Homoketenyl Cations in a Friedel–Crafts Acylation[1]

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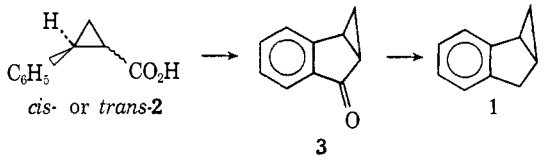
Abstract: Friedel–Crafts cyclization of the acid chloride from optically active *cis*- or *trans*-2-phenylcyclopropanecarboxylic acid (*cis*- and *trans*-**2**) gave racemic 1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-one (**3**). Uncyclized acid (from pure *cis*- or *trans*-**2**) was completely racemized, and was 15% *cis*-**2** and 85% *trans*-**2**; optically active **3** did not racemize under Friedel–Crafts conditions. Cyclopropane ring opening and complete equilibration occur among epimeric and enantiomeric species before acylation takes place; involvement of homoketenyl cations is proposed, and precedents are cited. Acid chloride from active *cis*-**2** with thionyl chloride in refluxing benzene gave no intramolecular acylation. There was also no effect on the activity of recovered starting material, but epimerized (trans) product was partly racemized; configurational inversion occurred predominantly at the asymmetric center bearing the acid chloride function. No evidence was obtained requiring that two-center inversions of cyclopropyl compounds be concerted.

Reversible solvolytic ring opening of substituted cyclopropanes has received much attention recently; evidence has been advanced for the interconvertibility of α-cyclopropylvinyl and homoallenyl cations,[2] and for racemization of suitably substituted cyclopropanes *via* ionic intermediates.[3] This paper reports evidence for what is believed to be the first example of racemizing interconversion of cyclopropacyl and homoketenyl cations.

Indications of this phenomenon were uncovered during attempts to establish the absolute configuration of 1,1a,6,6a-tetrahydrocycloprop[*a*]indene (**1**) through correlation with *cis*- or *trans*-2-phenylcyclopropanecarboxylic acid (*cis*- and *trans*-**2**), configurations of which are known.[4] The intramolecular Friedel–Crafts acylation reaction of acid chloride from racemic *trans*-**2**[5] was modified to give ketone **3** in over 70% yield.



cis- or *trans*-**2** **3** **1**

However, when acid chloride from (−)-*trans*-**2**, $[\alpha]^{26}D$ −309° (*c* 1.5, 95% ethanol), was subjected to the same Friedel–Crafts conditions, the ketone (**3**) obtained was racemic, as was all recovered uncyclized acidic material. The latter consisted of 15% *cis*-**2** and 85% *trans*-**2**. Hydrolysis of a sample of the same acid chloride which had not been exposed to Lewis acid afforded (−)-*trans*-**2** having essentially unchanged optical activity.

Optically active **3**, obtained by selective Schiff base formation with dehydroabietylamine,[6] was not detectably racemized under Friedel–Crafts conditions.

Racemization of the 2-phenylcyclopropanecarboxylic acid system described above requires configurational randomization at both C-1 and C-2; the data given establish that these processes occur only after exposure of acid chloride to Lewis acid and before acylation of the benzene ring. It was hoped that generation of the acylating species in the required configuration for acylation (*i.e.*, from the acid chloride of *cis*-**2**) would enable ketone formation to compete with racemization; however, acid chloride from (−)-*cis*-**2**, $[\alpha]^{25}D$ −28° (*c* 1.02, $CHCl_3$),[7] gave only racemic **3**. Recovered acid chloride, on hydrolysis, again gave a 15:85 mixture of *cis*- and *trans*-**2**.

