Thermal Isomerization of Arylmethylenecyclopropanes to Indenes: The Question of Orbital Symmetry Control as a Factor in Hydrogen Transport

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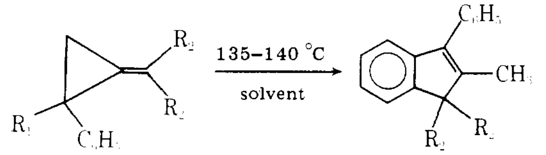
Examination of the deuterium distribution of the 2-methyl-3-phenylindene resulting from rearrangement of 2-phenyl-2-(perdeuteriophenyl)-1-methylenecyclopropane conclusively demonstrates that orbital symmetry does not control the net 1,5 migration of hydrogen required to produce the indene. An alternative explanation is offered for the necessity of having diaryl substitution of C-2 of the 1-methylenecyclopropane in order to observe the isomerization.

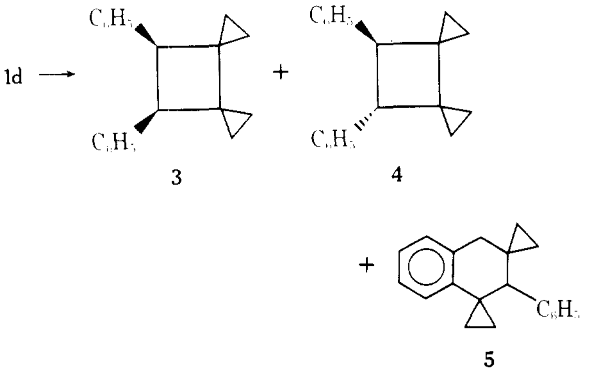
An earlier paper[1] that described the thermal rearrangements of 2-phenyl-1-methylenecyclopropanes to indenes (eq 1) included mention of an interesting dependence of the course of the reaction on the substitution pattern at C-2. So long as this carbon atom bears two phenyl groups as in **1a**, the reaction proceeds in a facile manner, and independently of the nature of the number of alkyl substituents on the double bond; cf **1b** and **1c**. However, 2-phenyl-1-methylenecyclopropane (**1d**) itself exhibited considerably greater thermal stability, surviving unchanged when heated for 16 h at 140 °C, conditions corresponding to about two half-lives of rearrangement for the diphenyl analogue **1a**. It did undergo reactions apparently thermal in nature under more forcing conditions (190 °C, 16 h) or when heated for extended periods of time (14–21 days) at 110–140 °C, but afforded a mixture of dimeric products (eq 2).[2] No 2-methylindene, the product of a molecular rearrangement analogous to that observed for **1a–c**, could be detected using analytical methods (^{1}H NMR) where as little as 5% of the indene would have been noted. The indene was separately shown to be stable to these reaction conditions.[4]



(1)

1 **2**

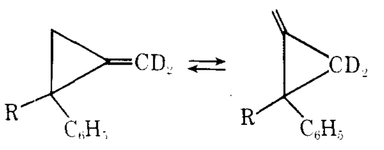
a, $R_1 = C_6H_5$, $R_2 = H$; **b**, $R_1 = C_6H_5$, $R_2 = H, CH_3$; **c**, $R_1 = C_6H_5$, $R_2 = CH_3$; **d**, $R_1 = R_2 = H$



