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# Scope and Mechanism of the Reaction of Olefins with Anhydrides and Zinc Chloride to Give β,γ-Unsaturated Ketones

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**Abstract:** The synthesis of β,γ-unsaturated ketones from carboxylic acid anhydrides, zinc chloride, and a variety of cyclic and acyclic olefins is found to be effective only for simple anhydrides and olefins. The conversions of 1-methylcyclohexene (**3**) to 6-acetyl-1-methylcyclohexene (**4**) and of methylenecyclohexane (**9**) to 1-cyclohexenylacetone (**10**) are illustrative of the 22 cases included. The observation of a product isotope effect in the absence of a corresponding kinetic isotope effect in the series methylenecyclohexane, methylenecyclohexane-2,2-$d_2$ (**9**-$d_2$), and methylenecyclohexane-2,2,6,6-$d_4$ (**9**-$d_4$) is compelling evidence for a reaction intermediate. Substituent effects are taken to support a carbocationic species and the regiospecificity of the reaction is consistent with intramolecular proton transfer in that intermediate. The value of the series **9**, **9**-$d_2$, and **9**-$d_4$ for distinguishing concerted and stepwise mechanisms for formal ene reactions is noted.

An intriguing aspect of the Friedel–Crafts acylation of olefins is the frequent, and sometimes exclusive, formation of β,γ-unsaturated ketonic products.[1] In fact, it often is found that the accompanying, and generally more stable, α,β-unsaturated ketones are produced by isomerization of the initially formed unconjugated isomer. Mechanistic postulates for the reaction have ranged from early suggestions of a carbonium ion intermediate[2-4] (**1**) to a more recent emphasis on a concerted process[5] (**2**).

The acylation of an olefin is conveniently carried out by reaction in acetic anhydride with zinc chloride catalyst. A seminal discovery was the report of Deno and Chafetz that the
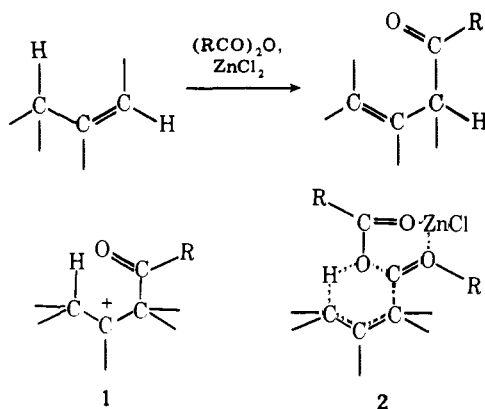
reaction of 1-methylcyclohexene (**3**) gives exclusively 6-acetyl-1-methylcyclohexene (**4**).[2] Further work has shown that **4** and related $\beta,\gamma$-unsaturated ketones from di- and trisubstituted medium ring carbocyclic olefins can be produced in 90% yields and that additions to 1-methyl-4-alkylcyclohexenes give predominantly the $\beta,\gamma$-unsaturated ketone formed by addition trans to the substituent.[3,5] While the reaction can be extended to acyclic olefins, it is usually most successful with acetic anhydride and 1-substituted cyclohexenyl and cyclopentenyl systems.[3,6]
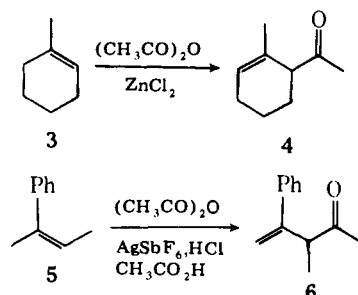


Our attention was drawn to this reaction by the conversion of **5** to **6** under acidic conditions encountered in the course of a different study.[7] We subsequently found those conditions to be suitable for the acylation of olefins to $\beta,\gamma$-unsaturated ketones; the conversion of **3** to **4** could be achieved in >95% yield.[8] However, the relative convenience, cost, and milder conditions of the acetic anhydride–zinc chloride acylation of olefins suggested that investigation of the latter processes would be more useful. We now wish to report a survey of the scope of that reaction and evidence which distinguishes between the concerted and stepwise processes. We provide definitive evidence for a stepwise mechanism and suggest that the regiospecificity of the reaction is determined by the energetically most favorable intramolecular proton transfer in a carbocationic intermediate.

## Results and Discussion

**Reactants and Products.** Acylations of olefins were carried out at ambient temperature with zinc chloride in acetic anhydride or with acetic anhydride, propionic anhydride, or butyric anhydride in a solvent to give the $\beta,\gamma$-unsaturated ketones in the yields given in Table 1. The reaction proceeds with yields of >90% for cyclopentene and cyclohexene derivatives which have at least one disubstituted carbon. Thus the 1-alkyl- and 1-arylcyclohexenes, the 1-alkylcyclopentenes, 1,6-dimethylcyclohexane, methylenecyclohexane, ethylidenecyclohexane, and ethylidenecyclopentane generally give high yields of a single $\beta,\gamma$-unsaturated ketone. The tetrasubstituted double bond of 1,2-dimethylcyclohexene also undergoes smooth reaction to give a quaternary carbon at the position of acylation.

Suitable solvents are methylene chloride, chloroform, carbon tetrachloride, chlorobenzene, bromobenzene, carbon disulfide, or nitromethane. The reaction does not proceed in acetonitrile, tetrahydrofuran, or dimethylformamide. The products were characterized by $^1$H NMR, IR, and MS methods. The yields in Table I were determined by GLC but comparable amounts could be isolated in the cases investigated. If the reactions are allowed to proceed for longer times or at higher temperatures, isomerization to the $\alpha,\beta$-unsaturated ketone is observed. 1-Cyclohexenylacetonitrile and ($E$)-3-hexene are unreactive while $\beta$-pinene and (1-cyclohexenylmethyl)trimethylsilane lead to tars. Reaction of **3** with acetic–formic anhydride gives **4** in ca. 90% yield, while reaction of **3** with trimethylacetic, chloroacetic, trifluoroacetic, benzoic, succinic, and 1,2-cyclohexenecarboxylic anhydrides does not give the desired unsaturated ketones.