The above data appear to be accommodated adequately by the interconversions formulated in Scheme I. Rate constants are subscripted as follows: k_{ot} and k_{oc} for trans and cis opening, k_{ct} and k_{cc} for trans and cis closure, k_b and k_k for benzyl and ketenyl epimerization. Some processes such as C′ ⇌ B′, D ⇌ **3**, and acid chloride–cyclopropacyl ion interconversions are omitted for simplicity. All of the observed racemizations and isomerizations are accounted for by mechanisms involving these species. The optical inactivity of the Friedel–Crafts product **3** (flat ORD curve down to 210 nm) and rotational strength of *partially* resolved **3** ($[\alpha]_{310} \sim 10^{4}$°) require that ring opening of D or D′ occur at least 10^4 times faster than acylation ($k_{oc} \gg k_{F-C}$). The identical distributions of racemic *cis*- and *trans*-**2** recovered from reaction of either optically active starting acid show that complete equilibration is achieved among the epimeric and enantiomeric cyclopropacyl cations before acylation takes place. Because acid chlorides of both *cis*- and *trans*-**2** can be hydrolyzed without interconversion or racemization, the 85:15 preference for the trans isomer after Lewis acid treatment must reflect the greater stability of the trans cyclopropacyl cation (A or A′), and probably indicates greater stability for "transoid" homoketenyl ions B and B′ than for the corresponding "cisoid" species C and C′.

(1) Part IV in a series on cyclopropylarene chemistry. Part III: R. C. Hahn and P. H. Howard, *J. Amer. Chem. Soc.*, **94**, 3143 (1972). A preliminary report of this work was given at the 164th National Meeting of the American Chemical Society, New York, N. Y., Aug 1972, Abstract ORGN-60.

(2) For leading references, see (a) D. R. Kelsey and R. G. Bergman, *J. Amer. Chem. Soc.*, **93**, 1941 (1971); R. S. Macomber, *ibid.*, **92**, 7101 (1970); (c) M. Hanack, *Accounts Chem. Res.*, **3**, 209 (1970).

(3) (a) E. W. Yankee, F. D. Badea, N. E.Howe, and D. J. Cram, *J. Amer. Chem. Soc.*, **95**, 4210 (1973); (b) N. E. Howe, E. W. Yankee, and D. J. Cram, *ibid.*, **95**, 4230 (1973).

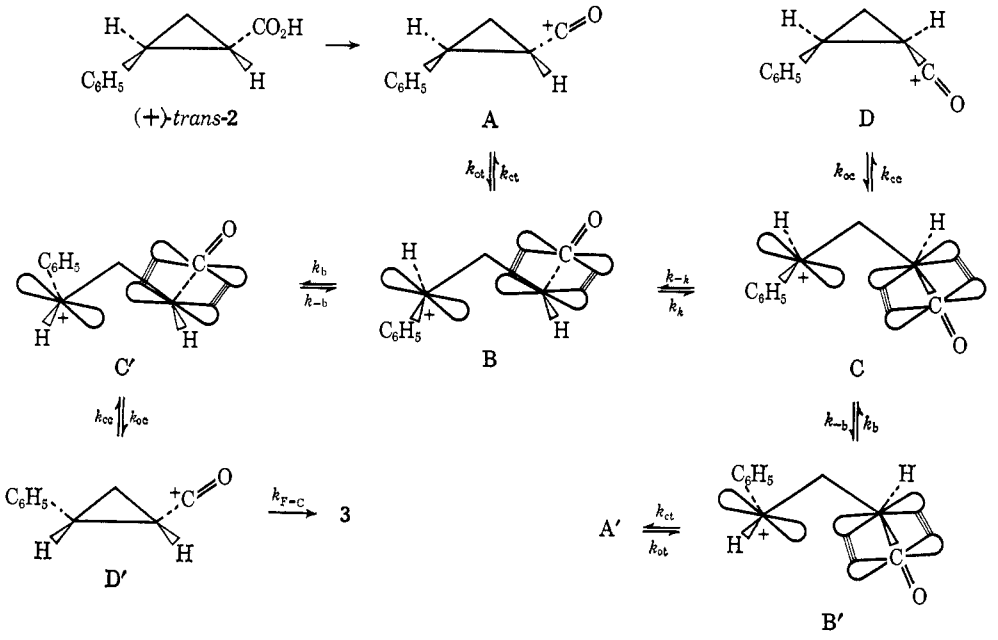
(4) (a) *trans*-**2**: Y. Inouye, T. Sugita, and H. M. Walborsky, *Tetrahedron*, **20**, 1965 (1964); (b) *cis*-**2**: T. Aratani, Y. Nakanisi, and H. Nozaki, *ibid.*, **26**, 1675 (1970).