3 **4** **5**

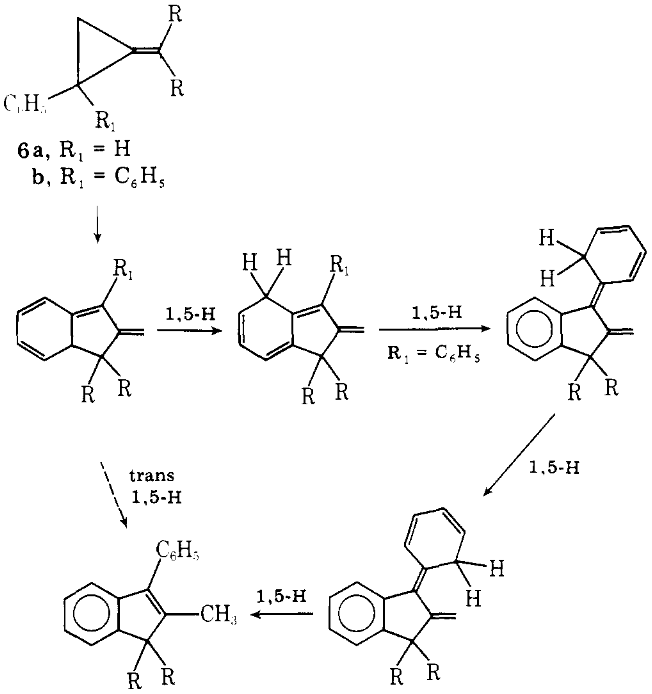
(2)

The thermal behavior of 2-phenyl-1-methylenecyclopropane (**1d**) is all the more perplexing in view of the observation that it undergoes automerization (eq 3) at a rate that is only one order of magnitude less than that of the corresponding process in the diphenyl compound **1a**.[5] Clearly, the allylic bond of the cyclopropane ring has similar lability in the two compounds, as measured by the facility of the automerization, but this lability does not translate into analogous behavior of the two molecules when higher energy reaction surfaces are probed.



(3)

Scheme I. Sequential 1,5-Hydrogen Migrations to Yield Indenes



To rationalize the anomalous thermal behavior of **1d** vs. **1a**, the seemingly key role of a second phenyl substituent at C-2 in facilitating the isomerization of methylenecyclopropanes to indenes was tentatively ascribed to the operation of a reaction mechanism in which a conducted tour of a hydrogen atom is essential to formation of product (Scheme I).[1] In this mechanism, the tetraene **6**, which possesses the carbon skeleton of the indene ultimately produced, is generated initially and this species is transformed to the indene by a succession of 1,5-hydrogen shifts, the second of which demands the presence of an aromatic ring as a crucial link in the transport chain. The postulated shifts are across a *cis*-1,3-pentadienyl system and have ample precedent.[6] A 1,5 shift that would convert the tetraene **6** in one step into the indene involves hydrogen atom migration across a *trans*-pentadienyl moiety, but there is, to our knowledge, no literature support for such an event occurring under control of orbital symmetry. The

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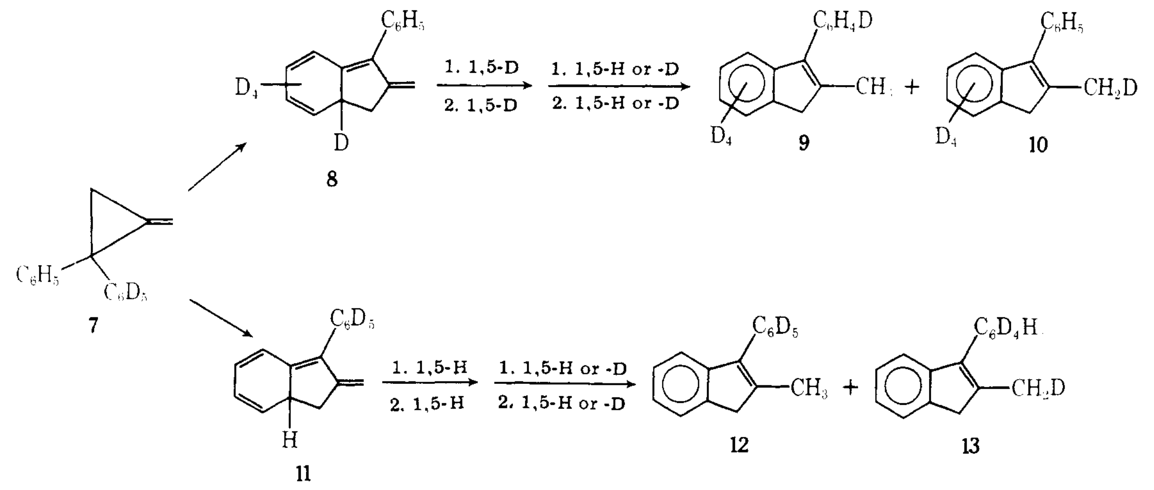
Scheme II. Rearrangements of Labeled 2,2-Diphenyl-1-methylenecyclopropane (7)



