Tetrahedron. Vol. 27, pp. 4889 to 4899. Pergamon Press 1971. Printed in Great Britain

CYCLOADDITION OF ISOPROPYLCYCLOPENTADIENES AND DICHLOROKETENE, AND THE SOLVOLYSIS OF THE ADDUCTS

SYNTHESIS OF β-THUJAPLICIN (HINOKITIOL)

K. TANAKA* and A. YOSHIKOSHI†

Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Sendai, Japan

(*Received in Japan* 13 *May* 1971; *Received in the UK for publication* 21 *June* 1971)

Abstract—Dichloroketene was allowed to react with a mixture of 1- and 2-isopropylcyclopentadienes (**1** and **2**) to afford a mixture of the cycloadducts **5**, **7** and **8**. The adducts **5** and **8** were isolated, and an adduct **7** was obtained as a mixture with **5**. The structures of these adducts were assigned. Some derivatives of the adducts were prepared and their structures discussed. A mixture of β- and γ-thujaplicins (**19** and **20**) were produced after a mixture of the adducts was heated in acetic acid containing potassium acetate, 2-Isopropylcyclopentadiene (**2**) was prepared from cyclopentadienylmagnesium bromide and isopropyl tosylate, and the adduct obtained gave only β-thujaplicin under the same solvolytic reaction conditions.

INTRODUCTION

THUJAPLICINS (isopropyltropolones) were isolated from *Chamaecyparis taiwanensis* Masamune et Suzuki[1] and *Thuja plicata* D. Don[2,20a,21] as the first members of naturally occurring terpenic tropolones, and their antibacterial and antifungal activities have been demonstrated. In spite of low content and laborious procedure, β-thujaplicin‡ (hinokitiol) (**19**) has been isolated on a commercial scale from the essential oils of plants, especially *Thujopsis dolabrata* Sieb. et Zucc.[3]

A useful synthetic process of tropolones consists of the cycloaddition of cyclopentadiene, its derivatives, or fulvene derivatives and dichloroketene, followed by the solvolytic fragmentation of the resulting adducts. This process has been successfully applied to the synthesis of tropolone,[4] β- and γ-methyltropolones,[5] β- and γ-ethyltropolones,[6] α-dolabrin,[7] and 4,5-benzotropolone.[8] However, in the synthesis of 4- or 5-alkyltropolones, as seen in the above examples, this process usually gives a mixture of both products which is not always easy to separate. Very recently, Nozoe[9] reported, without giving a detailed explanation, the synthesis of β- and γ-thujaplicins by the sovolysis of the cycloadducts obtained from isopropylcyclopentadienes and dichloroketene. We have also independently studied the structures of the adducts of isopropylcyclopentadienes and dichloroketene and on the correlation between each adduct and its solvolysis product, β- or γ-thujaplicin. The correlation was also expected to give a clue to the mechanism of this solvolytic fragmentation.[10]

Current experimental work has revealed that 1-isopropylcyclopentadiene (**2**) is

* Present address: Central Research Laboratory, Ogawa Perfumery Co., Horiagedori, Higashiyodogawa-ku, Osaka.

† Address correspondence to this author.

‡ The prefix α, β or γ indicates the tropolone to be 3-, 4-, or 5-substituted respectively

essential for the preparation of β-thujaplicin based upon this synthetic process.[11] 1-Isopropylcyclopentadiene was prepared from cyclopentadiene in high purity, and β-thujaplicin not contaminated with the γ-isomer was obtained from the dichloroketene adduct of the pure diene.

RESULTS AND DISCUSSION

A mixture of isopropylcyclopentadienes (**2** and **3**) was prepared, according to Ziegler *et al.*,[12] from LAH reduction of 6,6-dimethylfulvene[13] (**1**) which is easily obtainable from cyclopentadiene and acetone. Although the original authors have not mentioned the structure of the diene, it was shown to be a mixture of two dienes (1:1 in approximate ratio). This was demonstrated by GLC, wherein a dimethylsulfolane-Neopak 1B column[14] was used, and by the NMR spectrum of the mixture, which showed integrated areas at methyl and olefinic proton regions approximately corresponding to an isopropyl group and three olefinic protons, respectively. Of three possible dienes (**2**, **3** and **4**), 5-isopropylcyclopentadiene (**4**) might be ruled out for the following reasons; (a) in general, 5-alkylcyclopentadienes have been reported as more thermodynamically unstable than the other two isomers and as isomerizing readily to other isomers even at room temperature,[15] (b) no cycloadduct derived from 5-isopropylcyclopentadiene could be detected in the adducts of the diene mixture and dichloroketene (*vide post*). Hence, it was concluded that the diene mixture consisted of 1- and 2-isopropylcyclopentadienes (**2** and **3**).

