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PREPARATION AND PHOTOCHEMICAL ISOMERIZATION OF 2-CYCLODODECENONES

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Abstract—Treatment of *trans*- or *cis*-epoxycyclododecane (I and II) with n-butyllithium yields the same product, *trans*-2-cyclododecenol (III). Oxidation of III with chromic acid affords a 4:1 mixture of *trans*- and *cis*-2-cyclododecenones (IV and V) the isomers being separated chromatographically. The *cis* enone V is thermodynamically less stable and is isomerized spontaneously at room temp to the *trans* enone IV. Irradiation of a cyclohexane solution of IV with a high-pressure mercury lamp gives V and a β,γ-unsaturated ketone, *cis*-3-cyclododecenone (VII). This *cis* enone VII is thermally and photochemically stable.

PHOTOCHEMICAL behaviour of α,β-unsaturated cyclic ketones shows interesting correlation with the ring size. 2-Cyclopentenone is transformed into two isomeric cyclodimers.[1] Irradiation of five- and six-membered 2-cyclenones in the presence of alkenes[2] or alkynes[3] affords the corresponding cycloaddition products in excellent yields. Seven- and eight-membered 2-cyclenones, however, undergo neither dimerization nor cycloaddition, but highly strained *trans* isomers are produced.[4–6] Irradiation of open chain α,β-unsaturated ketones results in the *trans* to *cis* isomerization, and in the presence of γ-hydrogen isomerization leading to the β,γ-unsaturated ketones is observed.[7] In view of these previous findings we have been interested in the photochemistry of 2-cyclododecenone as an extension of studies on the photochemical isomerization of twelve-membered cyclic olefins.[8]

Both *trans* and *cis* isomers of the 2-cyclenone (IV and V) have been prepared as follows. *trans*-2-Cyclododecenol (III) was obtained by treating *trans*-epoxycyclododecane (I) with n-butyllithium.[9] Analogous isomerization of *cis*-epoxycyclododecane[10] afforded the same *trans* cyclenol (III) in 62% yield, whose IR spectrum (Fig. 1) indicated clearly the presence of little *cis*-2-cyclododecenol, if any.[11] Oxidation of the cyclenol III with chromic acid[12] gave a mixture of *trans*- and *cis*-2-cyclododecenones in 85% yield. GLC analysis indicated the abundance ratio of 4(IV):1(V) and both

[1] P. E. Eaton, *J. Amer. Chem. Soc.* **84**, 2454 (1962).
[2] E. J. Corey, J. D. Bass, R. LeMahieu and R. B. Mitra, *J. Amer. Chem. Soc.* **86**, 5570 (1964) and Refs cited therein.
[3] P. E. Eaton, *Tetrahedron Letters* 3695 (1964); R. Criegee and H. Furrer, *Chem. Ber.* **97**, 2949 (1964).
[4] P. E. Eaton and K. Lin, *J. Amer. Chem. Soc.* **86**, 2087 (1964).
[5] P. E. Eaton and K. Lin, *J. Amer. Chem. Soc.* **87**, 2052 (1965).
[6] E. J. Corey, M. Tada, R. LeMahieu and L. Libit, *J. Amer. Chem. Soc.* **87**, 2051 (1965).
[7] N. C. Yang and M. J. Jorgenson, *Tetrahedron Letters* 1203 (1964).
[8] H. Nozaki, Y. Nisikawa, Y. Kamatani and R. Noyori, *Tetrahedron Letters* 2161 (1965).
[9] L. I. Zakharkin, *Izv. Akad. Nauk SSSR. Otd. Khim. Nauk* 2245 (1961); *Chem. Abstr.* **57**, 11040 (1962).
[10] H. Nozaki and R. Noyori, *J. Org. Chem.* **30**, 1652 (1965).
[11] W. Kirchhof, *Chem. Ber.* **93**, 2712 (1960).
[12] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.* **83**, 2952 (1961).