temperatures required to promote the rearrangement are commensurate with our proposed mechanism given the activation parameters expected for the postulated hydrogen shifts; e.g., $\Delta S^{\ddagger} = -3$ eu and $\Delta H^{\ddagger} = 35.1$ kcal/mol for the 1,5-hydrogen shift in *trans*-5,6-dimethyl-1,3-cyclohexadiene.[7]

It was felt significant, therefore, to subject the hypothesized role of the second phenyl group to a sensitive experimental test. From our prior work,[5] it was known that free-radical chain inhibitors such as diphenylamine did not suppress the overall rate of production of the indene from **1a** and that an increase in the surface to volume ratio had only a slight accelerating effect on the rate of reaction. Although the latter observation suggested that heterogeneous pathways were not of importance, such an interpretation must be viewed with caution. This is because it is likely that the rate-determining step in the rearrangement actually involves cyclization to the tetraene **6** and thus occurs *prior* to any hydrogen shift(s), for which heterogenous catalysis is a possibility. If this is the case, absence of a significant change in reaction rate as a function of variation of the surface to volume ratio cannot be taken as definitive support for the orbital symmetry controlled mechanism. Consequently, it was necessary to devise an experimental test that had the potential to provide unambiguous evidence for the homogeneous mode even in the presence of a heterogenous component and to discriminate between these two pathways under conditions where the rate-determining step of the rearrangement most probably occurs prior to any hydrogen migrations. These goals could be achieved with the aid of isotopic labeling in the following manner.

Consider the anticipated consequence of rearrangement of 2-phenyl-2-(perdeuteriophenyl)-1-methylenecyclopropane (**7**) as shown in Scheme II. If product formation depends upon transportation of hydrogen (deuterium) through the pendant phenyl ring of **8** or **11**, it can be seen that the final two [1,5] sigmatropic shifts allow for operation of intramolecular kinetic isotope effects. Because the isotope effect is expected to be normal and large, e.g., $k_H/k_D = 12.2$ (25 °C) in *cis*-1,3-pentadiene,[8] the preferential formation of **9** from **8** and of **12** from **11** would be predicted. Production of isomer **9** is a particularly sensitive probe for the postulated mechanism as its formation relative to **10** is favored by two separate steps in which an isotope effect favoring retention of deuterium in the ring is a factor.

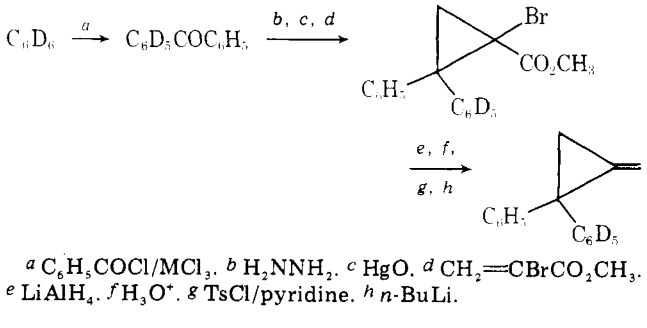
The synthesis of **7** is outlined in Scheme III and is described in detail in the Experimental Section. The key step in the entire sequence is the first one, in that the homogeneity of the label must be assured. Reference to earlier literature suggested that the benzoylation would be uncomplicated since Adams and Tarbell have reported the preparation of benzophenone-d_5 from Friedel-Crafts reaction between perdeuteriobenzene and benzoyl chloride.[9] In our hands, repetition of the published procedure, except that unsublimed aluminum chloride was used in place of sublimed material, afforded a chemical yield (44%) similar to that reported (50%), but gave ketone in which loss of isotope and scrambling were evident as indicated by the following isotope distributions: 5% d_6, 65% d_5, 25% d_4, 5% d_3. Use of carefully sublimed aluminum chloride gave inconsistent results both in terms of yields and the extent of scrambling and loss of deuterium. These results may be the consequence of the difficulty in protecting the catalyst from exposure to atmospheric moisture.