CHART 1

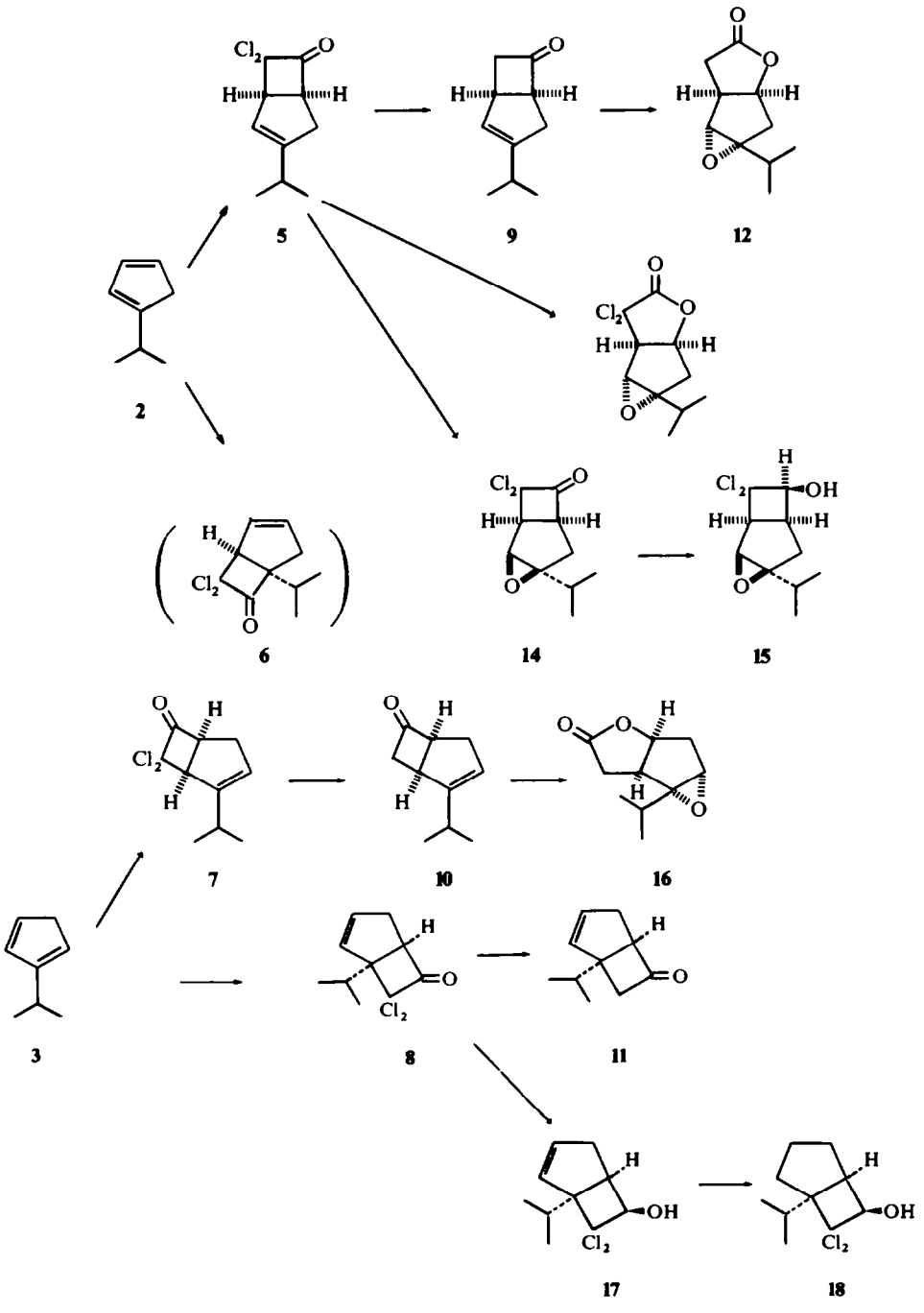
1 **2** **3** **4**

The reaction of the diene mixture with dichloroketene (dichloroacetyl chloride and triethylamine) produced a mixture of adducts in 80% yield. The mixture was separated into two pure adducts, **5** and **8**, and a mixture of the adducts (**5** + **7**) by means of chromatography. Another possible adduct **6** could not be isolated. The structures of these adducts will be discussed later.

In order to check the ratio of the formation, a total mixture of the cycloadducts was reductively dechlorinated by chromous chloride quantitatively, giving a mixture of the corresponding cyclobutanones, **9**, **10** and **11**, because insufficient separation (or decomposition) was observed for the former mixture in GLC. The GLC of the resulting cyclobutanone mixture showed that it consists of three ketones in the ratio of 4:67:29. Each cyclobutanone was separated by preparative GLC. On the other hand, the pure adducts **5** and **8**, were similarly treated with chromous chloride to give the cyclobutanones **9** and **11**, respectively, and the mixture fraction of the adducts **5** and **7** was also dechlorinated into a mixture of **9** and **10**. As demonstrated by the retention times, the largest peak in GLC of the total mixture of cyclobutanones was the peak for **9**, and the smallest one was that for **11**. It would be reasonable to estimate that the above

ratio of the cyclobutanones was approximately parallel to the formation ratio of the cycloadducts. These cyclobutanones (**9**, **10** and **11**) were characterized as crystalline semicarbazones.

CHART 2



The structures of the cycloadducts **5**, **7** and **8** were assigned as follows: the adduct **5**, most abundantly produced in the cycloaddition of the diene mixture and dichloroketene, was a 1:1 adduct of the diene and dichloroketene, and its NMR spectrum showed the presence of an olefinic proton. Although the NMR signals of **5** were insufficiently separated, they were assignable as shown in the structure **5**, except for the orientation of the dichloroketo group, by means of decoupling experiments (Experimental). On the other hand, in the epoxylactone **13**, which was obtained from oxidation of **5** with excess *m*-chloroperbenzoic acid, the signals were separated sufficiently to be easily assignable by a simple first-order treatment. The spectrum of the epoxylactone was consistent with the structure **13**, and the coupling constant J_{fg} (0 Hz) (formula **13a**) indicated that the oxirane ring was *trans* to the lactone ring. These observations showed that the structure of the adduct is **5**. The cyclobutanone **9** was also oxidized to the epoxylactone **12** in a similar manner.

