Acknowledgment. We wish to thank Mr. E. B. Banta for technical assistance.

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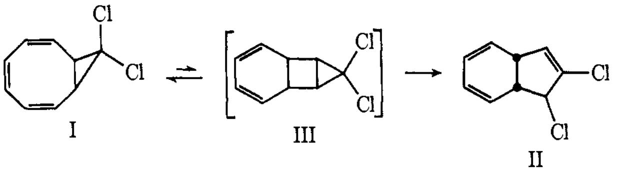
Received November 2, 1970

Thn Thermal Bicyclo[6.1.0]nonatrienyl Chloride–Dihydroindenyl Chloride Rearrangement

Sir:

In 1961 Vogel and Kiefer[1,2] reported the first observations dealing with rearrangements of bicyclo[6.1.0]-nonatrienes, a field which subsequently has been rather extensively investigated.[2–8] 9,9-Dichlorobicyclo[6.1.0]-nonatriene (I) upon heating gave 1,2-dichloro-*cis*-8,9-dihydroindene (II); the intermediacy of the tricyclic valence tautomer III was proposed to explain this result.[1,2]



Subsequent investigations have shown that this reaction course is exceptional. For example, 9,9-dideuteriobicyclo[6.1.0]nonatriene gives mainly 1,1-dideuterio-*cis*-dihydroindene,[3] while 9,9-dimethylbicyclo-[6.1.0]nonatriene rearranges to 1,1-dimethyl-*trans*-dihydroindene.[6] The behavior of the monochlorides IV and V related to I has appeared not to follow the mechanism proposed by Vogel and Kiefer. Regardless of the stereochemistry at C-9, IV and V were found to rearrange at about equal rates to give the same product, 1-chloro-8,9-dihydroindene (VI).[4,5,9] LaLancette and Benson[5] suggested that "chlorocyclononatetraene (VII) may be a common intermediate in these transformations."

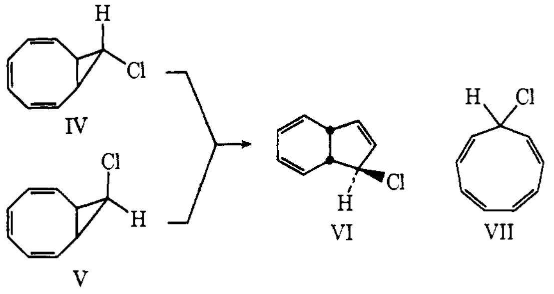
We have investigated the apparent discrepancy between the behavior of dichloride I and monochlorides IV and V. Because of the known propensity of disrotatory *syn*-bicyclocyclopropyl chloride ring opening,[10a] V, at least, might be expected to react *via* the Vogel–Kiefer mechanism.[10b]

Table I. Thermolysis and Solvolysis Rates, 75°

Compd	Solvent	k, sec^{-1}	k_{rel}	$\Delta H^{\ddagger}$, kcal	$\Delta S^{\ddagger}$, eu
IV	CCl_4	$2.60 \times 10^{-4\,a}$	1.0	25	−2.3
	CH_2Cl_2	$6.53 \times 10^{-4\,a}$	2.5		
	90% acetone	$2.43 \times 10^{-3\,b}$	9.4		
	70% acetone	$2.97 \times 10^{-3\,b}$	11.3		
V	CCl_4	$2.46 \times 10^{-4\,a}$	0.95	23	−8.7
	CH_2Cl_2	$1.13 \times 10^{-4\,a}$	0.44		
	90% acetone	$2.64 \times 10^{-4\,b}$	1.01		
	80% acetone	$1.81 \times 10^{-4\,b}$	0.70		
I	CCl_4	$3.74 \times 10^{-5\,a}$	0.14		
	CH_2Cl_2	$6.29 \times 10^{-5\,a}$	0.41		
	80% acetone	$3.80 \times 10^{-5\,b}$	0.15		
	70% acetone	$4.04 \times 10^{-5\,b}$	0.16		

[a] Thermolysis rates were obtained by measuring the rate of disappearance of absorptions in the nmr due to H_1 and H_8. [b] Solvolysis rate, determined conductometrically.

Quantitative measurements (Table I) confirmed that IV and V rearrange to VI at nearly the same rate in aprotic solvents. Furthermore, neither thermolysis was significantly enhanced if more polar solvents like CH_2Cl_2 were employed. This shows that the rate-determining step was in neither case the formation of an ion pair similar to that involved in the thermal rearrangements of di-



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(1) E. Vogel, *Angew. Chem.*, 73, 548 (1961); H. Kiefer, Dissertation, Köln, 1962.

