. The simplest interpretation of our experiments is that caryophyllene and *iso*caryophyllene oxides have identical configurations of the oxide ring at $C_{(4)}$ but differ in configuration at $C_{(5)}$. That *iso*caryophyllene is a geometrical isomer of caryophyllene is thus proved.

A decision has now to be made as to which of the structures (I) and (X) is caryophyllene and which is its stereoisomer. The phenyl azide reaction (Ziegler and Wilms, *Annalen*, 1950, **567**, 1; Blomquist, Liu, and Bohrer, *J. Amer. Chem. Soc.*, 1952, **74**, 3643) is not applicable since neither stereoisomer reacts. Prelog, Schenker, and Küng (*Helv. Chim. Acta*, 1953, **36**, 471) have shown that the strained *trans-cyclo*nonene reacts with per-acid faster than does the strain-free *cis-cyclo*nonene. A similar situation obtains in the *cyclo*decene series (Prelog, Schenker, and Günthard, *ibid.*, 1952, **35**, 1602). We find that caryophyllene reacts much faster with perphthalic acid than does *iso*caryophyllene. On this basis caryophyllene is the *trans*-isomer (I) and *iso*caryophyllene is the *cis*-isomer (X). The relative reactivities of the two isomers towards the electrophilic reagent nitrous acid (see above) are in agreement. These configurational assignments would also explain the modes of genesis of *iso*caryophyllene. The latter is obtained by steam-distillation of the mother-liquors from the preparation of caryophyllene nitrosite or by digestion of the nitrosite with alcohol. In the first method a derivative of *iso*caryophyllene does not appear to be an intermediate (see Experimental section) and the reaction can be regarded as the well-known isomerisation of a less stable to a more stable ethylenic linkage induced by nitrous acid. In the second method elimination of NO_2^- and NO^+ from the nitrosite by reversal of the addition mechanism must generate nitrous acid, which then isomerises the less stable *trans*- to the more stable *cis*-isomer in the usual way.

Before the successful completion of the experiments outlined above an attempt had been made to decide the relative stability of the caryophyllenes by determining the relative stabilities of their dihydro-derivatives. Dihydro- and dihydro*iso*-caryophyllene, prepared by palladium-catalysed hemihydrogenation, were heated with naphthalene-β-sulphonic acid. In both cases there was no apparent isomerisation, as judged by the rotation,* whereas according to Ziegler and Wilms (*loc. cit.*) and Blomquist *et al.* (*loc. cit.*) the *trans*-compound should have afforded the *cis*-isomer. A comparison of the infra-red spectra of dihydro- and dihydro*iso*-caryophyllene then revealed that they were identical, apart from very minor differences in the relative intensities of a few bands in the finger-print region. The infra-red spectra of caryophyllene and *iso*caryophyllene, compared at the same time, revealed marked differences. We conclude therefore that isomerisation takes place on the palladium catalyst during hydrogenation, so that the dihydrocaryophyllene described in the literature (see Simonsen and Barton, *op. cit.*) is really dihydro*iso*caryophyllene (XI). In agreement with this view " dihydrocaryophyllene," dihydro*iso*caryophyllene, and *iso*-caryophyllene all react with perphthalic acid at the same rate.

(X)   (XI)

The glycol (IV) has also been prepared by Atwater and Reid (personal communication from Dr. Evans B. Reid, Johns Hopkins University) by treatment of caryophyllene with performic acid, followed by alkaline hydrolysis. Thence the derived diketone (VI) was also obtained.

Experimental

For general experimental directions see *J.*, 1952, 2339. Infra-red spectra, in carbon disulphide solution, were kindly determined by Dr. J. E. Page and his staff (of Messrs. Glaxo Laboratories Ltd.), using a Perkin–Elmer double-beam instrument. $[\alpha]_D$'s are in chloroform; ultra-violet absorption spectra are in ethanol unless specified to the contrary.

*Dihydro*iso*caryophyllene.*—Caryophyllene (for physical constants see Barton and Lindsey, *J.*, 1951, 2988) was hydrogenated according to the directions of Naves and Perrottet (*Helv. Chim. Acta*, 1941, **24**, 789). The " dihydrocaryophyllene " obtained had b. p. 96°/3 mm., α_D −29°. This hydrocarbon (5 g.) was heated with quinol (100 mg.) and naphthalene-β-sulphonic acid (100 mg.) in nitrogen at 150° (sealed tube) for 1½ hr. (cf. Blomquist, Liu, and Bohrer,

* The rotations of the dihydro-compounds described here, although not in perfect agreement, are more nearly identical than any of those reported previously (for summary see Naves and Perrottet, *Helv. Chim. Acta*, 1941, **24**, 789). The lack of agreement is doubtless due to the difficulty of carrying out a truly selective hemihydrogenation.