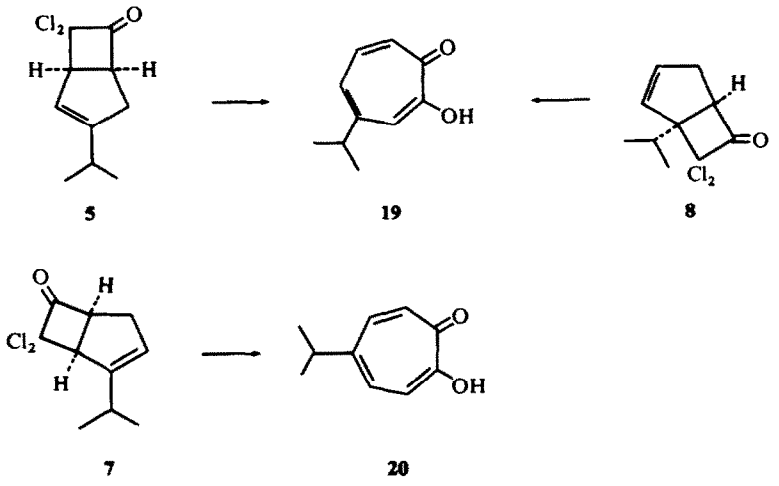
The NMR spectrum of the minor cycloadduct **8**, which was also a 1:1 adduct, showed that this compound possesses two olefinic protons of an AB-system (J = 5·6 Hz). Consequently, the structure **6** or **8**, or the structures in which dichloroketo groups are oppositely oriented respectively, may be assigned to it. Sodium borohydride reduction of this cycloadduct selectively yielded the *endo*-alcohol **17**. The IR spectrum of this alcohol indicated the presence of an intramolecular H-bonding of the OH group at 3568 cm^{-1}, while in the NMR spectrum the α-proton of the OH group showed a quartet signal (J = 7·5 and 10 Hz). Treatment with deuterium oxide changed the quartet into a doublet (7·5 Hz). The dihydro alcohol **18**, resulting from hydrogenation of **17**, no longer showed intramolecular H-bonding in the IR spectrum, and the NMR signal of the α-proton was observed as a doublet (J = 9·0 Hz). Accordingly, it was concluded that the larger coupling constants of the α-proton of **17** was due to the coupling between the α-proton and the OH proton, and that the H-bonding observed was the bonding between the OH and the double bond (formula **17a**). The above results are consistent with the formula **8** assigned to this minor cycloadduct.

Both the cycloadduct **8** and the corresponding cyclobutanone **11** resisted Baeyer-Villiger oxidation.

As described earlier, the adduct **7**, which was obtained as a mixture with **5** from column chromatography, afforded the cyclobutanone **10** by chromous chloride reduction of the adduct mixture following separation of the product by preparative GLC. The cyclobutanone, whose NMR and IR spectra showed an isopropyl group, an olefinic proton and carbonyl absorption due to cyclobutanone at 1782 cm^{-1}, was oxidized to the epoxylactone **16** with *m*-chloroperbenzoic acid. The NMR signals were assigned by NMDR experiments (Experimental). These results suggested the structure **7** to the cycloadduct.

A total mixture of the cycloadducts resulting from the diene mixture was heated in acetic acid containing potassium acetate,[4] and the tropolones formed were extracted with phosphoric acid from the mixture in 46% yield. Phosphoric acid-impregnated paper chromatography[16] showed, on comparison with authenic specimens, that the tropolone mixture seemed to consist of β- (**19**) and γ-thujaplicins (**20**). In fact, both thujaplicins were separated from the mixture by chromatography using a column packed with phosphoric acid-impregnated Celite,[17] and identified by their m.ps and spectral comparison. These results were in accordance with those reported by Nozoe.[9] On the other hand, the pure cycloadducts **5** and **8** were solvolyzed under

CHART 3



similar reaction conditions. Both yielded only β-thujaplicin (**19**), in 50% and 20% yields respectively.† However, the mixture fraction of the adducts **5** and **7** afforded, on solvolysis, a mixture of β- and γ-thujaplicins, as identified by phosphoric acid-paper chromatography. This indicated us that β-thujaplicin resulted from both adducts **5** and **8**, while the adduct **7** gave rise to the formation of the γ-isomer, and this correlation was also compatible with the reaction mechanisms recently proposed by two groups[11] for this solvolytic fragmentation. Consequently, it was found that 1-isopropylcyclopentadiene (**2**) is essential for the preparation of β-thujaplicin (**19**), provided no double bond migration takes place in the diene during the cycloaddition reaction with dichloroketene.

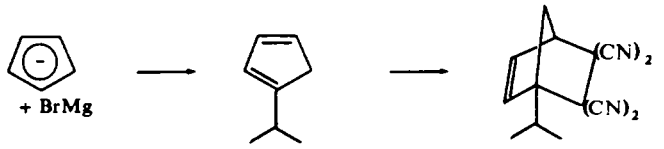
In order to examine this deduction, we attempted to prepare pure 1-isopropylcyclopentadiene from cyclopentadiene. A means of preparing 1-alkylcyclopentadiene from cyclopentadiene has been reported for the methyl derivative by Mironov *et al.*,[15] who have alkylated cyclopentadienylmagnesium bromide with dimethyl sulfate. In THF, cyclopentadienylmagnesium bromide (**23**) was alkylated with isopropyl tosylate to give a diene. The diene showed a single peak in GLC and was identified to be one of the two aforementioned dienes. The NMR spectrum showed no characteristic

† The selective formation of β-t-butyltropolone (**22**) from the adduct **21** has been found by Bartlett and Ando. See Ref 11*b*.

21 **22**

signals at δ *ca* 5·95 ppm which appeared in the spectrum of the diene mixture. This single diene isomerized easily to the same diene mixture as that obtained earlier on heating or especially on the addition of triethylamine, and was added to tetracyanoethylene at ice-bath temp, giving the single adduct **24** whose structure was proved by IR and NMR. These facts showed the single diene to be desired 1-isopropylcyclopentadiene (**2**).