(2) E. Vogel, *Angew. Chem.*, 74, 829 (1962); *Angew. Chem., Int. Ed. Engl.*, **2**, 1 (1963).

(3) W. Grimme, *Chem. Ber.*, 100, 113 (1967); *cf.* E. Vogel, W. Wiedemann, H. Kiefer, and W. F. Harrison, *Tetrahedron Lett.*, 673 (1963).

(4) T. J. Katz and P. J. Garratt, *J. Amer. Chem. Soc.*, **86**, 5194 (1964).

(5) E. A. LaLancette and R. E. Benson, *ibid.*, **87**, 1941 (1965).

(6) S. W. Staley and T. J. Henry, *ibid.*, **91**, 1239 (1969); *cf.* S. W. Staley and T. J. Henry, *ibid.*, **91**, 7787 (1969).

(7) W. Grimme, Habilitationsschrift, Köln, 1968; P. Radlick and W. Fenical, *J. Amer. Chem. Soc.*, **91**, 1560 (1969); G. J. Fonken and W. Moran, *Chem. Ind.* (*London*), 1841 (1963); K. F. Bangert and V. Boekelheide, *J. Amer. Chem. Soc.*, **86**, 905 (1964); S. Masamune, P. M. Baker, and K. Hojo, *Chem. Commun.*, 1203 (1969); P. Radlick and G. Alford, *J. Amer. Chem. Soc.*, **91**, 6529 (1969); G. Boche, H. Boehme, and D. Martens, *Angew. Chem., Int. Ed. Engl.*, **8**, 594 (1969).

(8) (a) W. H. Okamura and T. W. Osborn, *J. Amer. Chem. Soc.*, **92**, 1061 (1970); (b) C. S. Baxter and P. J. Garratt, *ibid.*, **92**, 1062 (1970); (c) A. G. Anastassiou and R. P. Cellura, *Tetrahedron Lett.*, 911 (1970).

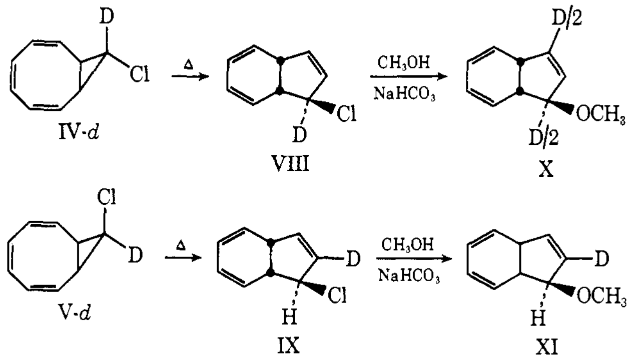
(9) We have established by nmr analysis in comparison with literature values and separately synthesized reference compounds that chloride VI, as well as the corresponding alcohol and methyl ether (*e.g.*, X) resulting from solvolysis of VI, possess the cis-exo stereochemistry.

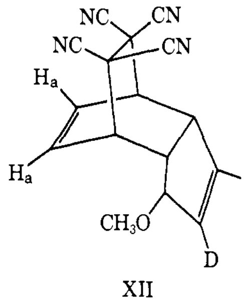
(10) (a) P. v. R. Schleyer, T. M. Su, M. Saunders, and J. C. Rosenfeld, *J. Amer. Chem. Soc.*, **91**, 5174 (1969), and references cited therein. (b) Precedence for the formation of postulated intermediate XIII (similar to Vogel and Kiefer's III) is found in observations of R. Huisgen, G. Boche, A. Dahmen, and W. Hechtl, *Tetrahedron Lett.*, 5215 (1968) (cyclooctatetraene oxide in equilibrium with 8-oxatricyclo-[4.3.0.0^{7,9}]nonadiene) and Okamura and Osborn,[8a] Baxter and Garratt,[8b] and Boche and Konz[11] (who were able to trap tricyclo[4.3.0.0^{7,9}]-nonadiene, a valence tautomer of bicyclo[6.1.0]nonatriene, as Diels–Alder adducts).