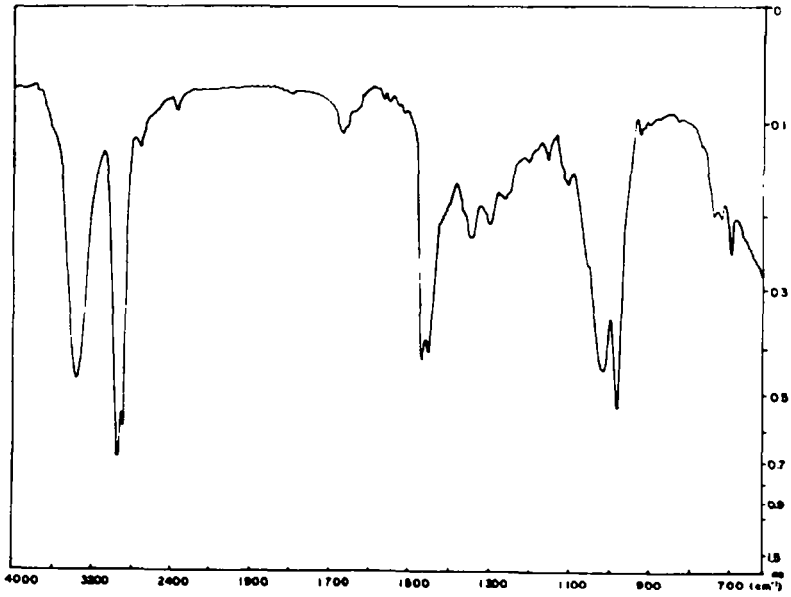
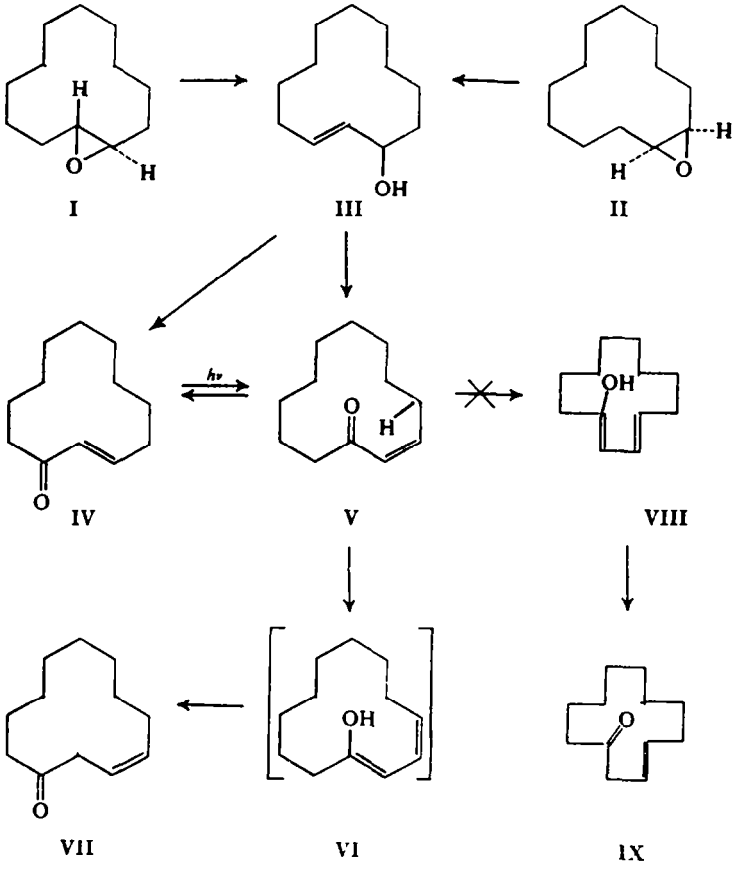


FIG. 1. IR of *trans*-2-Cyclododecenol (III)



isomers were readily isolated by chromatography on a silica-gel column. The IR spectra were given in Fig. 2 and 3. 2-Cyclododecenone containing mainly the *trans* isomer (IV) has previously been obtained by pyrolytic dehydration of 2-hydroxycyclododecanone on alumina,[13] but some differences were noticed between the recorded and now observed UV absorptions.