CHART 4



23 **2** **24**

Triethylamine was added to a solution of the single diene and dichloroacetyl chloride in light petroleum at ice-bath temp to provide an adduct, whose spectra were superimposable with those of the adduct **5**. The identification of the adduct demonstrated that no double bond migration was observable under the conditions used. That this adduct afforded only β-thujaplicin on heating in acetic acid containing potassium acetate was a matter of course. The crude adduct was treated with excess peracid, and the product was chromatographed. Thus a small amount of the epoxyketone **14** could be separated from the major oxidation product **13**.

The NMR spectrum of the epoxyketone **14** (Experimental) gave no decisive evidence for its stereochemistry; however the corresponding epoxyalcohol **15**, obtained from **14** by sodium borohydride reduction, showed the presence of an intramolecular H-bonding between the OH and the epoxy groups in the IR and NMR spectra (formula **15a**), *viz.*, the OH group absorbed at 3412 cm^{-1}, and the α-proton and the OH proton appeared as a double quartet (J = 14·0, 7·0, and 3·2 Hz) and a doublet (J = 14·0 Hz), respectively. Treatment of **15** with deuterium oxide, concurrently with disappearance of the signal of the OH proton, changed the signal due to the α-proton into a quartet (J = 7·0 and 3·2 Hz). These observations supported that the epoxy ring in **14** was *cis* to the cyclobutane ring.

Thus we failed to observe the formation of the adduct **6** in the cycloaddition reaction, however, according to the proposed mechanism,[10] this adduct may not produce any tropolonic product.

EXPERIMENTAL

M.ps were uncorrected. IR spectra were run on a Hitachi EPI-S2 spectrophotometer, and a Perkin–Elmer Model 125 spectrophotometer was also used for measurements of diluted solns. NMR spectra of CCl_4 solns (unless otherwise stated) containing Me_4Si (δ = 0 ppm) as internal standard were taken on a JEOL JNMC-60-HL spectrometer (60 MHz) or Varian HA-100 spectrometer (100 MHz), and coupling constants were given in Hz. Mass spectra were obtained using a Hitachi RMU-6D spectrometer.

Isopropylcyclopentadienes (**2** *and* **3**)

According to Ziegler *et al.*,[9] an ethereal soln of freshly distilled 6,6-dimethylfulvene[10] was allowed to

react with LAH to obtain a mixture of **2** and **3**. After the ether was removed, the residue was distilled *in vacuo* (5 mm) in a bath keeping the temp below 10°, and the distillate was trapped in a cooled receiver at −20°. The distillate showed two peaks (51:49 in relative area) in GLC (dimethylsulfolane-Neopak 1B column;[11] ϕ 3 mm × 1·5 m; column temp., 40°; He flow, 164 ml/min) at the retention times of 18·5 and 22 min, respectively.

1-*Isopropylcyclopentadiene* (**2**)

To a THF soln of EtMgBr prepared from 14·0 g EtBr and 3·0 g Mg, 8·0 g of cyclopentadiene was added, and the mixture was refluxed for 8 hr under N_2. A soln of 27·0 g isopropyl tosylate[18] in THF was added to the above Grignard reagent soln at 0°, and after standing for 13 hr at the same temp, the mixture was poured into a cold NH_4Cl aq. The product was extracted with light petroleum and the combined extracts were dried over $MgSO_4$. The diene thus obtained showed a single peak at the retention time of 22 min in GLC. In GLC the diene mixture (*vide supra*) showed enhancement of the peak at 22 min by addition of this single diene; δ 1·13 (6H, d, J = 7·5), 2·7 (1H, sept., J = 7·5), 2·8 (2H, m), 6·05–6·45 (3H, m).

The diene was isomerized slowly into a mixture of **1** and **2** by refluxing its ethereal soln and the isomerization was remarkably accelerated by addition of Et_3N to afford a 1:1 mixture after 1·5 hr.

Diels–Alder adduct **24** *of* 1-*isopropylcyclopentadiene and tetracyanoethylene*

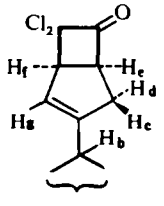
An ethereal soln of tetracyanoethylene and a small excess of 1-isopropylcyclopentadiene was allowed to stand in an ice-bath for 2 hr, and the ether was distilled off *in vacuo* at room temp. The solid residue was recrystallized from $CHCl_3$ to give the adduct **24** as colorless prisms, m.p. 165–165·5°, ν (KBr) 2230 cm^{-1}, δ (C_5D_5N) 0·95 (3H, d, J = 7·0), 1·30 (3H, d, J = 7·0), 2·00 (2H, t, J = 2·0), 2·45 (1H, sept., J = 7·0), 4·16 (1H, quint., J = 2·0), 6·72 (2H, d, J = 2·0). (Found: C, 71·28; H, 4·88. $C_{14}H_{12}N_4$ requires: C, 71·16; H, 5·12%).

Cycloaddition of the diene mixture (**2** + **3**) *and dichloroketene*

Et_3N (4·7 g) was added to an ethereal soln of the diene mixture obtained from 5·3 g 6,6-dimethylfulvene in the manner described. A soln of dichloroacetyl chloride (3·5 g) in the same solvent was added to the stirred diene soln at 5° dropwise over a period of 40 min. Stirring was continued for an additional 2 hr at the same temp. The precipitated salts were filtered off, and the filtrate was washed with 1N HCl and then water, and dried over $MgSO_4$. After removal of the solvent, the oily residue was poured onto a silica gel column and eluted with n-hexane–$CHCl_3$ (4:1) to separate the adducts from resinous products. The eluate was distilled *in* vacuo to give 4·2 g of the adduct mixture (80% on the basis of the dichloroacetyl chloride used). An aliquot (2·0 g) of the adduct mixture was carefully chromatographed on a silica gel column using n-hexane–benzene (10:1) as the eluting solvent. The adduct **5**, a mixture of **5** and **7** and **8** were eluted in this sequence. The pure adducts **5** and **8** weighed 647 and 60 mg, respectively.