(5) R. Jacquier and P. Besinet, *Bull. Soc. Chim. Fr.*, 989 (1957).

(6) W. J. Gottstein and L. C. Cheney, *J. Org. Chem.*, **30**, 2072 (1965).

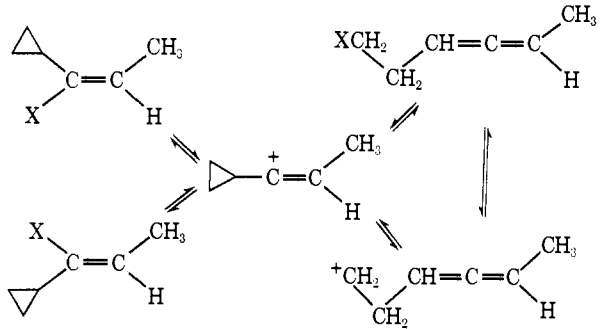
(7) Data of Aratan, *et al.*,[4b] indicate that optically pure *cis*-**2** should have $[\alpha]^{25}D$ ~30° ($CHCl_3$); the present study has established that this rotation corresponds to $[\alpha]D$ 24° (CH_3OH).

Scheme I



While there is no direct evidence for the participation of homoketenyl cations in the interconversions reported here, their involvement is reasonable in light of the interconversions reported on solvolysis of α-cyclopropylvinyl and homoallenyl systems.[2,8] Involvement of equilibrating α-cyclopropylvinyl cations and homoallenyl cations was postulated for these solvolyses, as exemplified[2a] in Scheme II.

Scheme II



In addition to the precise nature of the species generated in the presently reported reactions, the manner in which some of these species interconvert merits discussion. While Scheme I pictures all racemizations as proceeding *via* sequential epimerizations, the acylation experiments do not exclude the possibility that A–A′ and B–B′ interconversions (and thus production of racemic **3** from optically active *cis*-**2**) are at least in part results of simultaneous inversion of benzyl and ketenyl centers. However, there is no reason to assign concerted processes a major role in these interconversions. Concerted inversions cannot account for any of the cis–trans interconversions noted, or for formation of ketone **3** from *trans*-**2**. Also, the cis–trans equilibrations observed, particularly starting from *cis*-**2**, suggest that stepwise inversions are more facile than concerted ones, although the slowness of the acylation step relative to *all* other processes may effectively mask any such rate differences. Thus, none of the data cited above require concerted inversions, while some of the results do demand stepwise inversions. It is of interest that calculations on terminal methylene rotation modes in trimethylene ($CH_2CH_2CH_2$),[9a] and experiments on gas-phase racemization and isomerization of optically active 1-ethyl-2-methylcyclopropanes,[9b] although not directly comparable with our system, also make no case for dominance of concerted processes.

Because the slow acylation step in Scheme I (formation of ketone **3** from D or D′) prevents assessment of the relative rates of inversion at the benzyl and ketenyl centers (k_b and k_{-b} *vs.* k_k and k_{-k}, respectively) as well as assessment of the relative roles of stepwise and concerted inversions, conditions were sought under which inversions might occur without acylation. An earlier report[10] of epimerization of racemic *cis*-**2** acid chloride to the trans compound led us to perform a similar experiment with acid chloride from (+)-(1*S*,2*R*)-*cis*-**2** ([α]D 16.6° (CH_3OH), ~70% optically pure). Refluxing this acid chloride with thionyl chloride in benzene, followed by hydrolysis, diazomethane esterification, and glc separation, afforded *cis*-**2** methyl ester ([α]D 50.5° (CH_3OH)) and *trans*-**2** methyl ester ([α]D ~97° (CH_3OH)). The cis ester was shown to have the same relative optical purity (~70%), within experimental error, as the starting acid chloride, while the trans ester was only ~30% optically pure.