It has been reported that 1-ethylcyclohexene (**11**) undergoes reaction with acetic anhydride and zinc chloride to give 2-acetyl-1-ethylidenecyclohexane (**19**), in addition to 6-acetyl-1-ethylcyclohexene (**12**).[3] Similarly the reaction of 1-ethylcyclopentene (**15**) is reported to give 2-acetyl-1-ethylidenecyclopentane (**20**) along with 6-acetyl-1-ethylcyclopentene (**16**).[3] However, as Table I shows, we find **11** and **15** to give only **12** and **16**, respectively, in high yield. By repeating the earlier work we have found that the materials assigned structures **19** and **20**, in fact, are 3-(1-cyclohexenyl)-2-butanone



**19**, $n = 2$
**20**, $n = 1$
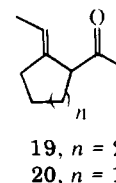
(**14**) and 3-(1-cyclopentenyl)-2-butanone (**18**). That these products are obtained from 1-ethylidenecyclohexane (**13**) and 1-ethylidenecyclopentane (**17**), which are logical impurities in 1-ethylcyclohexene and 1-ethylcyclopentene, was confirmed by the NMR spectra of the olefins. Independent reactions of pure **13** and **17** confirmed the conversions of these olefins to only **14** and **18**, respectively. The present work then shows the reactions of **11** and **15** in fact to be regiospecific. The difficulties in the earlier work are understandable as we were unable to achieve even analytical separation of the olefinic mixtures by GLC.

Reaction of 1-methylcyclooctene with acetic anhydride and zinc chloride gives a mixture of the two possible $\beta,\gamma$-unsaturated ketones which could result directly from the olefin, 2-acetyl-1-methylenecyclooctane and 8-acetyl-1-methylcyclooctene, as well as 1-cyclooctenylacetone. That the latter could arise by isomerization of the starting olefin under the reaction conditions prior to acylation is confirmed by NMR analyses of an incomplete reaction which shows signals attributable to 1-methylenecyclooctane. A similar mixture of $\beta,\gamma$-unsaturated ketonic products is produced from a 10:1 mixture of 1-methylcycloheptene and 1-methylenecycloheptane. Again it appears the reaction may be regiospecific and that the isomers are produced by isomerization of the starting material.

The last four entries in Table I summarize the reactions of acyclic olefins. While 2-ethyl-1-butene gives a 90% yield of ($Z$)- and ($E$)-4-ethyl-4-hexen-2-one in 7:3 ratio, 2-methyl-2-butene gives a 38% yield of 3,4-dimethyl-4-penten-2-one. We also find that 2-ethyl-1-butene provides 4-ethyl-4-hexen-2-one in a $Z:E$ ratio of 3:2 on reaction with acetylium hexafluoroantimonate under the conditions of Hoffmann.[9] Submission of the latter mixture of isomers to the former conditions does not cause any change in the $Z:E$ ratio. Apparently the products from the acetic anhydride reaction are determined by kinetic control. The $\beta,\gamma$-unsaturated ketones from ($Z$)-3-hexene and 1-hexene and acetic anhydride and zinc chloride

**Table 1.** Reactions of Olefins with Acetic Anhydride and Zinc Chloride at 25 °C for 12 h

| olefin | product | yield,[a] % | olefin | product | yield,[a] |
|---|---|---|---|---|---|
| **3** | **4** | 90 | **13** | **14** | 95 |
| (D-labeled) | **8**[d] | 90 | **15** R = CH$_3$ | **16** R = CH$_3$ | 90[g] |
| | | | R = C$_2$H$_5$ | R = C$_2$H$_5$ | 80 |
| **7** | | | **17** | **18** | 95 |
| | Ar = C$_6$H$_5$ | 90 | | | 100[h] |
| | Ar = C$_6$D$_5$ | 90 | **10 : 1** | | |
| | Ar[b] = p-CH$_3$OC$_6$H$_4$ | 90 | | | |
| | Ar = p-BrC$_6$H$_4$ | 90 | | | |
| | Ar = p-CH$_3$C$_6$H$_4$ | 90 | | | 90[h] |
| | Ar[c] = p-FC$_6$H$_4$ | 30 | | | |
| | R[e] = CH$_2$CH$_3$ | 90 | | | |
| | R[f] = (CH$_2$)$_2$CH$_3$ | 90 | | | 90[i] |
| | | 80 | | | |
| | | 80 | | | 38 |
| **9** | **10** | 95 | | | 30 |
| **11** | **12** | 95 | | | 10[j] |

[a] GLC. [b] 2 h. [c] 72 h. [d] Material tentatively identified as 2-aryl-2-cyclohexenyl acetate is found in less than 5% yields in some reactions. [e] Reactant is propionic anhydride. [f] Reactant is butyric anhydride. [g] 5 h at 10–15°C. [h] The ratio is 4:3:3 in the order shown above. [i] The *Z:E* ratio is 7:3. [j] The material is a mixture of geometrical isomers.

are obtained in yields of 10 and 30%, respectively. While the latter yield is ten times that previously reported[5] for these reactants, it is still about half that obtained by Smit et al. from acetylium salts and 1 olefins and the product under both conditions does contain small amounts of α,β-unsaturated isomer.[10] In general the reaction of olefins with alkyl anhydrides–zinc chloride to give β,γ-unsaturated ketones appears to be more selective and convenient than the alternatives, although this advantage may be offset for some cases by a more limited scope.

**Mechanism.** The exclusive formation of β,γ-unsaturated ketones in the acylations of olefins by acetic anhydride–zinc chloride has led to the recent proposal of Dubois et al. of transition state **2** in which electrophilic attack of an acetic anhydride–zinc chloride complex on the double bond is concerted with breakage of the γ-carbon–hydrogen bond.[4] Such a mechanism is symmetry allowed and analogous to the ene reaction suggested by Hoffmann and Tsushima for the reaction of acetylium ions with olefins.[9] On the other hand, many earlier proposals for the acylation of olefins under similar conditions have been convincingly formulated in terms of a carbonium

intermediate **1** on the basis of product and rate studies.[1,2,3,6,10] In the case of the reaction of cyclohexenes with acetic anhydride and zinc chloride, Groves and Jones have suggested that an intermediate produced by axial addition of the acetylium electrophile provides a cation which undergoes stereoelectronically controlled loss of the γ proton.[3]

Clearly the question of the existence of an intermediate on the pathway must be settled if the origin of the regioselectivity in this reaction is to be understood. We have carried out studies of substituent and isotope effects to settle that issue.