The pure *cis* isomer (V) appears to be novel. In contrast with *cis*-cyclododecene,[8] which can be stored without any appreciable isomerization, the *cis*-2-cyclenone (V) was spontaneously isomerized to the *trans* isomer (IV). After standing at room tem-

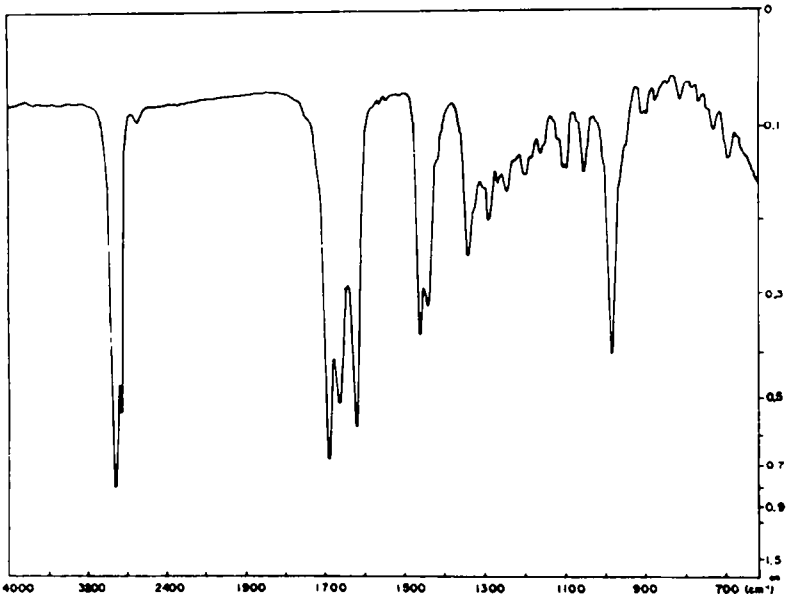


FIG. 2. IR of *trans*-2-Cyclododecenone (IV)

perature in the dark for two weeks, GLC and IR spectrum indicated that in V (neat) a change into a mixture of 2(IV):1(V) had occurred.

Photochemical transformation of the *trans*-2-cyclenone (IV) was effected by irradiating a 5% cyclohexane solution in a Pyrex vessel with a 200 W high-pressure mercury lamp externally at room temperature and was traced by IR spectrometry and GLC. Irradiation for 2 hr afforded a mixture of 1(IV):3(V) and a trace of another isomer (VII) while after 15 hr of exposure the sole isolable product was VII (over 92% yield) and either IV or V was completely absent. Further irradiation brought about no change. Irradiation of IV dissolved in *cis*-1,2-dichloroethylene or furan under analogous conditions caused neither photochemical cycloaddition nor Diels–Alder reaction, but gave exclusively the isomer VII.

The IR absorption of VII at 1715 cm^{-1} (Fig. 4) indicated that this was no longer a conjugated ketone. In the UV spectrum (99% ethanol) the strong π–π^* band of conjugated ketone was lost and the blue shift of n–π^* band to 289 mμ (log ϵ 1·95) appropriate to an unconjugated system was noted. NMR spectrum also was consistent with