J. Amer. Chem. Soc., 1952, **74**, 3643). The recovered hydrocarbon had b. p. 96°/3 mm., α_D −29° (l = 1).

Similar hydrogenation of *iso*caryophyllene afforded dihydro*iso*caryophyllene (XI), b. p. 96°/3 mm., α_D −31°. Treatment of this hydrocarbon with naphthalene-β-sulphonic acid as indicated above gave back a product, b. p. 96°/3 mm., α_D −33°.

Hydration of Caryophyllene Oxide (III).—The oxide (Treibs, *Chem. Ber.*, 1947, **80**, 56; Barton and Lindsey, *J.*, 1951, 2988) (10 g.) in a mixture of acetone (40 ml.), water (5 ml.), and 50% v/v sulphuric acid (2 ml.) was refluxed for 2 hr. on the steam-bath. The acetone was removed *in vacuo* and, after working up in the usual way, the product was crystallised from light petroleum (b. p. 80—100°), to give 4 : 4 : 8-*trimethyl*tricyclo[6 : 3 : 1 : $0^{1,5}$]*dodecane*-2 : 9-*diol* (IV) (4·1 g.) as needles, m. p. 152—153°, $[\alpha]_D$ +5° (*c*, 1·9) (Found: C, 75·4; H, 11·2. $C_{15}H_{26}O_2$ requires C, 75·55; H, 11·0%). Experiments on the hydration of caryophyllene oxide with formic or hydrochloric acid in place of sulphuric acid gave lower yields of the same glycol. The yield was also lowered when the acetone was replaced by dioxan, or when the reaction was conducted at room temperature.

The glycol was acetylated with pyridine–acetic anhydride overnight at room temperature. Recrystallisation of the product from methanol gave the *diacetate* as prisms, m. p. 96—97°, $[\alpha]_D$ −54° (*c*, 2·05) (Found: C, 70·6; H, 9·0. $C_{19}H_{30}O_4$ requires C, 70·75; H, 9·4%).

Chromic Acid Oxidation of 4 : 4 : 8-*Trimethyl*tricyclo[6 : 3 : 1 : $0^{1,5}$]*dodecane*-2 : 9-*diol* (IV).—The glycol (1·0 g.) in "AnalaR" acetic acid was treated with chromium trioxide (550 mg.) in aqueous "AnalaR" acetic acid (10 ml., 80%) at room temperature and left overnight. Working up in the usual way (continuous ether-extraction) afforded an oil (900 mg.) which was chromatographed over alumina (14 fractions). Fractions 2—4, eluted with light petroleum (b. p. 40—60°), gave 4 : 4 : 8-*trimethyl*tricyclo[6 : 3 : 1 : $0^{1,5}$]*dodecane*-2 : 9-*dione* (VI) (200 mg.). Recrystallised from light petroleum (b. p. 60—80°) as long needles this had m. p. 50—51°, $[\alpha]_D$ −109° (*c*, 1·9), $\lambda_{max.}$ 291—294 mμ, ε = 50 (Found: C, 77·2; H, 9·2. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·45%). Fractions 6—10, eluted with benzene, gave 4 : 4 : 8-*trimethyl*-2-*oxo*tricyclo[6 : 3 : 1 : $0^{1,5}$]*dodecan*-9-*ol* (V; R = H) (450 mg.). Recrystallised from light petroleum (b. p. 60—80°) as needles, this had m. p. 84—85°, $[\alpha]_D$ +11° (*c*, 1·7) (Found: C, 76·4; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%). A better yield of keto-alcohol was obtained in the following way. The glycol (1·0 g.) in "AnalaR" acetic acid (6 ml.) was treated with chromium trioxide (260 mg.) in aqueous acetic acid (20 ml.; 90%) at room temperature and left for 5 hr. Working up as above gave 400 mg. of pure keto-alcohol.

The diketone was characterised by conversion into the bis-2 : 4-*dinitrophenylhydrazone* in the usual way. Chromatographed in benzene solution over alumina and recrystallised from ethyl acetate–ethanol, this had m. p. 240—241° (Found: C, 54·1; H, 5·0. $C_{27}H_{30}O_8N_8$ requires C, 54·5; H, 5·1%).

The keto-alcohol was characterised by conversion into the 2 : 4-*dinitrophenylhydrazone*. Recrystallised from ethanol as needles, this had m. p. 179—180° (Found: C, 61·1; H, 7·05; N, 13·7. $C_{21}H_{28}O_5N_4$ requires C, 60·6; H, 6·8; N, 13·5%). Acetylation of the keto-alcohol with pyridine–acetic anhydride overnight at room temperature afforded the *acetate* (V; R = Ac). Purification by chromatography in benzene solution over alumina and recrystallisation from light petroleum (b. p. 40—60°) gave needles, m. p. 76—77°, $[\alpha]_D$ −34° (*c*, 1·35) (Found: C, 72·65; H, 9·4. $C_{17}H_{26}O_3$ requires C, 73·35; H, 9·4%). The keto-alcohol (100 mg.) in "AnalaR" acetic acid (2 ml.) was treated with chromium trioxide (50 mg.) in aqueous acetic acid (1 ml.; 80%) at room temperature and left for 2 days. The product was chromatographed over alumina [elution with light petroleum (b. p. 40—60°)], to give 4 : 4 : 8-trimethyl*tricyclo*[6 : 3 : 1 : $0^{1,5}$] dodecane-2 : 9-dione (see above) (80 mg.), identified by m. p. and mixed m. p.