The reactions of the 1-arylcyclohexenes provide an indication that the reaction can involve an intermediate. Although we find the conversions of 1-arylcyclohexenes with acetic anhydride–zinc chloride to 1-aryl-6-acetylcyclohexenes are not kinetically well behaved, the order of substituent reactivities of *p*-methoxy > *p*-methyl > *p*-fluoro > *p*-hydrogen > *p*-trifluoromethyl, as suggested by the reaction times in Table 11 and subsequently measured, is consistent with an intermediate which has substantial positive charge at the benzylic position.[11,12] A lack of a significant kinetic isotope effect for the reaction of 1-phenyl-2,6,6-trideuteriocyclohexene also can be

**Scheme I**



$(k_H/k_D)_3 = 1.0 \pm 0.3$



$(k_H/k_D)_9 = 1.0 \pm 0.3$
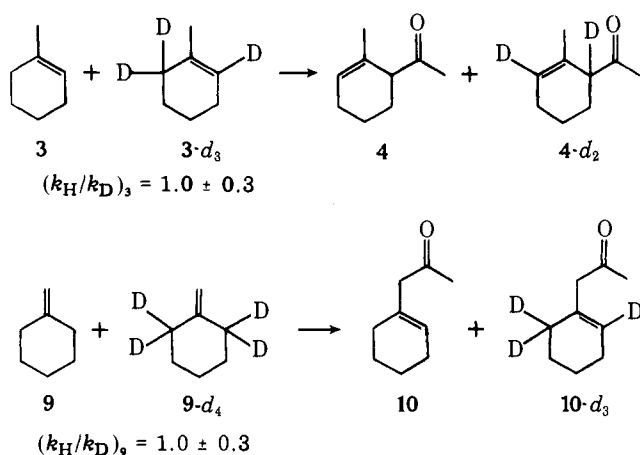
used to argue against a concerted process in the aryl cases.[12]

In order to definitively decide whether the reactions of alkyl-substituted cyclohexenes, as illustrated by the conversions of **3** to **4** and **9** to **10**, proceed by a stepwise process we have investigated kinetic and product isotope effects.

The essential kinetic comparisons are the relative rates of reaction of **3-3-$d_3$** and **9-9-$d_4$** to give **4-4-$d_2$** and **10-10-$d_3$**, respectively, as shown in Scheme I. Mixtures of the labeled and unlabeled materials, **3-3-$d_3$** and **9-9-$d_4$**, were allowed to react with acetic anhydride. The resulting kinetic isotope effects determined both from the rates of disappearance of the reactants and the rates of appearance of the products are $(k_H/k_D)_3$ = 1.0 ± 0.3 and $(k_H/k_D)_9$ = 1.0 ± 0.3. Clearly there is a negligible kinetic isotope effect in these reactions.

This absence of a kinetic isotope effect implies a lack of carbon–hydrogen bond breaking in the rate-determining step. While that result could be taken to support the existence of a reaction intermediate, the possibility of a highly unsymmetrical bond breaking in a concerted process cannot be rigorously excluded. The symmetry of **9** provides an opportunity to obtain definitive evidence on that point. The essential information can be obtained by determination of the product isotope effect for the reaction of 2,2-dideuteriomethylenecyclohexane (**9-$d_2$**) as shown in Scheme II. The ratio of the products, **10-$d_1$** and **10-$d_2$**, from **9-$d_2$** provides a measure of the isotope effect for $\gamma$-carbon–hydrogen bond cleavage regardless of whether or not this reaction occurs in the rate-determining step. If the low isotope effect is due to unsymmetrical carbon–hydrogen bond breaking in the rate-determining step, the ratios of **10-$d_1$** and **10-$d_2$** should be the same as the kinetic isotope effect. On the other hand, if the low kinetic isotope effect reflects a two-step reaction and the loss of the $\gamma$ hydrogen occurs in a second step, the product isotope effect obtained from the ratio of **10-$d_1$** and **10-$d_2$** will be different from the kinetic isotope effect.[13]

Reaction of **9-$d_2$** gives a mixture of unequal amounts of **10-$d_1$** and **10-$d_2$**. If the intensities of the molecular ion fragments are used to estimate the ratio of **10-$d_1$** and **10-$d_2$**, a product isotope effect of 2.8 ± 0.5 is obtained. If consideration

**Scheme II**



$10\text{-}d_2/10\text{-}d_1 = 3.2 \pm 0.7$
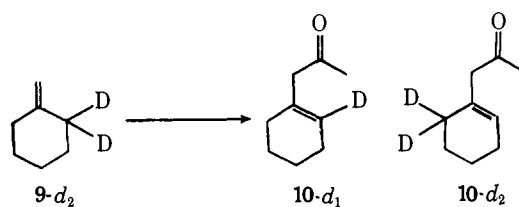
**Table II.** Reaction of Substituted 1-Arylcyclohexenes with Acetic Anhydride and $ZnCl_2$ to Give 1-Aryl-6-acetylcyclohexenes

| starting olefin Ar | reaction time, s | % composition[a] | | log $(k_X/k_H)$[b] |
|---|---|---|---|---|
| | | olefin | product | |
| $p\text{-}CH_3O\text{-}C_6H_4$ | 780 | 35.9 ± 4.9 | 53.8 ± 5.5 | 0.72 + 0.08 |
| $p\text{-}CH_3C_6H_4$ | 2360 | 13.2 ± 3 | 82.5 ± 3 | 0.53 ± 0.07 |
| $p\text{-}FC_6H_4$ | 2360 | 51.9 ± 0.5 | 32.7 ± 1.1 | 0.043 ± 0.03 |
| $p\text{-}C_6H_5$ | 4200 | 34.8 ± 1.7 | 56.1 ± 2.1 | 0.0 |
| $p\text{-}CF_3C_6H_4$ | 251 920 | 51.6 ± 1.4 | 37.6 ± 1.4 | −0.98 ± 0.04 |
| $C_6H_5$[c] | 4105 | 59.7 ± 2.7 | 59.7 ± 2.7 | 0.0 |
| | 10 850 | 27.2 ± 4.4 | 72.8 ± 4.4 | |

[a] Error limits are one standard deviation. [b] Error limits in $k_X/k_H$ result from the use of the entire range of % composition instead of the mean value; $k_X/k_H$ calculated using percentage of olefin remaining after the reaction is quenched. [c] 1-Phenyl-2,6,6-trideuterio-cyclohexene.
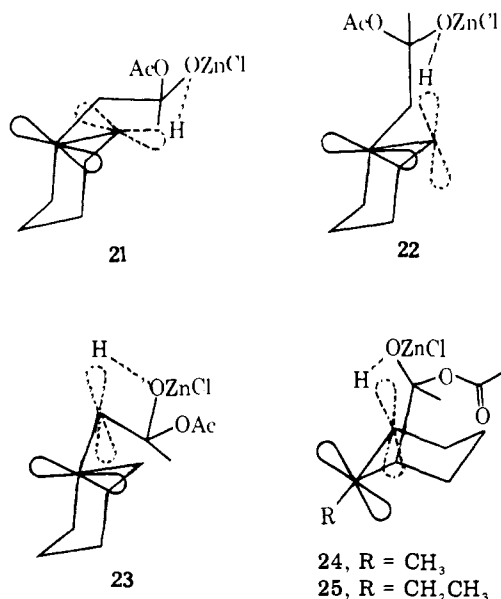
**Scheme III**
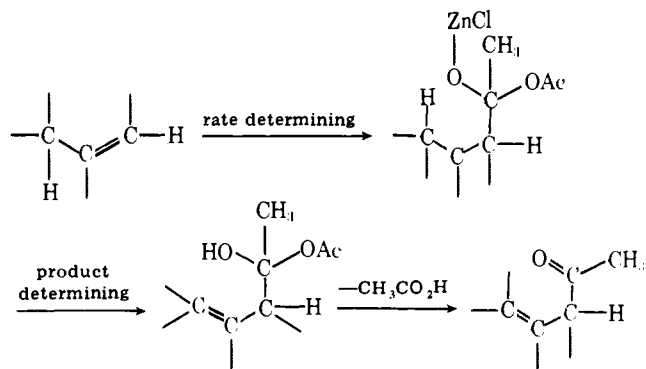