The above data show that, under conditions which allow cis → trans acid chloride epimerization, *some* inversion occurs at *both* asymmetric centers; no evidence is provided for concerted inversion. Also, under these conditions (in contrast to Friedel–Crafts conditions), the cyclopropane ring-opening process which must occur to allow racemization is essentially irreversible for the cis acid chloride, or trans → cis epimerizations do not occur, or both. Finally, the formation of levorotatory trans ester, which corresponds to (−)-(1*R*,2*R*)-*trans*-**2**,[4a] shows that the pre-

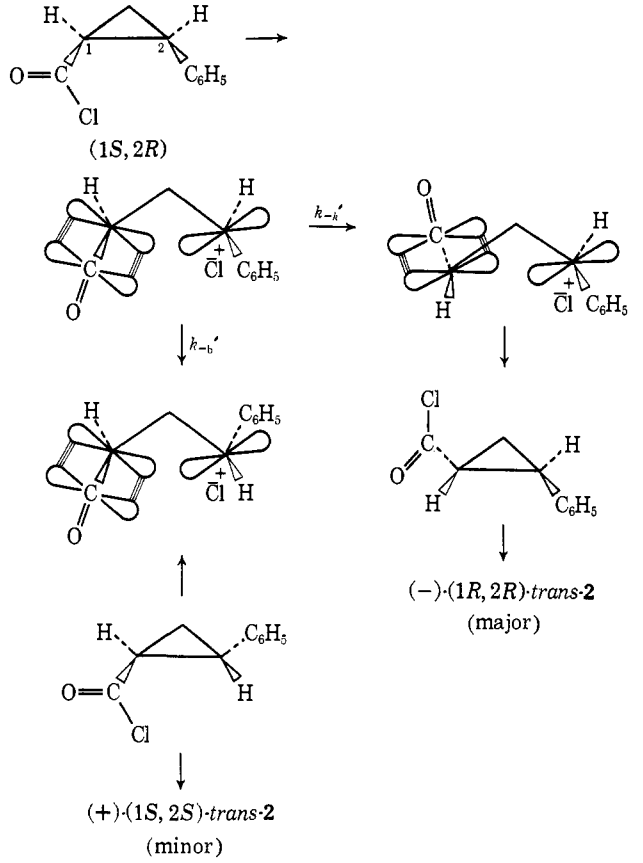
(8) T. Von Lehman and R. S. Macomber, Abstracts, 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, No. ORGN-122.

(9) (a) R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968); (b) R. G. Bergman and W. L. Carter, *ibid.*, **91**, 7411 (1969).

(10) A. Burger and W. L. Yost, *J. Amer. Chem. Soc.*, **70**, 2198 (1948).

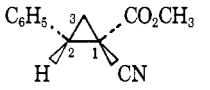
ponderance of configurational inversion occurs at the asymmetric center bearing the acid chloride moiety. These conclusions are incorporated into Scheme III.

Scheme III



Depiction of all processes as irreversible indicates only lack of evidence for reversibility.

The reactions described and the transition states or intermediates suggested here have features similar to those reported by Howe, Yankee, and Cram[3b] for epimerization and racemization of methyl 1-cyano-2-phenylcyclopropanecarboxylate (**4**). Compound **4** undergoes



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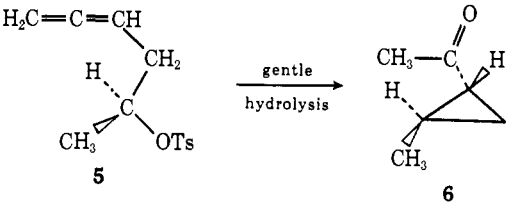
inversion at C-1 faster than at C-2; the epimer is stable under the conditions employed. Sensitivity of reactions of **4** to solvent polarity led to postulation of intervention of zwitterionic species as being very likely to be involved in the epimerizations. As formulated in Scheme III, *cis*-**2** acid chloride, under the influence of the relatively weak Lewis acid thionyl chloride (not shown), can be postulated to give rise to a homoketenyl ion pair. Association of the chloride ion with the benzylic cation would render epimerization at the benzyl center more difficult than at the ketenyl center ($k'_{-k} > k'_{-b}$); with the more powerful Lewis acid aluminum chloride, the negative charge associated with the chloride ion would be more effectively dispersed. More complete removal of the chloride ion from the vicinity of a cationic species (Friedel–Crafts conditions) also should minimize steric hindrance to trans → cis epimerization, and/or to closure of a cisoid open species; lack of *cis*-**2** acid chloride racemization with thionyl chloride thus may also be attributed to the weakness of the latter as a Lewis acid.[11]