The adduct **5** was an oil, ν_{max}(neat) 1807 cm^{-1}, δ (C_6D_6)* (see formula **5a**) 0·82 (H_a, 6H, d, J_{ab} = 7·5), 2·01 (H_d, d.m., J_{cd} = 16·3, J_{de} = 7·5), 2·04 (H_b, sept, J_{ab} = 7·5), 2·42 (H_c, dm, J_{cd} = 16·3), 3·57 (H_f, m), 3·71 (H_e, dt, J_{ef} = 7·5, J_{ee} = 1·8), 5·12 (H_g, m). (Found: C, 55·00; H, 5·36; Cl, 34·28. $C_{10}H_{12}OCl_2$ requires: C, 54·81; H, 5·52; Cl, 32·36%).

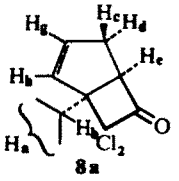
The adduct **8** was also an oil, ν_{max}(neat) 1807 cm^{-1}, δ* (see formula **8a**) 0·81, 1·10 (H_a, 3H, d, J_{ab} = 7·5 each), 2·45 (H_d, 1H, a pair of dt, J_{dc} = 17·5, J_{de} = J_{dh} = 1·95), 2·60 (H_b, 1H, sept, J_{ab} = 7·5), 2·77 (H_c, 1H.



5a

* These NMR spectra were measured at 100 MHz, and the signals were assigned by decoupling experiments.

brd, J_{cd} = 17·5), 3·63 (H_c, 1H, brd, J_{de} = 7·5), 5·75 (H_h, 1H, m), 6·05 (H_g, 1H, d.t., J_{gh} = 5·6). (Found: C, 54·41; H, 5·52; Cl, 32·64. $C_{10}H_{12}OCl_2$ requires: C, 54·81; H, 5·52; Cl, 32·36%).



8a

Cycloaddition of 1-*isopropylcyclopentadiene* (**2**) *and dichloroketene*

Dichloroacetyl chloride (8·0 g) was added to a stirred light petroleum soln of **2** prepared from 8·0 g cyclopentadiene as described, and then the soln was cooled to 0°. A soln of 7·0 g Et_3N in the same solvent was added to the stirred soln of the diene during a period of 40 min, and the mixture was stirred for an additional 4 hr at the same temp. The precipitated salts were filtered off, and the filtrate was washed with 1N HCl and then water, and dried over $MgSO_4$. The soln was poured onto a silica gel column, and the product was eluted with a mixture of light petroleum–ether (10:1). Removal of the solvent left a residue, which was then distilled *in vacuo* to give 5·88 g of an oil (79% yield on the basis of the dichloroacetyl chloride used). The oil was identical with the adduct **5** on a comparison of IR and NMR spectra.

Chromous chloride reduction of cycloadducts

2·19 g of a mixture of the cycloadducts, obtained from the mixture of 1- and 2-isopropylcyclopentadienes, was dissolved into 200 ml acetone. $CrCl_2$ aq (100 ml) prepared according to Djerassi *et al.*[19] was added to this acetone soln. The soln was allowed to stand at room temp under N_2 for 3 hr. and diluted with water. The product (1·33 g) was extracted with ether, and its IR spectrum showed no absorption at 1807 cm^{-1} (α-dichlorocyclobutanone). In GLC (PEG 20M-Celite column, ϕ 3 mm × 1·5 m; column temp, 155°; He flow, 12 ml/min), the product showed three peaks at the retention times of 9·5, 11 and 13 min in the ratio of 4, 67 and 29%, respectively. Each cyclobutanone was also isolated by preparative GLC.

The cycloadducts **5** and **8**, isolated by column chromatography, were similarly treated with $CrCl_2$ aq, and the resulting **9** and **11** were checked for their retention times by GLC. The comparison indicated that the first peak corresponded to **11** and the second one to **9**. On the other hand, similar treatment of the mixture fraction (**5** + **7**) gave a mixture of cyclobutanones which showed two peaks at the retention times of 11 and 13 min in GLC. The peak which eluted faster was identified as **9** by the peak enhancement experiments.

The isolated cyclobutanones were characterized as follows.

(a) Cyclobutanone **9**; ν_{max}(neat) 1782 cm^{-1}, δ 1·05 (6H, d, J = 7·0), 2·0–4·0 (7H), 5·40 (1H, quint, J = 1·9). Its semicarbazone was colorless leaflets and melted at 183–184°. (Found: C, 63·96; H, 7·74; N, 20·10. $C_{11}H_{17}ON_3$ requires: C, 63·74; H, 8·27; N, 20·27%).

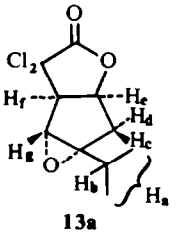
(b) Cyclobutanone **11**; ν_{max}(neat) 1783 cm^{-1}, δ 0·85, 0·96 (3H, d, J = 7·0 each), 1·6–3·5 (7H), 5·73 (2H, s, accompanied by satelite bands). The semicarbazone, m.p. 189–189·5°, was obtained as colorless leaflets. (Found: C, 63·97; H, 8·35. $C_{11}H_{17}ON_3$ requires: C, 63·74; H, 8·27%).