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

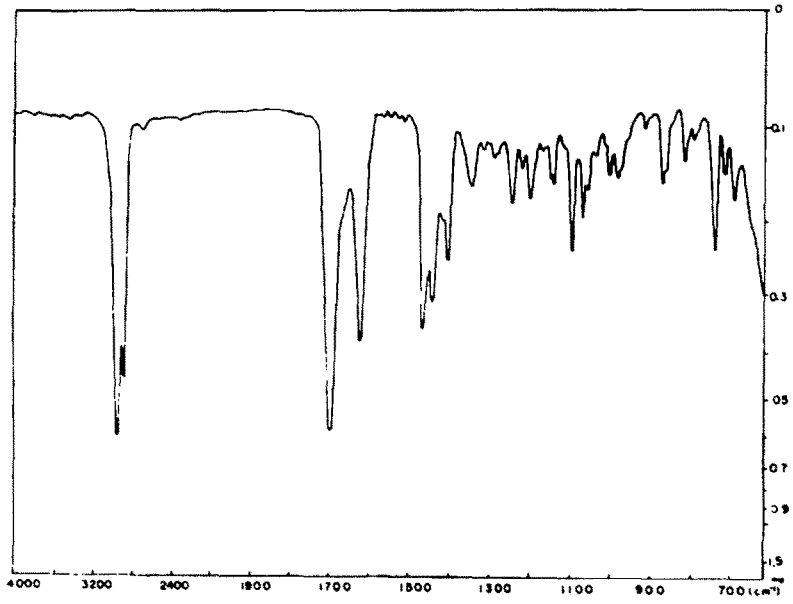


FIG. 3. IR of *cis*-2-Cyclododecenone (V)

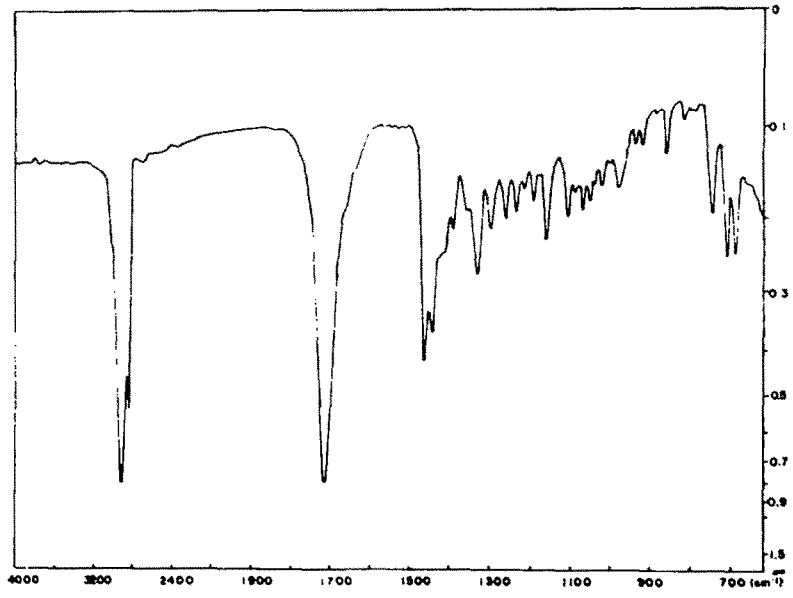


FIG. 4. IR of *cis*-3-Cyclododecenone (VII)
All spectra were taken with neat liquid films.

the β,γ-unsaturated structure.[14] Hydrogenation of VII over Pd-C resulted in absorption of one mole hydrogen and afforded cyclododecanone quantitatively, while ozonolysis of VII yielded sebacic acid. The 3-cyclenone (VII) and its 2,4-dinitrophenylhydrazone were found homogeneous on TLC and only single peak was observed on GLC of VII. The *cis* configuration of the ethylenic bond of VII was based on the absence of usually strong IR band of *trans* olefins at 970–980 cm^{-1}.

Irradiation of the *cis*-2-cyclenone (V) was carried out under monitoring similarly. Exposure for a $\frac{1}{2}$ hr afforded a mixture of 1(IV):3(V):13(VII) and after 15 hr only VII was obtained in almost quantitative conversion.

Clearly, the *trans*- and *cis*-2-cyclenones (IV and V) are in photochemical equilibrium with predominance of the thermodynamically less stable *cis* isomer (V) and this is in turn transformed into *cis*-3-cyclododecenone (VII) upon prolonged irradiation. This second stage would probably proceed by the scheme as suggested by Yang and Jorgenson[7] *via* a six-membered cyclic transition state involving the enone system and the adjacent bonding of γ-carbon to hydrogen which is abstracted. This is feasible only with the *cis*-2-cyclenone (V) in its O-inside conformation and affords selectively the *trans, cis* dienol (VI) which is finally transformed into the *cis*-3-cyclenone (VII). Consideration on the Dreiding models shows that very little chances are left for the formation of *trans, trans* dienol (VIII) leading to *trans*-3-cyclenone (IX). The thermal and photochemical stability of *cis*-3-cyclododecenone is remarkable in view of the recorded *trans* to *cis* isomerization of open chain β,γ-unsaturated ketones[15] and the unusually facile intramolecular hydrogen transfer of cyclododecanone affording a cyclobutanol derivative upon irradiation.[16,17]