is given to the lack of quantitative labeling in the olefin **9-$d_2$** and the above value of 2.8 is used to estimate the product isotope effect for the impurities **9-$d_1$** and **9-$d_3$** present in the starting material, a product isotope effect of 3.2 ± 0.7 is calculated. This value is close to the isotope effect attributed to the ene reaction.[14] Regardless of the exact value the observation of a product isotope effect in the absence of a kinetic isotope effect for the conversion of **9** to **10** is unambiguous evidence for the presence of an intermediate on the reaction pathway.

If that intermediate is considered to be a carbocationic species, a generalized reaction for the formation of $\beta,\gamma$-unsaturated ketones from olefins with acetic anhydride–zinc chloride can be drawn as shown in Scheme III. The irreversible rate-determining step involves electrophilic attack on the olefin by the acetic anhydride–zinc chloride complex to give an intermediate. The product-determining loss of a $\gamma$ proton from the intermediate is envisioned as an intramolecular process. While the rate-determining step is not subject to a significant deuterium isotope effect, the product-determining step involves carbon–hydrogen bond breaking and is subject to the expected partitioning.

The key to understanding the exclusive formation of $\beta,\gamma$-unsaturated ketones in this reaction lies in analysis of the product-determining paths available to the reaction intermediate.[15] If breakage of the $\gamma$-carbon–hydrogen bond is considered to be an intramolecular process, the results in Table I can be readily rationalized. For example, for the reaction of **9** with acetic anhydride–zinc chloride the proposed intermediate may be seen to have a transition state for $\gamma$-proton loss which can be represented as **21**.[16]

In **21** the stereoelectronically controlled removal of an axial $\gamma$ hydrogen as shown is clearly preferred over the transition states which would be required for removal of an equatorial $\gamma$ hydrogen, shown as **22**, or an $\alpha$ hydrogen, shown as **23**. In

21                    22



23                    24, R = CH₃
                      25, R = CH₂CH₃

**Scheme IV**



9-*d*₂

a, NBS (42%); b, *t*-BuOH, *t*-BuOK (60%); c, BH₃S(CH₃)₂ (70%); d, TsCl (80%); e, collidine, 100°C (50%).

the latter cases achievement of proper orbital alignment would require substantial twisting from the structure depicted.

The reaction of **3** and other 1-substituted cyclohexenes can be envisioned to involve similar intramolecular proton transfers. For example, **24** would be formed from **3**. In fact the structure for **24** is similar to the earlier proposal of Groves and Jones[3] except that the determining factor in proton loss is the relative energies of the respective transition states for proton loss rather than the stereochemistry of the initial addition. In accord with the regiospecific reaction of **11** the transition state represented by **25** appears to have less encumbrance than do alternatives in which a proton would be removed from the methylene of that ethyl group. On the other hand, the *Z*/*E* product ratio from 2-ethyl-1-butene cannot be readily rationalized in similar terms; presumably the transition state for proton removal in this case has less conformational restrictions than for the cyclic olefinic systems.

## Summary

The reaction of olefins with alkyl anhydrides and zinc chloride to give a β,γ-unsaturated ketone is synthetically useful for disubstituted and higher olefins. On the basis of divergent kinetic and product isotope effects, the mechanism of the reaction must involve at least two steps. The regiochemistry and substituent effects may be understood by rate-determining electrophilic attack to give a carbocationic intermediate which undergoes intramolecular transfer of a γ hydrogen under stereoelectronic control. It is interesting that this reaction, which has been recently formulated as a concerted process which would be symmetry allowed, in fact proceeds by a stepwise mechanism. It is also noted that the series **9**, **9**-*d*₂, and **9**-*d*₄ provides a useful test of mechanism for formal ene reactions in which stepwise and concerted processes are possible.[13]

## Experimental Section[17]

**Materials.** Commercially available olefins, analyzed by gas–liquid phase chromatography (GLC) and NMR, were used. Olefins used for deuterium isotope effect studies and kinetic studies were purified by GLC, spinning-band column distillation, or medium-pressure liquid chromatography (MPLC). Acetic anhydride was heated to reflux over P₂O₅ for 2 days, then distilled under dry N₂. Zinc chloride (ZnCl₂) was ground to a fine powder under dry N₂, heated to 210 °C at less than 0.05 Torr for 5 days, ground to a fine powder under dry N₂, and stored in an air-tight container in the dry N₂ atmosphere of a glovebag. Solvents were dried by standard procedures prior to use. Air- or moisture-sensitive reactions were conducted under an N₂ atmosphere in glassware which had been oven dried.
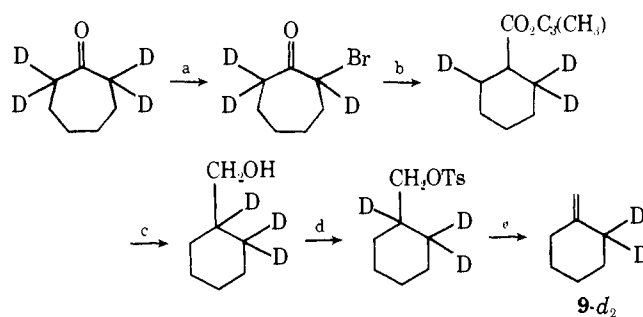
**Gas–Liquid Phase Chromatography (GLC).** Preparative GLC separations were carried out with a ¹⁄₂ in. by 10 ft copper column packed with 26% Carbowax 20M or 20% FFAP on 60/80 mesh Chromosorb. For analytical GLC 20% Carbowax 20M, SE-20, 15% Dow 710 and 5% Bentone mixture, 15% FFAP, 5% DEGS, and 5% QF1 mixture, 15% XF 1150, and 10% OV17 were used.

**Determination of Yields.** Determinations of yields of β,γ-unsaturated ketone products were carried out by GLC and NMR with chlorobenzene as an internal standard. In some cases *n*-propyl benzoate was used as the internal standard for GLC. In cases where material was isolated by evaporation of the pentane extracts, the yields were comparable to GLC yields unless otherwise noted. The yields reported are corrected for unreacted olefin, which is less than 5% except as noted. Yields determined by NMR are for only the β,γ-unsaturated ketone products and do not include any α,β isomer which may be observed. The IR spectra of the crude reactions were used for detection of the presence of α,β-unsaturated ketone isomers.