(c) Cyclobutanone **10**; ν_{max}(neat) 1782 cm^{-1}, δ 1·05, 1·10 (3H, d, J = 7·0 each), 2·0–4·0 (7H), 5·40 (1H, s). The semicarbazone was colorless leaflets and melted at 182–183°. (Found: C, 63·64; H, 8·27; N, 20·54. $C_{11}H_{17}ON_3$ requires: C, 63·74; H, 8·27; N, 20·27%).

Epoxylactone **13**

A soln of 104 mg of the adduct **5** and 312 mg of *m*-chloroperbenzoic acid in 6 ml CH_2Cl_2 was allowed to stand for 20 hr at room temp. Na_2SO_3 was added to destroy the excess oxidant. The resulting mixture was extracted with ether, and the combined extracts were washed with $NaHCO_3$ aq and then water, and dried over $MgSO_4$. Removal of the ether left 89 mg of a residue, which was then chromatographed on a silica gel column. Colorless needles (35 mg) were eluted by n-hexane–$CHCl_3$ (5:1), and an analytical sample, m.p. 77–77·2°, was obtained by recrystallization from light petroleum. (Found: C, 47·95; H, 5·10. $C_{10}H_{12}O_3Cl_2$ requires: C, 47·83; H, 4·82%); ν_{max}(KBr) 1805, 1187, 1170 cm^{-1}; δ* (see formula **13a**) 0·98,

1·01 (H_a, 3H, d, J_{ab} = 6·8 each), 1·90 (H_b, sept, J_{ab} = 6·8), 2·03 (H_c, dd, J_{ce} = 4·0, J_{cd} = 14·8), 2·44 (H_d, dd, J_{de} = 6·8, J_{cd} = 14·8), 3·55 (H_f, d, J_{ef} = 6·8), 3·63 (H_g, s), 4·79 (H_e, dt, J_{ce} = 4·0, J_{de} = J_{ef} = 6·8).



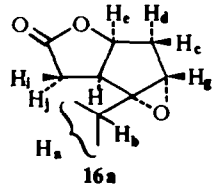
13a

Epoxylactone **12**

A soln of 177 mg of the ketone **9** and 503 mg of *m*-chloroperbenzoic acid in 20 ml CH_2Cl_2 was allowed to stand for 12 hr at room temp. After worked up as described, 160 mg of the crude product was obtained and purified by preparative TLC employing $CHCl_3$ as the eluting solvent, giving 67·5 mg of the oily lactone **12**; ν_{max}(neat) 1783 cm^{-1}, δ* ($CDCl_3$) 0·98, 1·00 (3H, d, J = 7·0 each), 1·88 (1H, sept, J = 7·0), 1·92 (1H, dd, J = 15·3 and 3·5), 2·31 (1H, dd, J = 18·2 and 7·0), 2·45 (1H, dd, J = 7·0 and 15·3), 2·72 (1H, dd, J = 10·4 and 18·2), 3·11 (1H, dt, J = 10·4, 7·0 and 7·0), 3·22 (1H, s), 4·81 (1H, dt, J = 3·5, 7·0 and 7·0), M^+ = 182. (Found: C, 66·20; H, 8·23. $C_{10}H_{14}O_3$ requires: C, 65·91; H, 7·74%).

Epoxylactone **16**

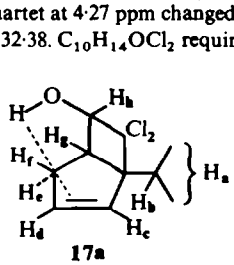
A CH_2Cl_2 soln of 100 mg of the ketone **10** and 350 mg of *m*-chloroperbenzoic acid was similarly worked up after standing for 24 hr at room temp, affording 92 mg of the crude product. The latter was purified, employing $CHCl_3$ as the eluting solvent, by preparative TLC to give 22 mg of **16**; ν_{max}(neat) 1783 cm^{-1}, δ ($CDCl_3$) (formula **16a**) 0·82, 1·05 (H_a, 3H, d, J_{ab} = 7·0 each), 1·79 (H_c, a pair of dd, J_{ce} = 1·5, J_{cd} = 15·0, J_{ce} = 5·0), 2·12 (H_b, sept, J_{ab} = 7·0), 2·28 (H_i, dd, J_{fi} = 9·6, J_{ij} = 17·5), 2·54 (H_j, dd, J_{fi} = 9·6, J_{ij} = 17·5), 2·56 (H_d, dd, J_{ce} = 7·5, J_{cd} = 15·0), 3·08 (H_f, dt, J_{ef} = 7·5, J_{fj} = J_{if} = 9·6), 3·37 (H_g, d, J_{eg} = 1·5), 4·64 (H_e, dt, J_{ce} = 5·0, J_{de} = J_{ef} = 7·5), M^+ = 182. (Found: C, 65·57; H, 7·70. $C_{10}H_{14}O_3$ requires: C, 65·91; H, 7·74%).



16a

Alcohol **17**

30 mg of $NaBH_4$ was added to a soln of 102 mg of the adduct **8** in 5 ml of MeOH, and the soln was allowed to stand at room temp for 2 hr. The MeOH soln was diluted with water and extracted with ether. The combined extracts were washed with water and dried. Removal of the ether left 94·6 mg of a crystalline residue, which was shown as an almost single spot on TLC. Recrystallization from n-hexane gave colorless plates, m.p. 84·5–85·0, ν_{max} 3564 cm^{-1} (c = 10^{-3} mol/l), δ* (formula **17a**) 0·65, 0·98 (H_a, 3H, d, J = 7·0 each), 1·97 (1H, d, J = 10·0, OH), 2·13–2·72 (H_b, H_e and H_f, 3H, m), 2·82 (H_g, 1H, t, J = 7·0), 4·27 (H_h, q, J = 10·0 and 7·0), 5·67, 6·05 (H_c and H_d, m each). The quartet at 4·27 ppm changed into a doublet (J = 7·0) by treatment with D_2O. (Found: C, 54·34; H, 6·06; Cl, 32·38. $C_{10}H_{14}OCl_2$ requires: C, 54·24; H, 6·38; Cl, 32·07%).