It is to be noted that Adams and Tarbell assessed the deuterium content of their benzophenone-d_5 by measurement of its density.[9] Precise determination of total deuterium content is not possible from such data, and isotopic distributions, of course, cannot even be estimated by this method.

Substitution of anhydrous ferric chloride as the Lewis acid catalyst in the procedure gave the desired ketone in reproducibly satisfactory yields (66%) in a reaction accompanied by only slight loss of total label. Specifically, benzene-d_6 having the isotopic content 97.8% d_6 and 2.2% d_5 afforded benzophenone-d_5 with the deuterium distribution 45.8% d_5 and 4.3% d_4. Analysis of the mass spectrum in the region where benzoyl carbocations appear showed that less than 0.3% of the d_1 species was present, thereby demonstrating that an inconsequential amount of scrambling occurred during benzoylation.[10] Our results are in line with the observation made by Olah and co-workers that H–D exchange was difficult to avoid when attempting Friedel–Crafts alkylation of perdeuteriobenzene with strong Lewis acid catalysts, whereas weaker catalysts such as ferric chloride suppressed any exchange.[12]

A critical element in the success of the investigation was development of a satisfactory mass spectral method for analyzing deuterium content in the aromatic rings of the indenes **9**, **10**, **12**, and **13**. Fundamentally, what was required was a

Scheme III. Synthesis of Labeled 2,2-Diphenyl-1-methylenecyclopropane (7)



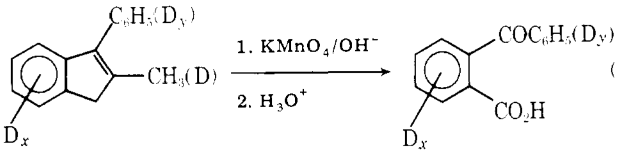
^{a} C_6H_5COCl/MCl_3. ^{b} H_2NNH_2. ^{c} HgO. ^{d} $CH_2{=}CBrCO_2CH_3$. ^{e} $LiAlH_4$. ^{f} H_3O^+. ^{g} TsCl/pyridine. ^{h} *n*-BuLi.

Table I. Deuterium Analyses (%) of Reactants and Products

compd	d_0	d_1	d_2	d_3	d_4	d_5
benzophenone-d_5[a]	49.1	0.2	0.2	0.4	4.3	45.8
o-benzoylbenzoic-d_x acid						
phenyl group[b]	47.6	0.5	0.1	1.9	3.7	45.9
benzo group[c]	49.6	0.1	0.4	4.0	45.7	

[a] Data from mass spectral analysis at 70 eV; uncorrected for isotope effects in the fragmentation; estimated error ±1%. [b] Benzoyl carbocations (*m/e* 105–110) were analyzed. [c] *o*-Carboxybenzoyl carbocations (*m/e* 149–153) were analyzed.

method for assessing the deuterium distribution in each ring separately. This goal could not be achieved by mass spectral analysis of the indenes themselves because of the extent and complexity of their fragmentation patterns even under conditions of low ionizing voltage. The desired analysis could be accomplished on the *o*-benzoylbenzoic acids arising from oxidative cleavage of the indenes (eq 4). As would be expected,[13] a major mass spectral fragmentation pathway involves rupture of bonds to the ketonic carbon atom to afford carbocations of the benzoyl and *o*-carboxybenzoyl varieties. The former ions allow for the crucial measurement of deuterium distribution in the phenyl ring and the latter in the benzo moiety.