EXPERIMENTAL

All temps were uncorrected. Microanalyses were performed at Elemental Analyses Centre of Kyôto University.

Preparation of trans-2-*cyclododecenol* (III). This was prepared according to the method of Zakharkin[9] with a few modifications under more moderate condition. A solution of 25·0 g (0·14 mole) *trans*- I[18] containing ca. 10% *cis* isomer II in 250 ml anhydrous ether was kept at −40°. To this 180 ml ethereal solution containing 0·23 mole of n-BuLi was added dropwise during 30 min under stirring and then the mixture was warmed up to room temp slowly, allowed to stand overnight, and then heated under gentle reflux for 1 hr. After treating with water, the organic layer was separated and the aqueous layer thoroughly extracted with ether. The combined extracts were washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. Distillation of the residual oil under red. press. gave 18–20 g (72–80% yield) *trans*- III as a highly viscous oil, b.p. 110–120°/3 mm.

[14] The spectrum was taken in CCl_4 solution on 60 Mc machine and chemical shifts are given in ppm from internal TMS reference: a multiplet of vinylic protons on C_3 and C_4 centred at 5·50 (2H), a multiplet of protons at C_2 centred at 3·05 (2H), a multiplet of methylene protons at C_5 and C_{12} centred at about 2·2 (4H) and a broad signal of methylene protons of C_6 through C_{11} at about 1·8 to 1·0 (12H).

[15] H. Morrison, *J. Amer. Chem. Soc.* **87**, 932 (1965).

[16] B. Camerino and B. Patelli, *Experientia* **20**, 260 (1964).

[17] All cyclododecenone isomers (IV, V and VII) were highly unstable under basic conditions. Treatment with dil alcoholic KOHaq at room temp gave a difficulty separable mixture with IR absorptions (neat) at 1720–1710 cm^{-1} (unconjugated carbonyl) and 1100–1080 cm^{-1}. Polymeric products were also produced. No cyclenones either unchanged or interconverted could be detected by GLC and IR spectroscopy.

[18] Prepared from *cis, trans, trans*-1,5,9-cyclododecatriene according to G. Wilke, *Angew. Chem.* **69** 397 (1957).

Similarly, 5·0 g (0·027 mole) *cis*- II[8] afforded 3·1 g (62% yield) the same alcohol III.

Comparison of the IR spectrum (Fig. 1) with the reported one[11] showed the presence of little *cis* isomer, if any. Though the previous authors[9,11] recorded separation of the *cis* isomer as a solid on long standing, the specimen obtained above did not give any precipitates even after storing for a month or more. GLC (high vacuum silicone grease, He) and TLC (silica-gel G, n-hexane and ethyl acetate mixture (4:1)) also indicated that this was homogeneous.