**Isotopic Ratios.** The quantitative analysis of deuterated olefins and ketones was carried out by examination of the molecular ion peaks obtained by field ionization mass spectrometry (FIMS). The method was established, by use of standard mixtures, to give reproducible and accurate results within the indicated error limits of one standard deviation. Almost no M − 1 or other fragmentation peaks are observed with this analysis, which was carried out on both purified olefin and crude reaction mixtures.

The pattern for the protio isomer was used to establish the natural distribution of the heavy-atom isotopes for dissection of the observed molecular ions into the actual distribution of deuterio species which are reported herein.[12] Analysis of the kinetic and product isotope effects was carried out on reactions which were quenched at between 20 and 72% conversion, as determined by GLC, by the application of eq 1 and 2 to the FIMS data.

$$\text{isotope effect in the olefin} = k_H/k_D = \frac{\log\,(a_H a^0{}_H)}{\log\,(a_D/a^0{}_D)} \quad (1)$$

$$\text{isotope effect in the ketone} = k_H/k_D = \frac{\log\,(1 - b_H/a^0{}_H)}{\log\,(1 - b_D/b^0{}_D)} \quad (2)$$

where $a^0$ = initial olefin concentration, $a$ = final olefin concentration, and $b$ = final ketone concentration. In the analyses of isotope effects on ketone formation account is taken of the actual deuterium content of the starting olefin. In all cases, however, the results obtained with this correction are within experimental error of those obtained by simple direct analysis.[12]

**Preparation of Substituted 1-Phenylcyclohexenes.** Aryllithiums and arylmagnesium bromides were allowed to react with cyclohexanone to produce substituted 1-phenyl-1-cyclohexanols. After chromatography, the alcohols were dehydrated by heating in benzene at reflux with a catalytic amount of *p*-toluenesulfonic acid and azeotropic distillation of the water formed. With the exception of deuterio compounds the olefins prepared are known compounds. The NMR, UV, and MS spectral data are consistent with the assigned structures.

**1-Phenyl-2,6,6-trideuteriocyclohexene:** NMR (CCl₄) δ 7.17 (5 H, m, aromatic), 2.13 (2 H, t, *J* = 1 Hz, CH₂C=C), 1.70 (4 H, m, aromatic); MS (70 eV) *m/e* 161 (M⁺).

**1-Methyl-2,6,6-trideuteriocyclohexene.** Olefin 3-*d*₃ was prepared by the method of Kinstle and Stark[18] and purified by preparative GLC on a 10 ft by ¹⁄₄ in. copper column on Carbowax 20M. The compound

was found to be >95% trideuterated by NMR analysis of the integrations of the vinyl and aliphatic regions. MS analysis indicated ca. 87% $m/e$ 99 ($C_7D_3H_9$), 10% $m/e$ 98 ($C_7D_2H_{10}$), 2% $m/e$ 97 ($C_7D_1H_{11}$).

**1-Methylene-2,2,6,6-tetradeuteriocyclohexane.** Olefin 9-$d_4$ was prepared from 2,2,6,6-tetradeuteriocyclohexanone by reaction with the ylide generated from equal molar amounts of triphenylmethylphosphonium bromide and *n*-butyllithium according to the procedure of Atkinson et al.[18,19] The olefin was purified by distillation through a spinning-band column, bp 102–103 °C. NMR analysis indicated >95% tetradeuteration by integration of the vinyl and aliphatic regions. MS analysis indicated ca. 95% $m/e$ 100 ($C_7D_4H_8$), 4% $m/e$ 99 ($C_7D_3H_9$).

**2,2,7,7-Tetradeuteriocycloheptanone.** The ketone was prepared according to the procedure of Kinstle and Stark for tetradeuteriocyclohexanone but with cyclohepanone as the starting material.[18] NMR analysis indicated >95% tetradeuteration, ^{1}H NMR ($CDCl_3$) $\delta$ 1.70 (s). MS analysis indicated 94.6% $m/e$ 112 ($C_7D_4H_8O$), 5.4% $m/e$ 111 ($C_7D_3H_9O$). Assignments for the ^{13}C NMR were made based on comparisons with reported values for similar compounds:[20] ^{13}C NMR cycloheptanone ($CDCl_3$) chemical shift (intensity) $\delta$ 214.9 (584, C=O), 43.8 (7852, $C_{2,7}$), 30.5 (8250, $C_{3,6}$), 24.4 (8604, $C_{4,5}$); 2,2,7,7-tetradeuteriocycloheptanone ($CDCl_3$) $\delta$ 214.8 (300, C=O), 43.8 (300–900, 30.4 (8082, $C_{3,6}$), 24.3 (8212, $C_{4,5}$).

**2,2-Dideuteriomethylenecyclohexane** was prepared as outlined in Scheme IV.

**2-Bromo-2,7,7-trideuteriocycloheptanone.** Freshly distilled cycloheptanone-$d_4$ and *N*-bromosuccinimide provided the bromo ketone in 42% yield according to the procedure of Corey.[21] NMR analysis shows absences of the $\alpha$ proton ($\delta$ 4.37, double doublet, CHBr) observed in protio material. ^{13}C NMR 2-bromocycloheptanone ($CDCl_3$): $\delta$ 206 (2877, C=O), 53.8 (9218, $C_2$), 39.4 (9801, $C_7$), 34.3 (9661, $C_3$), 29.6 (9500, $C_6$), 26.8 (9304, $C_4$), 25.0 (9450, $C_5$). ^{13}C NMR 2-bromo-2,7,7-trideuteriocycloheptanone ($CDCl_3$): $\delta$ 205.6 (397, C=O), 53.9 (600–1200, m, $C_2$), 39.5 (400, m, $C_7$), 34.1 (6630, $C_3$), 29.5 (6087, $C_6$), 26.8 (6960, $C_4$), 24.8 (5981, $C_5$).

**1,2,2-Trideuterio-*tert*-butyl Cyclohexanecarboxylate.** To dry, distilled *tert*-butyl alcohol-*O-d* (17 g, 226 mmol) was added clean K (3.9 g, 99.7 mmol) under a dry $N_2$ atmosphere. The mixture was stirred and heated until all K was consumed, 150 mL of dry THF was added, the reaction mixture was cooled to 0°C, and bromo ketone (10.2 g, 52.8 mmol) in 15 mL of dry THF was added with rapid stirring over a 5-min period. The mixture was allowed to slowly warm with stirring to room temperature over a period of 10 h. The solution was poured into 200 mL of saturated NaHCO₃, the organic layer separated, and the reaction mixture worked up by extraction with diethyl ether. The residue remaining after concentration at reduced pressure was used for GLC purification, which gave the product in ca. 60% yield. ^{13}C NMR *tert*-butyl cyclohexanecarboxylate[22] ($CDCl_3$): $\delta$ 175.5 (719, C=O), 60.0 (460, $CMe_3$), 44.2 (2554, $C_1$), 29.15 (4739, $C_{2,6}$), 28.1 (7734, $CMe_3$), 25.9 (3955, $C_4$), 25.5 (5265, $C_{3,5}$). ^{13}C NMR 1,2,2-trideuterio-*tert*-butyl cyclohexanecarboxylate ($CDCl_3$): $\delta$ 175.6 (368, C=O), 60 (451, $CMe_3$) 44.0 (140–330, m, $C_1$), 29.0 (1300, m, $C_2$, $C_{2,6}$), 28.1 (6805, $CMe_3$), 25.9 (1885, $C_4$), 25.3 (2918, $C_{3,5}$).