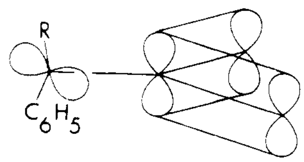


(4)

Thermolysis of 4 yielded the desired indenes in 80% yield following purification by column chromatography; oxidation provided the *o*-benzoylbenzoic acids which were purified by recrystallization. The results of mass spectral analysis of these acids, as well as of the benzophenone-d_5 used to prepare the methylenecyclopropane 7, are collected in Table I.

First, it is of importance to note in the table that the ratios d_0/d_5 and d_0/d_4 in the phenyl and benzo moieties, respectively, of the product indene are within experimental error of that of the benzophenone-d_5 from which the methylenecyclopropane 7 was prepared. This observation renders untenable a mechanistic proposal in which the cyclization of 7 to give the tetraenes 8 and 11 is considered reversible. Were this the case, consideration of primary isotope effects would dictate that the major pathway for product formation be by way of **11**, even though initial cyclization to 8 would be favored slightly owing to secondary deuterium isotope effects.[14] The postulation of reversal, therefore, would require a preference for the perdeuteriophenyl ring of **7** to appear as the phenyl ring of the indene. Such is clearly not the case.

The ratio d_0/d_1 in the benzoyl cations arising from fragmentation of 14 potentially represents the most sensitive measure available to us for detection of the orbital symmetry controlled pathway. This is because production of the indenes **9** and **10** that would define this ratio eventually requires the operation of two sigmatropic shifts in which competition between deuterium and hydrogen migration could occur. Consequently, significant accumulation of deuterium in the phenyl ring would be predicted and would be reflected in a dramatic change in the d_0/d_1 ratio. In contrast, formation of products **11** and **12**, although also resulting from a similar competition in migration of hydrogen and deuterium, is measured by the ratio d_5/d_4, and consideration of isotope effects prompts the conclusion that a less dramatic change in this ratio would be anticipated.



14a, R = H
b, R = C_6H_5

The data in Table I show that regardless of which ratio is examined, its value is within experimental error of that measured for the benzophenone-d_5 from which **7** was prepared. The evidence is unambiguous that the orbital symmetry plays, at best, a minor role in defining the nature of hydrogen migrations that occur in the rearrangement of 2,2-diphenyl-1-methylenepropanes to indenes. The apparent requirement of having two phenyl groups at C-2 to promote the rearrangement is obviously not associated with the hydrogen transport phenomenon.

This being so, it becomes difficult to rationalize the difference in the propensities of tetraenes **6a** and **6b** to suffer a catalyzed isomerization if both tetraenes are, in fact, being produced. Consequently, our present explanation for the function of the second phenyl group in facilitating the rearrangement (eq 1) rests on its ability to relax geometrical constraints placed on the biradical-like (biradicaloid) species **14** that reasonably can be proposed as a precursor to the indene skeleton. Thus, rotation about the C-3, C-4 bond in the trimethylenemethane skeleton is expected to be more restricted in **14a** than in **14b**; that is, the cost in energy for disrupting delocalization through one of the two phenyl rings in **14b** undoubtedly is less than the comparable process in **14a**. Such rotations may be crucial to the development of the 1,5 overlap necessary for transformation of **14** to the indene skeleton. In the absence of the second phenyl group, tetraene **6a** is not accessible from **14a**.

Experimental Section

Proton magnetic resonance (^1H NMR) spectra were recorded with a Varian Associates A-60 spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from Me_4Si (0.00 ppm). All melting points were obtained on a Hoover-Thomas apparatus and are uncorrected.

Exact mass determinations were obtained at 70 eV on a Dupont (CEC) 21-210 high-resolution mass spectrometer. This instrument, operating at an ionizing potential of 70 eV, was also used for measuring isotopic distributions, except in the case of C_6D_6 where a potential of 10 eV was used.