The racemizations found in the present system stand in contrast to the results of Bertrand and Santelli,[12] who "gently" hydrolyzed the homoallenyl tosylate **5** and obtained the *trans*-methyl cyclopropyl ketone **6**



5 **6**

(>95% optical activity preserved)

with almost no detectable racemization. This difference in results may be accounted for in part by the greater ability of the phenyl group (in homoketenyl ions derived from **2**) to stabilize positive charge and thereby facilitate racemization; however, ordinary hydrolysis conditions and Friedel–Crafts conditions are so different as to render such comparisons of these experiments quite tenuous. Parallel experiments with more closely structurally related homoallenyl and homoketenyl systems clearly are in order.

In summary, there appears to be adequate evidence to justify the addition of homoketenyl cations to the host of species postulated to intervene in chemical reactions of cyclopropyl compounds. However, the present study has unearthed no evidence requiring that two-center inversions of cyclopropyl compounds occur in concert.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were obtained with a Perkin-Elmer 137 Infracord, nmr spectra with a Varian A-60, and ORD and CD spectra with a Durrum-Jasco spectropolarimeter Model J-20.

1,1a,6,6a-Tetrahydrocycloprop[*a*]inden-6-one (3). Racemic *trans*-2-phenylcyclopropanecarboxylic acid chloride (73.3 g, 0.407 mol; from reaction of *trans*-**2**[10] with thionyl chloride) was added during 3 hr to a suspension of aluminum chloride (70 g, 0.525 mol) in 100 ml of methylene chloride at 0°. The mixture was stirred at 0° for 22 hr and poured into 1000 ml of ice–water, and 200 ml of concentrated hydrochloric acid was added. The organic phase was separated and the aqueous phase extracted with methylene chloride. Work-up of the organic phase gave a mixture of ketone and unreacted acid chloride, which was refluxed 1 hr with excess 10% aqueous sodium carbonate and extracted with ether. The aqueous phase on acidification yielded 14.2 g of *trans*-**2**; no attempt was made to recover the more soluble *cis*-**2**. The organic phase was dried and stripped of solvent, and the residue was distilled at 0.07 mm to yield 34.2 g (74% based on unrecovered acid) of ketone **3**: bp 68° (0.06 mm) (lit.[13] 80° (0.4 mm)); ir (neat, NaCl) 1701, 1601, 1460, 1300, 1202, 1102, 916, 866, 795, 760, and 698 cm^{-1}; nmr ($CDCl_3$) τ 2.60 (4 H, broad m; aryl H's), 7.15 (1 H, m, benzyl H), 7.60 (1 H, m, α-keto H), 8.5 (1 H, m, anti H), and 8.8 (1 H, m, syn H).

Partial Resolution of Ketone 3. A solution of **3** (28.8 g, 0.2 mol) and dehydroabietylamine (28.6 g, 0.1 mol) in 100 ml of dry benzene was refluxed with continuous removal of water (Dean–Stark trap) for 4 hr. Removal of benzene and distillation of the residual syrup at 0.05 mm yielded 15.1 g of unreacted **3** which was slightly levorotatory. The residue from the distillation was dissolved in 95% ethanol and partly hydrolyzed with an excess of 1 *N* hydrochloric acid. Extraction with ether and work-up yielded 2.06 g of (−)-**3**

(11) A referee has pointed out that the Principle of Least Motion also would account for the preference for C_1–C_3 over C_1–C_2 rotation; *cf.* J. Hine, *J. Org. Chem.*, **31**, 1236 (1966).

(12) M. Bertrand and M. Santelli, *Chem. Commun.*, 718 (1968).

(13) M. M. Fawzi and C. D. Gutsche, *J. Org. Chem.*, **31**, 1390 (1966).