**(1,2,2-Trideuteriocyclohexane)methanol.** To 1,2,2-trideuterio-*tert*-butyl cyclohexanecarboxylate (3.0 g, 17.5 mmol) and 150 mL of dry THF at room temperature was added an excess of $BH_3\cdot Me_2S$ (5.2 mL, 10 M, 52 mmol) with stirring. Stirring was continued for 18 h, and $H_2O$ was added, followed by $K_2CO_3$ until the water layer separated. Extractive workup with diethyl ether gave material which was purified by GLC to yield 1.3 g of alcohol, ca. 70% yield. ^{13}C NMR cyclohexanemethanol ($CDCl_3$): $\delta$ 68.4 (4491, COH), 40.6 (3508, $C_1$), 29.8 (7346, $C_{2,6}$), 26.8 (4015, $C_4$), 26.0 (8215, $C_{3,5}$). ^{13}C NMR (1,2,2-trideuteriocyclohexane)methanol ($CDCl_3$): $\delta$ 68.5 (5641, COH), 40.0 (ca. 300, m, $C_1$), 29.5 (5295, $C_{2,6}$), 26.6 (6777, $C_4$), 25.9 (9696, $C_{3,5}$).

**(1,2,2-Trideuteriocyclohexyl)carbinyl Tosylate.** The method of Wilcox and Chibber was used to prepare the trideuterated tosylate.[23] Purification by medium-pressure liquid chromatography (MPLC) using a 1 m by 3 cm silica gel column and 6% ethyl acetate in $CCl_4$ as elution solvent gave 80% of the tosylate, mp 30–32 °C (lit. protio isomer 31–33 °C).[23] MS analysis (10 eV) indicated $m/e$ 271 parent ion ($M^+$). ^{13}C NMR cyclohexanemethanol ($CDCl_3$): $\delta$ 144.7 (2493, aromatic), 133.5 (1801, aromatic), 129.9 (10 284, aromatic), 127.8 (10 288, aromatic), 75.3 (5236, $COSO_2$), 37.3 (4498, $C_1$), 29.1 (8580,

$C_{2,6}$), 26.1 (4404, $C_4$), 25.4 (8455, $C_{3,5}$), 21.51 (2995, *p*-CH₃). ^{13}C NMR (1,2,2-trideuteriocyclohexyl)carbinyl tosylate ($CDCl_3$): $\delta$ 144.6 (437, aromatic), 133.4 (200, aromatic), 129.8 (3334, aromatic), 127.9 (3200, aromatic), 75.2 (1287, $COSO_2$), 37.0 (ca. 350, m, $C_1$), 28.9 (2154, $C_{2,6}$), 26.1 (1244, $C_4$), 25.4 (1525, $C_{3,5}$), 21.6 (935, *p*-CH₃).

**2,2-Dideuteriomethylenecyclohexane** (9-$d_2$). (1,2,2-Trideuteriocyclohexyl)carbonyl tosylate (0.70 g) and 30 mL of dry collidine were heated for 3 h at 110 °C under a $N_2$ atmosphere. The collidine–olefin mixture was distilled under reduced pressure at ca. 100°C and 15–20-mL portions of distillate were collected. After addition of 10 mL $CH_2Cl_2$, 2 mL of $CDCl_3$, and 2 mL of $CCl_4$ to each portion, these solutions were washed with ice-cold 10% aqueous HCl until no collidine remained as determined by NMR. The organic layer was dried ($Na_2SO_4$) and concentrated by distillation of the solvents. The deuteriochloroform–carbon tetrachloride solution containing 9-$d_2$ was used without further purification in subsequent studies. A 50% yield of olefin was estimated by ^{1}H NMR by comparison with standard solutions of protio olefin.

NMR analysis indicated that no isomeric olefin was detectable in the solution of olefin. NMR 2,2-dideuteriomethylenecyclohexane ($CCl_4$): $\delta$ 4.50 (s, ca. 2 H, $CH_2$=C), 2.06 (m, ca. 2 H, $CH_2C$=$CH_2$), 1.52 (m, 6 H, aliphatic protons). ^{13}C NMR methylenecyclohexane ($CDCl_3$): $\delta$ 150.1 (795, $C_1$), 106.5 (2877, $C_7$), 35.4 (6075, $C_{2,6}$), 28.3 (5936, $C_{3,5}$), 26.4 (3364, $C_4$). ^{13}C NMR 2,2-dideuteriomethylenecyclohexane ($CDCl_3$ and $CCl_4$, dilute sample): $\delta$ 106.4 (100, $C_7$), 35.3 (140, position deuterated, $C_{2,6}$), 28.2 (330, $C_{3,5}$), 256.2 (180, $C_4$). FIMS analysis of olefin indicated 5.8% $m/e$ 96 ($C_7H_{12}$), 5.8% $m/e$ 97 ($C_7DH_{11}$), 71.9% $m/e$ 98 ($C_7D_2H_{10}$), 15.7% $m/e$ 99 ($C_7D_3H_9$), 0.8% $m/e$ 100 ($C_7D_4H_8$). High-resolution mass spectral analysis indicated the formula for $m/e$ 98 as $C_7D_2H_{10}$ and for $m/e$ 99 as $C_7D_3H_9$.

**General Procedures for the Conversion of Olefins and Acetic Anhydride and Zinc Chloride to $\beta,\gamma$-Unsaturated Ketones. Method A.** Under an $N_2$ atmosphere, dry zinc chloride ($ZnCl_2$, 0.11 g, 0.80 mmol) was added with stirring to a mixture of olefin (2 mmol) and 20 mL of acetic anhydride over 5 min at ca. 20 °C. A water bath was used to prevent large temperature increases in these exothermic reactions. For products which tended to be converted to $\alpha,\beta$-unsaturated isomers lower temperatures could be used to reduce isomerization; ca. 0 °C was the lowest temperature used. Reaction times varied from 2 to 48 h, but usually were 12 h. After the appropriate reaction time an internal standard, *n*-propyl benzoate or chlorobenzene, 50 mL of pentane, and 50 mL of saturated $Na_2CO_3$ solution were added to the reaction mixture, and the solution was worked up extractively with pentane. The yield was determined by GLC and, after removal of the solvent under reduced pressure, preparative GLC separation provided the $\beta,\gamma$-unsaturated ketone, usually in 90% yield. It should be noted that a small amount of $Na_2CO_3$ stabilizes the $\beta,\gamma$ products in long-term storage. The NMR, IR, and MS of known compounds are consistent with the assigned structures and reported values unless otherwise noted.