Benzophenone-d_5. A slurry of benzene-d_6 (5.0 g, 60 mmol), benzoyl chloride (9.2 g, 66 mmol), and anhydrous ferric chloride (11.6 g, 72 mmol) in carbon disulfide (48 mL) was stirred at reflux for 8 h under an atmosphere of dry nitrogen. The reaction mixture was cooled to 0 °C and quenched by addition of water. After low-boiling substances were removed by rotary evaporation, the two-phase solution was heated at reflux for 0.5 h to hydrolyze residual benzoyl chloride. The resulting mixture was extracted with ether, and the ethereal extracts were washed with 1 M NaOH, dried ($MgSO_4$), and filtered. Benzophenone-d_5, mp 47–49 °C, was isolated in 66% yield following removal of solvent.

The benzophenone-d_5 was transformed to diphenyldiazomethane-d_5 by the published procedure,[15] and the diazo compound was added to methyl α-bromoacrylate according to the method described previously,[16] except that the reaction was carried out at 0 °C rather than at reflux. The yield of desired product, mp 105–107 °C (lit.[16] 105–107 °C), was 85%.

Reduction of the ester to the alcohol and transformation to the tosylate were accomplished according to literature methods.[17]

2-(Perdeuteriophenyl)-2-phenyl-1-methylenecyclopropane (7). To a solution of 2-(perdeuteriophenyl)-2-phenyl-1-bromocyclopropanecarbinol tosylate (9.3 g, 26 mmol) in dry THF (100 mL), held at 0 °C and protected from moisture, was added 32 mL (53 mmol) of 1.6 M *n*-BuLi during 5 min. After the mixture was allowed to stir for 1 h, it was quenched by addition of water, salt was added, and the aqueous solution was thoroughly extracted with ether. Drying ($MgSO_4$) of the solution and removal of solvents left 4.5 g of crude product. Column chromatography over neutral alumina with pentane gave 4.0 g (73%) of pure **7**.

***o*-Benzoylbenzoic Acid.** To a stirred mixture of 2-methyl-3-phenylindene-d_x (686 mg, 3.3 mmol) and 25 mL of 0.04 M NaOH was added $KMnO_4$ (2.1 g, 13 mmol). The reaction mixture was stirred for 48 h at ambient temperature, after which excess permanganate was destroyed by addition of ethanol. Celite was added to facilitate the subsequent filtration. The filtrate was extracted once with ether to remove neutral organics, acidified, and further extracted with ether. Drying of the latter ethereal solution followed by removal of solvent afforded 129 mg (50% yield) of crude product. Recrystallization from CCl_4 gave 85 mg of pure acid, mp 125.0–125.5 °C (lit.[18] 127.5–128.5 °C), whose ^1H NMR spectrum matched that published.[19]

Thermal Rearrangements. A 10% solution of 2-(perdeuteriophenyl)-2-phenyl-1-methylenecyclopropane in CCl_4 or hexane was degassed, and the Pyrex ampule containing it was sealed. The ampule was heated at ~141 °C for 40–50 h. The solvent was then removed, and the desired indene was purified by elution from neutral alumina with pentane. The yield of pure indene was 65–80%.

Acknowledgment. The support of this research by the Robert A. Welch Foundation is gratefully noted.

Registry No.—**7,** 69795-95-5; benzophenone-d_5, 2694-78-2; benzene-d_6, 1076-43-3; benzoyl chloride, 98-88-4; diphenyldiazomethane-d_5, 69795-96-6; methyl α-bromoacrylate, 4519-46-4; 2-(perdeuteriophenyl)-2-phenyl-1-bromocyclopropanecarbinol, 69795-97-7; 2-(perdeuteriophenyl)-2-phenyl-1-bromocyclopropanecarbinol tosylate, 69795-98-8; 2-methyl-3-phenylindene-d_x, 69795-99-9; *o*-benzoylbenzoic-d_x acid, 69796-00-5; methyl 2-(perdeuteriophenyl)-2-phenyl-1-bromocyclopropanecarboxylate, 69796-01-6.