(fraction A) (methanol, 23°, *c* 1.54): $[\alpha]_{360}$ −3585°, $[\alpha]_{353}$ −4030° (tr), $[\alpha]_{311}$ +13,950° (pk).

Further boiling of the Schiff base with 1 *N* hydrochloric acid for 0.5 hr and work-up as before yielded 2.3 g of (+)-**3** (fraction B) (methanol, 23°, *c* 1.74): $[\alpha]_{360}$ +4020°, $[\alpha]_{352}$ +4880° (pk), $[\alpha]_{310}$ −18,100° (tr).

Optically Active *trans*-2-Phenylcyclopropanecarboxylic Acid (*trans*-2). Racemic trans acid[10] was resolved by fractional crystallization of the brucine salt[14] and work-up to give material having mp 49.5–50° and $[\alpha]^{26}D$ −309° (*c* 1, 95% ethanol) (lit.[14] mp 51–52°, $[\alpha]^{22}D$ 311.7°).

Friedel–Crafts Cyclization of Acid Chloride from Active *trans*-2. The acid chloride was prepared by reaction of *trans*-**2**, $[\alpha]^{25}D$ −259° (*c* 8.5 × 10^{-2}, methanol), with oxalyl chloride. A 1.0-g sample (5.6 mmol) in 10 ml of dichloromethane was added slowly to a stirred suspension of 1.1 g (8.6 mmol) of aluminum chloride in 25 ml of dichloromethane at 0°. The mixture was kept at 0° for 2 hr and worked up; distillation afforded ketone **3** which showed no detectable rotation in the accessible uv–visible region. Isolated acidic material (0.17 g) also was optically inactive; esterification (diazomethane) and vpc analysis (10% QF-1, DMCS on Chromosorb W, 5 ft × 1/8 in. column, 135°) showed a cis–trans ester ratio of 15:85.

Configurational Stability of Acid Chloride from Active *trans*-2. A portion of *trans*-**2** having $[\alpha]^{26}D$ −309° (*c* 1.0, 95% ethanol) was converted to acid chloride (as above); hydrolysis back to *trans*-**2** afforded material having $[\alpha]^{26}D$ −307° (*c* 0.189, 95% ethanol).

Optically Active *cis*-2-Phenylcyclopropanecarboxylic Acid (*cis*-2). Dehydroabietylamine (1,2,3,4,4a,9,10,10a-octahydro-7-isopropyl-1,-4a-dimethylphenanthrenemethylamine)[6] (25.3 g, 0.089 mol) was dissolved in a boiling mixture of 1200 ml of methanol and 320 ml of water, and 14.3 g (0.088 mol) of racemic *cis*-**2** was added. Slow cooling of the solutions gave, after 24 hr, 22 g of colorless needles, mp 185–187°. Recrystallization from 90% aqueous methanol yielded 12 g of salt, mp 200–201°. Work-up[6] afforded 4.18 g (95.4%) of *cis*-**2**, mp 83–84°, $[\alpha]^{25}D$ −28° (*c* 1.023, $CHCl_3$) (lit.[14] mp 78–98°, $[\alpha]^{23}D$ −20°). Resolved *cis*-**2** from another run had $[\alpha]^{23}D$ −27.6° ($CHCl_3$) and $[\alpha]^{23}D$ −22.1° (CH_3OH).

Friedel–Crafts Cyclization of Acid Chloride from (+)-*cis*-2. The acid chloride was made from *cis*-**2**, $[\alpha]^{22}D$ +16.6° (*c* 1, methanol), by reaction with oxalyl chloride. A 1.4-g sample was cyclized as described for active *trans*-**2**; work-up and distillation afforded optically inactive ketone **3**. Isolated acidic material (0.26 g) also was optically inactive; esterification (diazomethane) and vpc analysis showed a cis–trans ester ratio of 15:85.

Configurational Stability of Ketone 3. A mixture of (−)-**3** (2.0 g from fraction A, above) and an equivalent amount of aluminum chloride in 40 ml of methylene chloride was kept 20 hr at 0–7°. After a duplicate work-up and redistillation, recovered ketone (1.67 g, 83.5%) had the following ORD features (methanol, 24°, *c* 1.62): $[\alpha]_{360}$ −3400° (tr), $[\alpha]_{353}$ −3700° (tr), $[\alpha]_{311}$ +14,800° (pk).