Oxidation of trans-2-*cyclododecenol* (III). Chromic acid solution prepared from 13·1 g (0·044 mole) sodium dichromate dihydrate, 9·8 ml (0·18 mole) conc H_2SO_4 and 50 ml water was added dropwise to a solution of 20·0 g (0·11 mole) allyl alcohol (III) in 60 ml ether in the course of 30 min at 25° under stirring and the mixture maintained under the same condition for an additional 3 hr. The resulting green-coloured mixture was extracted with ether, the extracts were washed with water, dried and concentrated. Distillation of the residue *in vacuo* afforded 17·0 g (85% yield) 2-cyclododecenones, b.p. 95–105°/3 mm. GLC (high vacuum silicone grease, He) showed that this was a 1:4 mixture of *cis*- and *trans*-2-cyclenones (V and IV), whose relative retention times were 1·00 and 1·28, respectively. The mixture was subjected to chromatography on a silica-gel column. Elution with n-hexane and benzene mixture (1:3) gave V first. Redistillation afforded an analytical sample, b.p. 95–97°/2 mm, which crystallized on standing to give colourless needles, m.p. 15–16·5°. (Found: C, 79·83; H, 11·43. $C_{12}H_{20}O$ requires: C, 79·94; H, 11·18%.) UV absorptions (in 99% EtOH): λ_{max} 228 (log ε 3·72) and 320 mμ (1·67). IR spectrum was shown in Fig. 3. Orange-coloured 2,4-*dinitrophenylhydrazone of* V melted at 148–148·5° (from EtOH). (Found: C, 59·74; H, 6·86. $C_{18}H_{24}N_4O_4$ requires: C, 59·98; H, 6·71%.)

Further elution with pure benzene gave IV as a colourless oil, which was purified by redistillation, b.p. 97–100°/2 mm. (Found: C, 79·80; H, 11·34. Calc. for $C_{12}H_{20}O$: C, 79·94; H, 11·18%.) UV absorptions (in 99% EtOH): λ_{max} 230 (log ε 4·05) and 321 mμ (2·24). IR spectrum was given in Fig. 2.

2,4-*Dinitrophenylhydrazone of* IV formed deep red prisms, m.p. 130·5–131° (from ethyl acetate). (Found: C, 60·24; H, 6·95. $C_{18}H_{24}N_4O_4$ requires: C, 59·98; H, 6·71%.)

Both unsaturated ketones IV and V were dissolved in EtOH and hydrogenated on 10% Pd–C under ordinary press at room temp to afford cyclododecenone in almost quantitative yield, m.p. and m.m.p. 60–61°.

Lower yields (50–60%) of the ketones IV and V were obtained on Oppenauer oxidation of the allyl alcohol III, which may be ascribed to the basic reaction conditions favouring the side reactions.[17]

Photoisomerization of trans-2-*cyclododecenone* (IV). All isomerization experiments were monitored by GLC (high vacuum silicone grease, He) and IR spectroscopy. A solution of 4·0 g (0·022 mole) IV in 80 ml purified cyclohexane was placed in a Pyrex tube (25 mm diametre) and covered with N_2. Irradiation was effected externally with a Hg. lamp (200 W) from a distance of 20 mm at 20°. Exposure for 2 hr gave a mixture of *trans*- IV and *cis*- V in the ratio of 1:3, respectively. At the same time, a trace of the third isomeric ketone VII having the retention time of 1·08 relative to V was detected. After irradiation for 15 hr, IV and V completely disappeared and cis-3-*cyclododecenone* (VII) was found to be the sole ketonic product. Concentration followed by vacuum distillation gave 3·7 g (92% isolation yield) a colourless oil, which crystallized as needles, m.p. 38–39°. (Found: C, 80·24; H, 11·33. $C_{12}H_{20}O$ requires: C, 79·94; H, 11·18%.) UV absorption (in 99% EtOH): λ_{max} 289 mμ (log ε 1·95). IR spectrum was shown in Fig. 4. 2,4-*Dinitrophenylhydrazone of* VII formed orange-coloured prisms, m.p. 125·5–126° (from ethyl acetate). (Found: C, 60·44; H, 6·95. $C_{18}H_{24}N_4O_4$ requires: C, 59·98; H, 6·71%.) The homogeneity of this ketone was ascertained by GLC (silicone grease, He) and TLC (silica-gel G, n-hexane–EtOH (4:1)) of the 2,4-dinitrophenylhydrazone. Upon hydrogenation on 10% Pd–C, VII took up equimolar hydrogen to give cycledodecanone, m.p. and m.m.p. 60–61°. The ketone VII dissolved in CH_2Cl_2 was ozonized at −10°. The resulting ozonide was subjected to oxidative decomposition with H_2O_2 to give crude sebacic acid (55% yield), which was converted into dimethyl ester and identified by GLC and IR.

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