References and Notes

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(2) The dispirooctanes **3** and **4** are presumably formed by initial isomerization of **1d** to benzylidenecyclopropane followed by its [2 + 2] dimerization, a process that is well precedented for methylenecyclopropanes.[3] The observation of **5**, whose structure is only tentative at present, is novel, but could be rationalized by way of a [2 + 4] cycloaddition of benzylidenecyclopropane. We thank B. Brock for these results.

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(10) An *inverse* deuterium isotope effect, k_H/k_D, of 0.963 ± 0.008 appears to operate in the cleavage of benzophenone cation radicals to the phenyl radicals and benzoyl carbocations in the mass spectrometer. This value was calculated on the basis of the reasonable assumptions (1) that the sum of the benzoyl-d_5 and benzoyl-d_4 peaks represented the rate constant, k_D, for cleavage of the cation radical to generate the deuterated carbocation, whereas the benzoyl-d_0 peak corresponded to the analogous rate constant, k_H, and (2) that the deuterium isotope effect was the same for cleavage of the d_4 and the d_5 cation radicals. The d_1–d_3 peaks, the sum total of which was 0.9% of the total peak area for benzoyl carbocations, were neglected in the calculation, and all peak heights were corrected for contributions from carbon-13. The observation of an inverse isotope effect is consistent with the greater anticipated stability of benzoyl-d_5 carbocations relative to the undeuterated species, an expectation that is based on the inverse isotope effect noted in the solvolysis of ring-deuterated benzhydryl chloride.[11]

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Hexakis[μ-(ethyl chlorocarbamato-*N*,*O*)]-μ_4-oxo-tetrazinc and Its Thermolysis in Simple Olefins

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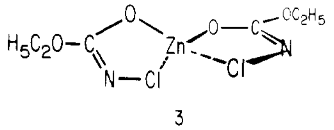
This report describes a new tetranuclear zinc compound, hexakis[μ-(ethyl chlorocarbamato-*N*,*O*)]-μ_4-oxo-tetrazinc, and its thermal decomposition in 2,3-dimethyl-2-butene and cyclohexene. Thermolysis in 2,3-dimethyl-2-butene gives mainly ethyl *N*(2,3-dimethyl-2-butenyl)carbamate, ethyl *N*-[3-(2,3-dimethyl-1-butenyl)]carbamate, five $C_{12}H_{22}$ isomers, and 2,3-dichloro-2,3-dimethylbutane. Studies with isotopically labeled reagents support the intermediacy of 2,3-dimethyl-2-butenyl cation. The cation partitions to products when captured by either olefin or a carbamate donor. Carbethoxynitrene is not an important intermediate. Thermolysis in cyclohexene gives very low yields of analogous products. This reaction does not appear to be general for olefins for reasons that are discussed.

Several well-characterized metal salts of *N*-chlorocarbamates (**1**) have been described.[1] Though they appear to be potential precursors for carboalkoxynitrenes (**2**) (eq 1), none have been reported to react this way.

$$\begin{array}{ll} M(ClNCO_2R) & \rightarrow MCl + NCO_2R \\ \mathbf{1}, M = Na, K, Ag & \qquad\qquad \mathbf{2} \end{array} \qquad (1)$$

However, Swern and Saika[2] obtained trace amounts of azabicyclo[4.1.0]heptane from the thermolysis of **1** (M = Ag, Na; R = C_2H_5) in cyclohexene, suggesting that some carbethoxynitrene might have formed in their experiments.

The original intent of our work was to examine those salts containing metals capable of intramolecular coordination with chlorine, such as the hypothetical ethyl *N*-chlorocarbamatozinc (**3**). Elimination of $ZnCl_2$ might be especially favorable



3

in this case since the zinc–chlorine bond would already be partially formed in the ground state. Moreover, **3** should be more soluble in olefins than the alkali metal and silver salts,

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