[With Dr. T. Bruun.] The keto-alcohol (100 mg.) in ethanol (1·5 ml.) containing dissolved sodium (56 mg.) was heated with hydrazine (1 ml.) at 180° overnight. The product was an oil. This was oxidised to the corresponding ketone by treatment with a slight excess of chromic acid in "AnalaR" acetic acid. The non-crystalline 4 : 4 : 8-trimethyl*tricyclo*[6 : 3 : 1 : $0^{1,5}$]-dodecan-9-one was characterised by conversion into the 2 : 4-*dinitrophenylhydrazone*, m. p. 190—191° (from chloroform–methanol), $\lambda_{max.}$ 369 mμ (in $CHCl_3$), ε = 20,500 (Found: N, 13·9. $C_{21}H_{28}O_4N_4$ requires N, 14·0%).

Bromination of 4 : 4 : 8-*Trimethyl*tricyclo[6 : 3 : 1 : $0^{1,5}$]*dodecane*-2 : 9-*dione* (VI).—The diketone (100·5 mg.) in "AnalaR" acetic acid (20 ml.) containing hydrogen bromide (1 drop of 50% hydrogen bromide in acetic acid) and twice the theoretical amount of bromine for the replacement of four α-hydrogen atom was left at room temperature in the dark for 48 hr. (uptake, determined by titration of an aliquot, 97·5%). There was no change in bromine uptake after

a further 7 days at room temperature. Working up and crystallisation of the product from ether afforded 3 : 3 : 10 : 10-*tetrabromo*-4 : 4 : 8-*trimethyl*tricyclo[6 : 3 : 1 : $0^{1:5}$]*dodecane*-2 : 9-*dione* (VII) as colourless plates, m. p. 190—192°, $[\alpha]_D$ −68° (*c*, 1·9) (Found : C, 33·1; H, 3·5; Br, 58·3. $C_{15}H_{18}O_2Br_4$ requires C, 32·7; H, 3·3; Br, 58·2%). This compound resisted further bromination under the same conditions (no bromine uptake, confirmed by isolation). The tetrabromo-diketone (400 mg.) in " AnalaR " acetic acid (20 ml.) was refluxed with zinc dust (1 g.) for 4 hr. The product, crystallised from light petroleum (b. p. 40—60°), gave back the parent diketone (250 mg.), identified by m. p. and mixed m. p.

Bromination of 4 : 4 : 8-*Trimethyl*-2-*oxo*tricyclo[6 : 3 : 1 : $0^{1:5}$]*dodec*-9-*yl Acetate* (V; R = Ac).—The keto-acetate (see above) (30·3 mg.) was treated with bromine (4 Br) as for the diketone. After 50 hr. the uptake was 96·6% of the theoretical, unchanged after a further 7 days. Working up and crystallisation of the product from ether afforded 3 : 3-*dibromo*-4 : 4 : 8-*trimethyl*-2-*oxo*-tricyclo[6 : 3 : 1 : $0^{1:5}$]*dodec*-9-*yl acetate* (VIII) as plates, m. p. 151—152°, $[\alpha]_D$ −14° (*c*, 0·9) (Found : C, 46·9; H, 5·3; Br, 36·5. $C_{17}H_{24}O_3Br_2$ requires, C, 46·7; H, 5·75. Br, 36·3%).

The dibromo-acetate (100 mg.) was refluxed with collidine (20 ml.; freshly redistilled) for 4 hr. Recrystallisation of the product from methanol gave 3-*bromo*-4 : 4 : 8-*trimethyl*-2-*oxo*-tricyclo[6 : 3 : 1 : $0^{1:5}$]*dodec*-9-*yl acetate* (20 mg.), m. p. 182—183°, no high-intensity selective absorption in the ultra-violet above 220 mμ (Found : Br, 20·8. $C_{17}H_{25}O_3Br,CH_3{\cdot}OH$ requires Br, 20·6%).

iso*Caryophyllene Oxide*.—*iso*Caryophyllene was prepared *via* caryophyllene nitrosite by the method of Deussen and Lewinsohn (*Annalen*, 1907, **356**, 1). It had b. p. 92°/3 mm., and gave no nitrosite under the conditions used above for caryophyllene nitrosite and did not react with phenyl azide. Treatment in ethereal solution with perphthalic acid (110%) gave iso*caryophyllene oxide*, m. p. 80—81° [from light petroleum (b. p. 40—60°)], $[\alpha]_D$ −4° (*c*, 1·0) (Found : C, 81·95; H, 11·0. $C_{15}H_{24}O$ requires C, 81·75; H, 11·0%). The oxide gave a marked depression in m. p. on admixture with caryophyllene oxide, m. p. 61°, $[\alpha]_D$ −69° (*c*, 3·8).