(11) G. Boche and W. E. Konz, unpublished results.

chlorocyclopropanes to 2,3-dichloroallyl products (*i.e.*, step III → II in the Vogel–Kiefer scheme).[12,13]

Despite this evidence, deuterium labeling studies show conclusively that IV and V *react by different mechanisms*. The thermolysis of IV-d^{14a} yielded dihydroindenyl chloride (VIII) with $>95\%$ D in the C_1 position, while the similar reaction of V-d^{14b} gave product IX with the deuterium label exclusively at C_2. Location of the deuterium labels was established by nmr analysis of VIII and IX, and of X and XI, the methanolysis products of VIII and IX, respectively. Compound VIII exhibited no detectable resonance at τ 5.1, assigned to the C*H*Cl proton (C_1), while X integrated for 0.5C*H*OCH$_3$ proton (C_1) at τ 5.7. Both IX and XI exhibited 1.0 proton in the C*H*Cl and C*H*OCH$_3$ regions, respectively; the deuterium was obviously in the complex olefinic region. The nmr spectrum of XII, the TCNE adduct of XI, showed a 2:1 H_a:H_b proton ratio;[15] this information restricts deuterium to C_2 of the dihydroindene product.

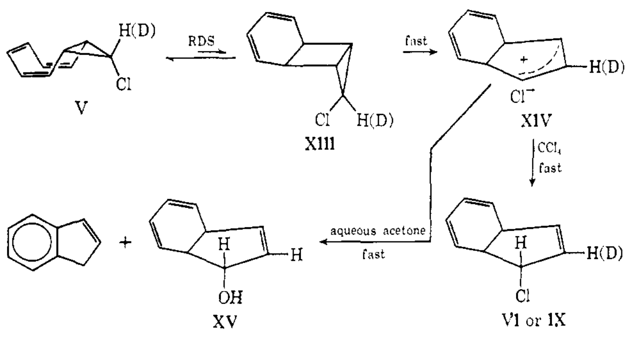




XII

Rate-determining formation of intermediate XIII followed by rapid rearrangement to ion pair XIV and product VI or IX provides an attractive explanation for the behavior of V and V-*d*.[10]

This mechanism is supported by solvolysis of V. In both 80 and 90% acetone, the conductometric rates are *virtually identical*, and are essentially the same as the thermolysis rates in aprotic solvents (Table I)!



The *solvolysis* products do not include chloride VI, even though it is stable under the solvolysis conditions.

Our reinvestigation of the behavior of dichloride I (Table I) shows that it behaves in the same manner as *syn*-monochloride V, in confirmation of Vogel and Kiefer's postulated mechanism.[15a] Both III (from I) and XIII (from V) contain *endo*-bicyclo[2.1.0]pentyl chloride systems, which should be exceedingly reactive toward concerted ring opening.[2,16]

The corresponding tricyclononadiene intermediate from chloride IV would possess exo stereochemistry, expected to be stable.[16] For this reason, the "normal" thermal rearrangement course (*via* VII?)[17] typically observed of 9-monosubstituted bicyclo[6.1.0]nonatrienes (to give VI or VIII)[2-8] is followed in aprotic solvents.

The solvolytic behavior of IV is of considerable interest. Although the solvolysis rates are somewhat faster than thermolysis, solvolysis does not appear to be the rate-determining step, since the rates in 70 and 90% acetone are virtually the same.[18] Solvolysis of IV also gives dihydroindenol (XV) as the only observable product. However, labeled IV-*d* gives dihydroindenol product with D *completely scrambled to all positions*. The simplest explanation consistent with these facts is rate-limiting thermal rearrangement of IV to VII, solvolysis of VII *via* the cyclononatetraenyl cation (which would necessitate complete D scrambling) to 9-hydroxycyclononatetraene, and rapid thermal conversion of the latter to product. Other explanations are possible. We are investigating the nature of the intermediate in these reactions.

Acknowledgments. This work was supported by grants from the National Science Foundation and the Petroleum Research Fund, administered by the Amer-

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[12] For example, R. C. DeSelms and C. M. Combs (*J. Org. Chem.*, **28**, 2206 (1963)) found that the rearrangement of 3,3-dichloro-*exo*-bicyclo[3.2.1.0^{2,4}]octane to 3,4-dichlorobicyclo[3.2.1]oct-2-ene proceeds 140 times faster in CH_2Cl_2 than in CCl_4.

[13] K. A. Holbrook and K. A. W. Parry, *J. Chem. Soc. B*, 1019 (1970).

[14] (a) Prepared by the method of Katz and Garratt[4] and appropriate deuterated reagents; (b) prepared by the method of LaLancette and Benson,[5] using cyclooctatetraene, methylene-d_2 chloride, and methyllithium. Deuterated products were purified by distillation and the major isomer was separated by chromatography on silica gel by elution with hexane.

[15] The nmr spectrum showed a 2:1 H_a:H_b proton ratio for the τ 3.3 and 4.0 absorptions, respectively. These assignments were based on comparisons with nmr spectra of the known TCNE–dihydroindenyl chloride adduct: T. Su, Ph.D. Dissertation, Princeton University, 1970.