**Method B.** In this procedure an aliquot of a homogeneous solution of $ZnCl_2$ in acetic anhydride (4.42 g/100.0 mL, 0.324 mmol/mL) was added to a solution of olefin and solvent. Olefin, anhydride, and $ZnCl_2$ portions were maintained at 2:20:1 in this procedure. Reaction times, temperatures, and workup were the same as in method A.

**Reaction of 1-Methylcyclohexene.** To a stirred heterogeneous mixture of acetic anhydride (20 mL) and $ZnCl_2$ (0.11 g, 0.80 mmol) at room temperature was added 3 (2 mmol). After 3 h the reaction mixture was worked up by preparative GLC to provide 6-acetyl-1-methylcyclohexene (4) in 90% yield.[3] The $\beta,\gamma$-unsaturated olefin could be converted to a 1:4 mixture with 2-acetyl-1-methylcyclohexene by treatment with sodium methoxide in methanol.

**Reaction of 1-Methyl-2,6,6-trideuteriocyclohexene (3-$d_3$).** Method B was used for the reaction of 3-$d_3$; the product obtained in >90% yield as judged by GLC was 6-acetyl-2,6-dideuterio-1-methylcyclohexene (4-$d_2$). The NMR spectrum was identical with that of 4 except for the absence of signals for the vinyl and $\alpha$ protons. MS 6-acetyl-1,2-dideuterio-1-methylcyclohexene (4-$d_2$) (10 eV): $m/e$ (rel intensity), 141 M + 1 (13.55), 140 parent ion ($M^+$) (100), 139 M − 1 (12.1), 98 (14.1), 97 (91.5), 96 (32.1).

**Reaction of 1-Phenylcyclohexene.** Method B was used for the reaction of 1-phenylcyclohexene to provide 6-acetyl-1-phenylcyclohexene in 90% isolated yield and (2-phenyl-2-cyclohexene) acetate in ca. 5% yield. The structure assignment for the latter is based on

NMR and MS data and is provisional.

6-Acetyl-1-phenylcyclohexene: NMR (CCl₄) $\delta$ 7.21 (5 H, m, aromatic), 6.18 (H, double triplet, vinyl), 3.71 (1 H, m, C*H*COCH₃), 2.21 (2 H, m, C*H*₂CH=C), 1.92 (3 H, s, COCH₃), 2.08-1.42 (4 H, m, aliphatic); MS (70 eV) *m/e* (rel intensity) 200 M⁺ (49.3), 158 (19.8), 157 (99.7), 129 (37.5), 115 (30.0), 91 (100.0), 43 (63.2); IR (neat) 1710 cm⁻¹.

Anal. Calcd for C₁₄H₁₆O: C, 83.96; H, 8.05. Found: C, 83.94; H, 8.03.

(2-Phenyl-1-cyclohexene) acetate: NMR (CCl₄) $\delta$ 7.17 (5 H, m, aromatic), 6.13 (1 H, triplet, vinyl), 5.78 (1 H, m, C*H*OOCCH₃), 2.20 (m, C*H*₂CH=C), 1.85 (COCH₃), 2.2-1.4 (m, aliphatic). HRMS analysis indicated C₁₄H₁₆O₂ for *m/e* 216; MS (70 eV) *m/e* 216 M⁺.

**Reactions of Substituted Phenylcyclohexenes.** The reactions were carried out according to method B as indicated.

1-Phenyl-2,6,6-trideuteriocyclohexene was converted, after 16 h at 25 °C, in 90% yield to 6-acetyl-2,6-dideuterio-1-phenylcyclohexene; IR (neat) 1705, 760, 700 cm⁻¹; NMR (CCl₄) $\delta$ 7.16 (5 H, s, aromatic), 2.22 (2 H, t, *J* = 5.4 Hz, C*H*₂CD=C), 1.81 (3 H, s, CH₃CO). 1.8 (4 H, m, aliphatic); MS *m/e* (rel intensity) 202 M⁺ (100), 159 (77.8); UV (CCl₄) λ_max 260 nm.

Anal. Calcd for C₁₄H₁₄D₂O: atom % D, 12.50. Found: atom % D, 12.25.

*p*-(1-Cyclohexenyl)anisole[24] was converted, after 2 h at 25°C, in 90% yield to *p*-(6-acetyl-1-cyclohexenyl)anisole: IR (neat) 1705, 840, 810 cm⁻¹; NMR (CCl₄) $\delta$ 7.05 (2 H, d, *J* = 9 Hz, aromatic), 6.67 (2 H, d, *J* = 9 Hz, aromatic), 5.97 (1 H, double triplet, *J* = 1, 4.5 Hz, vinyl), 3.63 (3 H, s, CH₃O), 3.50 (H, m, C*H*COCH₃), 2.19 (2 H, m, CH₂C=C), 1.82 (3 H, s, CH₃CO), 1.8 (4 H, m, aliphatic); MS (70 eV) *m/e* (rel intensity) 230 M⁺ (100), 188 (20.2), 187 (98.8), 160 (24.1), 121 (87.0), 79 (23.7), 43 (49.2); UV (CCl₄ λ_max 260 nm.

Anal. Calcd for C₁₅H₁₈O₂: C, 78.23; H, 7.88. Found: C, 78.58; H, 8.08.

*p*-Bromo(1-cyclohexenyl)benzene[25] was converted, after 16 h at 25°C, in 90% yield to *p*-(6-acetyl-1-cyclohexenyl)bromobenzene; IR (neat) 1710, 840, 810 cm⁻¹; NMR (CCl₄) $\delta$ 7.30 (2 H, d, *J* = 8 Hz, aromatic), 7.00 (2 H, d, *J* = 8 Hz, aromatic), 6.02 (1 H, t, *J* = 4 Hz, vinyl), 3.48 (1 H, m, C*H*COCH₃), 2.4-1.1 (m, aliphatic), 1.83 (3 H, s, CH₃CO); MS (70 eV) *m/e* (rel intensity) 280 (73.8), 278 M⁺ (76.6), 238 (18.1), 237 (97.9), 236 (26.7), 234 (95.0), 43 (100); UV (CCl₄) λ_max 260 nm.

Anal. Calcd for C₁₄H₁₅BrO: C, 60.23; H, 5.42; Br, 28.62. Found: C, 60.22; H, 5.34; Br, 28.41.