*iso*Caryophyllene oxide (1·0 g.) in ethyl acetate (15 ml.) with palladised calcium carbonate (5%; 100 mg.) was hydrogenated until 1 mol. had been absorbed. The product was an oil which resisted all attempts at crystallisation (also after extensive chromatography). The oil (3·8 g.) in dioxan (5 ml.) and aqueous sulphuric acid (5 ml.; 10% w/v of sulphuric acid) was left at room temperature for 6 days. Working up and crystallisation from light petroleum (b. p. 40—60°) furnished a *glycol* (340 mg.), m. p. 165°, $[\alpha]_D$ −3° (*c*, 2·0) (Found : C, 75·2; H, 11·6. $C_{15}H_{28}O_2$ requires C, 74·95; H, 11·75%). On titration with lead tetra-acetate the glycol took up 94% of the theoretical amount for one α-glycol system.

Similar hydrogenation of caryophyllene oxide afforded dihydrocaryophyllene oxide, m. p. 63—65° (Treibs, *Chem. Ber.*, 1947, **80**, 56). When this was subjected to the same acid-catalysed hydration no crystalline product could be obtained.

Action of Nitrous Acid on Caryophyllene.—Treatment of caryophyllene (50 g.) with nitrous acid according to Deussen and Lewinsohn (*loc. cit.*), removal of the precipitated nitrosite by filtration and washing of the residual light petroleum solution with aqueous sodium hydroxide (10%) gave a colourless oil. After distillation *in vacuo* there resulted almost pure *iso*caryophyllene (25 g.), b. p. 93°/3 mm., α_D −19°, characterised by conversion into the crystalline oxide (see above), identified by m. p., mixed m. p. and rotation {$[\alpha]_D$ −6° (*c*, 2·5)]} by treatment with perphthalic acid.

Hydration of iso*Caryophyllene Oxide*.—The oxide (7 g.) was hydrated as described above for caryophyllene oxide. Crystallisation of the product from ether–light petroleum (b. p. 40—60° gave 4 : 4 : 8-*trimethyl*tricyclo[6 : 3 : 1 : $0^{1:5}$]*dodecane*-2 : 9-epi-*diol*, m. p. 174—175°, $[\alpha]_D$ +19° (*c*, 0·6) (Found : C, 75·15, H, 11·3. $C_{15}H_{26}O_2$ requires C, 75·55; H, 11·0%).

The glycol (200 mg.) in " AnalaR " acetic acid (2 ml.) was treated with a solution of chromium trioxide (105 mg.) in aqueous acetic acid (5 ml.; 90% v/v) for 5 hr. at room temperature. Filtration of the product in benzene through alumina and crystallisation from light petroleum (b. p. 40—60°) afforded 4 : 4 : 8-trimethyl*tricyclo*[6 : 3 : 1 : $0^{1:5}$]dodecane-2 : 9-dione (180 mg.) (see above), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −106° (*c*, 0·8)}.

The glycol (200 mg.) in " AnalaR " acetic acid (2 ml.) was treated with chromium trioxide (48 mg.) in aqueous acetic acid (3 ml.; 90% v/v) for 3 hr. at room temperature. The product was chromatographed over alumina. Elution with benzene and crystallisation from light petroleum (b. p. 40—60°) furnished 4 : 4 : 8-*trimethyl*-2-*oxo*tricyclo[6 : 3 : 1 : $0^{1:5}$)]*dodecan*-9-epi-*ol* (90 mg.), m. p. 68—70°, $[\alpha]_D$ +31° (*c*, 0·6) (Found : C, 76·2; H, 10·3. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%).

Rates of Reaction with Perphthalic Acid.—Caryophyllene, *iso*caryophyllene, and their respec-

tive dihydro-derivatives were titrated in an ice-bath with ethereal perphthalic acid. The reaction solutions were 0·0252M with respect to perphthalic acid and 0·023M with respect to the hydrocarbons. The data in the Table are illustrative.

Reaction (%) with ethereal perphthalic acid.

Time (min.)	76	243	360	48 × 60
Caryophyllene (I)	56	78	100	—
*iso*Caryophyllene (X)	10	20	43	80
" Dihydrocaryophyllene "	12	21	47	80
" Dihydro*iso*caryophyllene "	12	20	43	78

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