17a

Dihydro alcohol **18**

A soln of 95 mg of the alcohol **17** in 5 ml of EtOH was hydrogenated over 10% Pd–C at room temp under atm pressure. After *ca* 1 mole equiv of H_2 was absorbed, the mixture was filtered. The filtrate was evaporated to leave a crystalline residue, which gave colorless needles, m.p. 73·0–73·5°, on recrystallization from n-hexane; $\nu_{max}(CCl_4)$ 3598 cm^{-1} ($c = 10^{-3}$ mol/l), δ 0·83, 0·95 (3H, d, J = 6·5 each), 1·1–3·1 (9H), 4·50 (1H, d, J = 9·0). (Found: C, 54·05; H, 7·65. $C_{10}H_{16}OCl_2$ requires: C, 53·82; H, 7·23%).

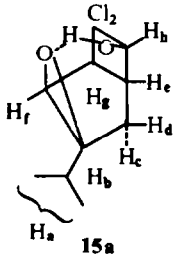
Epoxyketone **14**

2·9 g of the cycloadduct **5**, which was prepared from **2**, was oxidized with 8·0 g *m*-chloroperbenzoic acid as described earlier in the preparation of **13**. After worked up in a similar manner, the crystalline residue obtained was chromatographed on a column of silica gel (100 g) using $CHCl_3$ as the eluting solvent. From less polar fractions, 138 mg of the epoxyketone was left after evaporation of the solvent. Recrystallization of the epoxy-ketone gave colorless needles, m.p. 61·0–61·5; ν_{max}(KBr) 1806 cm^{-1}, δ ($CDCl_3$)* 0·97, 1·00 (3H, d, J = 6·5 each). 1·93 (1H, sept, J = 6·5), 2·07 (1H, dd, J = 14·5 and 9·0), 2·51 (1H, dd, J = 14·5 and 1·5), 3·33 (1H, dd, J = 8·0 and 2·3), 3·57 (1H, d, J = 2·3), 4·04 (1H, dt, J = 9·0, 1·5 and 8·0). (Found: C, 51·76; H, 5·28. $C_{10}H_{12}OCl_2$ requires: C, 51·08; H, 5·14%).

Epoxyalcohol **15**

46 mg of $NaBH_4$ was added to a soln of 110 mg of **14** in 5 ml MeOH, and the soln was allowed to stand at room temp for 2 hr. After dilution with H_2O the product was extracted with ether. Evaporation of the ether left 109 mg of an oil, which was chromatographed on a silica gel column. $CHCl_3$ eluted 103 mg of alcohol **15**, $\nu_{max}(CCl_4)$ 3412 cm^{-1} ($c = 10^{-3}$ mol/l), δ ($CDCl_3$)* (formula **15a**), 0·98, 1·01 (H_a, d, J_{ab} = 7 1·95 (H_b, sept, J_{ab} = 7), 1·92 (H_c, dd, J_{ce} = 8·5, J_{cd} = 15·0), 2·20 (H_d, dd, J_{cd} = 15·0, J_{de} = 1·8), 3·15–3·55 (H_e, H_f and H_g, m), 4·31 (H_h, a pair of quartets, J_{hg} = 3·2, J_{eh} = 7·0, J_{hi} = 14·0), 4·87 (H_i, d, J_{hi} = 14·0). Treatment with D_2O changed the pair of quartets at 4·31 ppm into a quartet (J_{hg} = 3·2, J_{eh} = 7·0).

Double resonance at about 3·4 ppm changed the signal of H_h into a sharp doublet (J = 14·0).



15a

β- *and* γ-*Thujaplicins* (**19** *and* **20**) *from the adduct mixture*

A soln of 1·0 g of the adduct mixture and 1·1 g of KOAc in 16 ml of 95% HOAc aq was refluxed for 12 hr, and then poured into water. The product was extracted with ether, and the extracts were extracted again with NaOH aq, separating the acidic product from colored material. After acidification of the aq extracts with HCl aq, the acidic product was collected in ether. The tropolonic product was extracted from the above ether extract with 85% H_3PO_4. Dilution of the H_3PO_4 extracts with H_2O gave a mixture of thujaplicins (322 mg), and the latter was collected in ether. In H_3PO_4-impregnated paper chromatography,[16] two spots were developed by sparying $FeCl_3$ soln, and their R_f values were identical with those of authentic specimens of β- and γ-thujaplicins. The mixture was then chromatographed on a column packed with H_3PO_4-impregnated Celtie[17] employing n-hexane–benezene mixture (4:1) as the eluting solvent. β- and γ-thujaplicins were obtained from less polar and polar fractions, respectively. The m.ps of β-thujaplicin (47·5–48·0°) and γ-thujaplicin (76·5–77·0°) thus separated were identical with the respective reported values (lit. β-isomer, 52–52·5°;[20] γ-isomer, 80–81°[21]), and showed no depression of the m.ps on admixture with authentic specimens. Their spectra were also superimposable with those of authentic specimens.

β-*Thujaplicin* (**19**) *from the adduct* **5**

A soln of 244 mg of **5** and 0·6 g of KOAc in 6·8 ml of 90% HOAc aq was refluxed for 20 hr, and then worked up similarly to give 92 mg (50%) of a crystalline tropolonic product. The latter showed a single spot in

paper chromatography, and by recrystallization from light petroleum afforded crystals melting at 47·2–47·8°. Its IR and NMR spectra were identical with those of β-thujaplicin.