[15a] NOTE ADDED IN PROOF. Professor E. Vogel (private communication) has also observed that the rate of thermal rearrangement of I is not solvent dependent.

[16] P. v. R. Schleyer, 20th National Organic Chemistry Symposium, American Chemical Society, Burlington, Vt., 1967, Abstracts, p 5.

[17] The detailed mechanism of the formation of *cis*-dihydroindenes remains unsolved.[2-8]

[18] Normally a rate difference of 10^1–10^2 is expected in these two solvents. See, for example, S. Winstein and A. Fainberg, *J. Amer. Chem. Soc.*, **79**, 5937 (1957).

ican Chemical Society. Professor M. Jones, Jr., provided helpful discussion.

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[19] National Institutes of Health Postdoctoral Fellow, 1969–1970.

[20] American Chemical Society–Petroleum Research Fund Fellow, 1968–1969; Ph.D. Thesis, Princeton University, 1970.

[21] Presented at the IUPAC Conference on Cycloaddition, Munich, Germany, Sept 1970.

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Received October 19, 1970

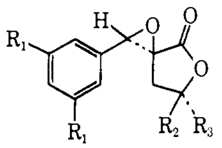
Darzens Condensation of α-Halolactones. Glycidic Lactones as Intermediates in Acetogenin Synthesis[1]

Sir:

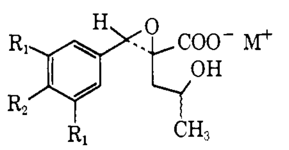
The development of methodology for synthesis of polyketide-derived natural systems has received much attention recently.[2] A major goal of these efforts remains the regulated elaboration of a ketide chain in open form and, toward this end, we have investigated procedures which would allow a homologation of the type ArCHO → $ArCH_2COCH_2COCH_3$. We wish to report that condensation of an aromatic aldehyde with α-bromo-γ-valerolactone, and subsequent transformation of the resulting glycidic lactone, provides a convenient sequence for effecting this construction.[3]

The full scope of the method is presently under investigation but the following example is illustrative. Addition of an equimolar mixture of 3,5-dimethoxybenzaldehyde and α-bromo-γ-valerolactone (**1**, mixture of cis and trans) to a solution of potassium *tert*-butoxide in *tert*-butyl alcohol–tetrahydrofuran (3:1) (1 hr at 0°, 20 hr at 25°) gave epimeric lactones **2**[4] (mp 102–103°; $\nu_{\max}$ 1780 cm^{-1}; nmr δ 1.33 (3 H, d, $J = 6$ Hz)) and **3** (mp 111–113.5°; $\nu_{\max}$ 1780 cm^{-1}; nmr δ 1.46 (3 H, d, $J = 6.5$ Hz)) in 78% yield (ratio 3:1, respectively). Lactone **3** is converted to **2** through saponification–relactonization cycles and this observation, taken with the deshielded methyl group in **3**, provides the basis for stereochemical assignment. As has been previously noted in connection with the Darzens reaction of α-chloro esters,[5] condensation at the carbonyl group proceeds with high stereoselectivity. Saponification of the mixture of **2** and **3** with 3 *M* sodium hydroxide in ethanol–acetone afforded carboxylate **4** (84%) (mp 184–194° dec; $\nu_{\max}$ 3400, 1600 (broad) cm^{-1}), which was irradiated (Hanovia 450-W lamp, Corex) in aqueous solution with provision for continuous removal of product by extraction into ether. After chromatography, hydroxy ketone **5** (62%) ($\nu_{\max}$ 3600, 1710 cm^{-1}; nmr δ 1.14 (3 H, d, $J = 6$ Hz), 2.58 (2 H, d, $J = 6$ Hz), 3.1 (1 H, broad, exchanged with D_2O), 3.60 (2 H, s), 3.76 (6 H, s), 4.20 (1 H, m), and 6.36 (3 H, s)) was obtained[6] accompanied by the secondary photolysis product **6**.[7] Oxidation of **5** with Jones' reagent produced **7**,[8] characterized as the copper(II) chelate, mp 201–202°; **7** has recently been converted in four steps to the anthraquinonoid pigment endocrocin.[9]