Epimerization of *cis*-2-Phenylcyclopropanecarboxylic Acid Chloride. A benzene solution of 1.4 g of acid chloride (from *cis*-**2**, $[\alpha]^{22}D$ +16.6°) and 1 ml of thionyl chloride was refluxed 4 hr and allowed to stand 20 hr at room temperature. Benzene and thionyl chloride were removed under reduced pressure. The residual red oil was stirred with 25 ml of water for 16 hr and extracted into ether. Washing, drying, and solvent removal afforded soft, brown crystals. These were charcoaled in benzene–hexane to give 450 mg of yellow, waxy solid, which was esterified by diazomethane in ether. Preparative vpc (20% QF-1, DMCS on Chromosorb W, 10 ft × 1/8 in. column, 135°) provided *trans*-**2** methyl ester, $[\alpha]^{22}D$ −97° (*c* 1.02, methanol), and *cis*-**2** methyl ester, $[\alpha]^{22}D$ +50.5° (*c* 1.11, methanol). Diazomethane esterification of independently prepared *trans*-**2**, $[\alpha]^{22}D$ −314° (~99% optical purity assumed),[4a] gave trans ester, $[\alpha]^{22}D$ −319°; similar esterification of *cis*-**2**, $[\alpha]^{21}D$ −10.6°, gave cis ester, $[\alpha]^{22}D$ −31°.

Acknowledgments. Financial support from the Research Corporation (Frederick Gardner Cottrell grant) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(14) H. M. Walborsky and L. Plonsker, *J. Amer. Chem. Soc.*, 83, 2138 (1961).

The Persistence of Stereoselectivity in the Intramolecular Diels–Alder Reactions of 5-Alkenylcyclohexa-1,3-dienes. A Novel Route to Functionalized Bridged Tricyclic Rings Using a Regenerable Diene[1]

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Abstract: Heating 5-(pent-4-enyl)cyclohexa-1,3-diene (**3**) at 210° leads to predominantly tricyclo[5.3.1.$0^{3,8}$]undec-9-ene (**11**) by direct stereoselective cyclization. Minor amounts of the epimeric tricyclo[5.2.2.$0^{1,5}$]undec-8-enes (**26** and **27**) are likely formed through a competing sequence involving the intermediate 1-(pent-4-enyl)cyclohexa-1,3-diene (**9**). Ketones corresponding in their skeletal structure to these tricyclic hydrocarbons have been obtained by heating α-pyrone with hepta-1,6-dien-3-one. These reactions are discussed in the context of the intramolecular Diels–Alder reaction.

The identification[1] of molecules **1** with C_s symmetry as the sole tricyclic products of the thermal Diels–Alder[2] reactions of 5-alkenylcyclohexa-1,3-dienes (**2**) (n = 0, 1, 2) prompted the investigation of the thermal behavior of higher homologs of this system.[3] These

(1) (a) Presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971, Abstract ORGN-95. (b) For a preliminary communication, see A. Krantz and C. Y. Lin, *Chem. Commun.*, 1287 (1971).

(2) (a) W. von E. Doering and A. Krantz, to be submitted for publication; (b) A. Krantz, Ph.D. Thesis, Yale University, 1967.

(3) For some general reviews of the Diels–Alder reaction, see (a) M. C. Kloetzel, *Org. React.*, 4, 1 (1948); (b) H. L. Holmes, *ibid.*, 4, 60 (1948); (c) K. Alder, in "Newer Methods of Preparative Organic Chemistry," Interscience, New York, N. Y., 1948, pp 381–511; (d) J. G. Martin and R. K. Hill, *Chem. Rev.*, 61, 537 (1961); (e) A. J. Onishchenko, "Diene Synthesis," Davey, New York, N. Y., 1964; (f) A. Wassermann, "The Diels–Alder Reaction," Elsevier, Amsterdam, 1965;