β-Thujaplicin (**19**) *from the adduct* **8**

A soln of 59 mg of **8** and 0·6 g of KOAc in 6·6 ml of 90% HOAc aq was similarly treated and worked up to give 30 mg of crystalline β-thujaplicin, which was identified by a comparison of the spectra.

β- and γ-Thujaplicins (**19** *and* **20**) *from the adduct mixture of* **5** *and* **7**

A soln of 2·00 g of the adduct mixture (**5** + **7**) obtained by column chromatography and 2·5 g of KOAc in 31 ml of 95% HOAc aq was similarly treated and worked up to afford 685 mg (46%) of an oil, which was a mixture of β- and γ-thujaplicins as demonstrated by paper chromatography and NMR.

β-Thujaplicin (**19**) *from the adduct obtained in cycloaddition of* 1*-isopropylcyclopentadiene* (**2**)

A soln of 2·19 g of the adduct, which was obtained from 1-isopropylcyclopentadiene and 3·0 g of KOAc in 31 ml of 95% HOAc aq was treated and worked up as described above, yielding 718 mg (44%) of crystals. The crystals showed a single spot on paper chromatography at R_f value identical with that of β-thujaplicin, and melted at 49·5–50·0° after recrystallization from ligroin. The IR and NMR spectra demonstrated the crystals to be β-thujaplicin. (Found: C, 73·34; H, 7·10. $C_{10}H_{12}O_2$ requires: C, 73·14; H, 7·37%).

Acknowledgement—We thank Professor K. Takase for providing an authentic sample of γ-thujaplicin, and Mr. S. Onodera of this Institute for measurements of the IR spectra of diluted solutions.

REFERENCES

[1] T. Nozoe, *Sci. Repts. Tohoku Univ.* I, **34**, 199 (1950); *Ibid.* **36**, 82 (1952); *Nature, Lond.* **167**, 1055 (1951)

[2] H. Erdtman and J. Gripenberg, *Acta Chem. Scand.* **2**, 625 (1948); J. Gripenberg, *Ibid.* **2**, 639 (1948); A. B. Anderson and J. Gripenberg, *Ibid.* **2**, 644 (1948); G. Aulin-Erdtman, *Ibid.* **4**, 1031 (1950); A. B. Anderson and E. C. Sheerard, *J. Am. Chem. Soc.* **55**, 3813 (1933)

[3] T. Nozoe, A. Yasue and K. Yamane, *Proc. Japan Acad.* **27**, 15 (1951)

[4] H. C. Stevens, D. A. Reich, D. R. Branat, K. R. Fountain and E. J. Gaughan, *J. Am. Chem. Soc.* **87**, 5257 (1965)

[5] J. H. Shim, *Daehan Hwahak Hwaejee* **13**, 83 (1969); *Chem. Abstr.* **72**, 3195q (1970)

[6] Idem, *Daehan Hwahak Hwaejee* **13**, 75 (1969); *Chem. Abstr.***72**, 3194p (1970)

[7] T. Asao, T. Machiguchi, T. Kitamura and Y. Kitahara, *Chem. Commun.* 89 (1970)

[8] R. W. Turner and T. Seden, *Ibid.* 399 (1966)

[9] T. Nozoe, *Recent Advances in the Chemistry of Troponoids and Related Compounds in Japan.* Invited lecture at the International Symposium on the Chemistry of Nonbenzenoid Aromatic Compounds, Sendai, August (1970)

[10] Recently two mechanism were proposed for this solvolysis. [a] T. Asao, T. Machiguchi and Y. Kitahara, *Bull. Chem. Soc. Japan* **43**, 2662 (1970); [b] P. D. Bartlett and T. Ando, *J. Am. Chem. Soc.* **92**, 7518 (1970)

[11] For other syntheses of β-thujaplicin, see T. Nozoe, S. Seto, K. Kikuchi, T. Mukai, S. Matsumoto and M. Murase, *Proc. Japan Acad.* **26**, 43 (1950); T. Nozoe, S. Seto, K. Kikuchi and H. Takeda, *Ibid.* **27**, 146 (1951); T. Nozoe, S. Seto and T. Sato, *Ibid.* **30**, 473 (1954); W. von E. Doering and L. H. Knox, *J. Am. Chem. Soc.* **75**, 297 (1953); J. W. Cook, R. A. Raphael and A. I. Scott, *J. Chem. Soc.* 695 (1951)

[12] K. Ziegler. H. G. Gellert, H. Martin, K. Nagel and T. Schneider, *Liebigs Ann.* **589**, 91 (1954)

[13] W. Freiesleben, Ger. Pat. 1, 146, 050; *Chem. Abstr.* **59**, 9914a (1963)

[14] S. M. Criesery, *J. Org. Chem.* **25**, 518 (1960)

[15] V. A. Mironov, E. V. Sobolev and A. N. Elizalova, *Tetrahedron* **19**, 1939 (1963)

[16] E. Zavarin and A. B. Anderson, *J. Org. Chem.* **21**, 332 (1956); *Chem. Ber.* **89**, 545 (1956); E. Zavarin, R. M. Smith and A. B. Anderson, *J. Org. Chem.* **24**, 1318 (1959)

[17] K. Ito, Dissertation Tohoku University (1961)

[18] R. Rumschneider and R. Nehring, *Monatsh.* **90**, 568 (1959)

[19] G. Rosenkranz, O. Mancera, J. Gatica and C. Djerassi, *J. Am. Chem. Soc.* **72**, 4077 (1950)

[20] [a] A. B. Anderson and J. Gripenberg, *Acta Chem. Scand.* **2**, 644 (1948); [b] T. Nozoe and S. Katsura, *Yakugaku Zasshi* **64**, 181 (1944)

[21] H. Erdtman and J. Gripenberg, *Nature* **161**, 716 (1948)