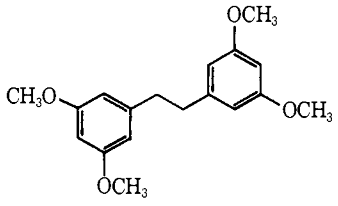
Alternatively, **5** was converted to the trans α,β-unsaturated ketone **8** (83%) ($\nu_{\max}$ 1690 cm^{-1}; nmr δ 1.83 (3 H, d of d, $J = 2$, 6.5 Hz), 3.70 (2 H, s), 3.72 (6 H, s), 6.10 (1 H, d of d, $J = 1.5$, 16 Hz), 6.33 (3 H, s), and 6.85 (1 H, d of q, $J = 6.5$, 16 Hz)) *via* acetoxy ketone **9** followed by chromatography on alumina. Extension of this procedure to the synthesis of **10**, an intermediate of potential utility for construction of various, natural pyronoquinonoid systems,[10] and which has recently found use in the total synthesis of mitorubrin,[11] was realized by condensation of **1** with 3,5-dibenzoyloxy-4-methylbenzaldehyde[12] to give lactone **11** as a mixture of epimers. Saponification of **11** (0.3 *M* potassium hydroxide in ethanol–acetone) afforded the resorcinol **12** which, without purification, was photolyzed as described above to give **13**. Dehydration of the latter (acetic acid containing *p*-toluenesulfonic acid) furnished the trans α,β-unsaturated ketone **10**.[11]



2, $R_1 = OCH_3$; $R_2 = H$; $R_3 = CH_3$
3, $R_1 = OCH_3$; $R_2 = CH_3$; $R_3 = H$
15, $R_1 = R_2 = H$; $R_3 = CH_3$
16, $R_1 = R_3 = H$; $R_2 = CH_3$



4, $R_1 = OCH_3$; $R_2 = H$
12, $R_1 = OH$; $R_2 = CH_3$
14, $R_1 = R_2 = H$



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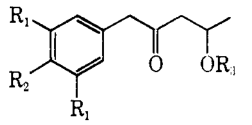

5, $R_1 = OCH_3$; $R_2 = R_3 = H$
9, $R_1 = OCH_3$; $R_2 = H$; $R_3 = Ac$
13, $R_1 = OH$; $R_2 = CH_3$; $R_3 = H$
18, $R_1 = R_2 = R_3 = H$

Photodecarboxylation of **14**, derived from the mixture of epimeric glycidic lactones **15** (mp 98–98.5°) and **16** (mp 150–151.5°), was excessively slow and, as an alternate route to the desired β-hydroxy ketone, **16** was

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[1] Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, Abstract P 170.

[2] T. Money, *Chem. Rev.*, 70, 553 (1970).

[3] M. S. Newman and B. J. Magerlein, *Org. React.*, 5, 413 (1949); M. Ballester, *Chem. Rev.*, **55**, 283 (1955).

[4] Satisfactory elemental analyses were obtained for all new compounds.

[5] F. W. Bachelor and R. K. Bansal, *J. Org. Chem.*, **34**, 3600 (1969).

[6] A mechanism has been proposed to account for formation of **5** [P. G. Sammes, *Quart. Rev., Chem. Soc.*, **24**, 37 (1970)]. Our own (unpublished) and related observations [J. W. Chamberlin, *J. Org. Chem.*, **31**, 1658 (1966)] support a process in which intramolecular energy transfer takes place from the initially excited aromatic nucleus to the carboxylate residue of **4** [for other examples, see C. Thiery, *Mol. Photochem.*, **2**, 1 (1970), and references cited]. It has not been ascertained whether this transfer takes place from an electronically excited state, as implied by Sammes, or *via* a vibrationally excited ground state.

[7] B. K. Bullimore, J. F. W. McOmie, A. B. Turner, M. N. Galbraith, and W. B. Whalley, *J. Chem. Soc. C*, 1289 (1967).

[8] H. Mühlemann, *Pharm. Acta Helv.*, **26**, 195 (1951).

[9] W. Steglich and W. Reininger, *Chem. Commun.*, 178 (1970).

[10] W. B. Whalley, *Pure Appl. Chem.*, 7, 565 (1963).

[11] R. Chong, P. W. Gray, R. R. King, and W. B. Whalley, *Chem. Commun.*, 101 (1970).

[12] Prepared from 3,5-dihydroxy-4-methylbenzoic acid [E. H. Charlesworth and R. Robinson, *J. Chem. Soc.*, 1531 (1934)] by (i) benzoylation (benzoyl chloride–pyridine), (ii) conversion to the acid chloride (thionyl chloride), and (iii) reduction with lithium aluminum tri-*tert*-butoxy hydride in diglyme at −78° [H. C. Brown and R. F. McFarlin, *J. Amer. Chem. Soc.*, **80**, 5372 (1958)].