*p*-Fluoro(1-cyclohexenyl)benzene[26] was converted, after 16 h at 25°C, in 90% yield to *p*-(6-acetyl-1-cyclohexenyl)fluorobenzene: IR (neat) 1710, 785, 685 cm⁻¹; NMR (CDCl₃) $\delta$ 7.05 (4 H, m, aromatic), 6.05 (1 H, double triplet, *J* = 1, 4 Hz, vinyl), 3.56 (1 H, m, C*H*COCH₃), 2.2 (m, CH₂C=C), 1.87 (3 H, s, CH₃CO), 1.8 (m, aliphatic); MS (70 eV) *m/e* (rel intensity) 218 M⁺ (29.6), 175 (66.2), 147 (20.1), 123 (25.0), 119 (25.1), 117 (32.3), 109 (80.7), 43 (100); UV (CCl₄) λ_max 260 nm.

Anal. Calcd for C₁₄H₁₅OF: C, 77.04; H, 6.93; F, 8.70. Found: C, 76.84; H, 6.91; F, 8.76.

*p*-(1-Cyclohexenyl)toluene[24] was converted, after 16 h at 25°C, in 90% yield to *p*-(6-acetyl-1-cyclohexenyl)toluene: IR (neat) 1705, 835, 805 cm⁻¹; NMR (CDCl₃) $\delta$ 7.05 (4 H, m, aromatic), 6.05 (1 H, t, *J* = 4 Hz, vinyl), 3.55 (1 H, m, C*H*COCH₃), 2.27 (3 H, s, CH₃PH), 2.2 (2 H, m, CH₂C=C), 1.88 (3 H, s, CH₃CO), 1.7 (m, aliphatic); MS (70 eV) *m/e* (rel intensity) 214 M⁺ (74.4), 172 (22.9), 171 (100), 143 (26.0), 129 (24.7), 105 (99.3), 79 (31.7), 43 (54.7).

Anal. Calcd for C₁₅H₁₈O: C, 84.07; H, 8.47. Found: C, 83.86; H, 8.39.

*p*-(1-Cyclohexenyl)trifluoromethylbenzene[27] was converted, after 3 days at 25°C, in 30% yield to *p*-(6-acetyl-1-cyclohexenyl)trifluoromethylbenzene: IR (neat) 1710 cm⁻¹; NMR (CCl₄) $\delta$ 7.52 (2 H, d, *J* = 9 Hz, aromatic), 7.03 (2 H, d, *J* = 9 Hz, aromatic), 6.24 (1 H, t, *J* = 4 Hz, vinyl), 3.70 (1 H, m, C*H*COCH₃), 2.27 (2 H, m, CH₂C=C), 1.98 (3 H, s, CH₃CO), 1.8 (4 H, m, aliphatic); MS (70 eV) *m/e* (rel intensity) 268 M⁺ (12.8), 225 (26.4), 43 (100); UV (CCl₄) λ_max 260 nm.

Anal. Calcd for C₁₅H₁₅OF₃: C, 67.16; H, 5.64; F, 21.24. Found: C, 66.53; H, 5.64; F, 21.04. HRMS analysis indicated *m/e* 268 (M⁺) to be C₁₅H₁₅OF₃.

Reactions of *m*-(1-cyclohexenyl)cyanobenzene[25] and *p*-(1-cyclohexenyl)benzoic acid[25] for 4 days at 25°C were judged to give less than 5% of the desired products.

**Reaction of 1-Methylcyclohexene with Propionic Anhydride.** Method B was used for the reaction of 1 (1.1 g, 1.4 mL, 17.9 mmol), propionic anhydride (13 g, 100 mmol), and ZnCl₂ (0.70 g, 5.1 mmol) which was allowed to proceed for 20 h at 34 °C. The yield of 6-propionyl-1-methylcyclohexene[28] was 90% as judged by GLC after the usual workup procedure.

**Reaction of 1-Methylcyclohexene with Butyric Anhydride.** Method B was used for the reaction of olefin with butyric anhydride and ZnCl₂. The yield of 6-butyryl-1-methylcyclohexene[28] was 90% as judged by GLC.

**Reaction of 1-Methylcyclohexene with Silver Hexafluoroantimonate, Hydrochloric Acid, and Acetic Acid.** The procedure of Beak and Hovey[8] was used for reaction of olefin 3 (0.74 g, 7.7 mmol), AgSbF₆ (4.0 g, ca. 11 mmol), 10% acetic anhydride, and 86 mL of gaseous HCl in acetic acid (20 mL). The mixture was allowed to stir for 12 h at ambient temperature, then worked up extractively to give 4 in 95% yield.

**Reaction of Methylenecyclohexane.** Methods A and B were used for the reaction of methylenecyclohexane with acetic anhydride and ZnCl₂ at room temperature for 8 h. Workup in the usual manner provided 1-cyclohexenylacetone[29] in 95% yield as judged by GLC and NMR.

**Reaction of 1-Ethylcyclohexene (11).** Methods A and B and the method of Groves and Jones were used for the conversion of 11 to acetyl-1-ethylcyclohexene[3,8] (12) in 95% yield as judged by GLC and NMR.

**Reaction of Ethylidenecyclohexane (13).** Methods A and B and the method of Groves and Jones were used for the conversion of 13 to 3-(1-cyclohexenyl)-2-butanone (14) in 95% yield as judged by GLC. The IR and NMR data for ketone correspond to values reported by Groves and Jones in their assignment to 6-acetyl-1-ethylidenecyclohexane.[3,8] The MS is consistent with the structure 14.

**Reaction of 1,2-Dimethylcyclohexene.** Methods A and B were used for the conversion of 1,2-dimethylcyclohexene to 6-acetyl-1,6-dimethylcyclohexene in 80% yield as judged by GLC. Material obtained from preparative GLC was taken up in pentane and filtered through a short column of silica gel and the solvent removed in vacuo to give pure 6-acetyl-1,6-dimethylcyclohexene: IR (neat) 1705 cm⁻¹; NMR $\delta$ 5.60 (1 H, m, vinyl), 2.09 (3 H, s COCH₃), 1.56 (3 H, m, CH₃C=C), 1.20 (3 H, s, CH₃C), 2.3-1.3 (6 H, m, aliphatic); MS (70 eV) *m/e* (rel intensity) 152 (9.7), 109 (100), 67 (43.5).

Anal. Calcd for C₁₀H₁₆O: C, 78.90; H, 10.59. Found: C, 78.51; H, 10.46.

**Reaction of 1,6-Dimethylcyclohexene.** Methods A and B were used for the conversion of 1,6-dimethylcyclohexene in 80% yield (GLC) to 6-acetyl-1,2-dimethylcyclohexene: IR (neat) 1705 cm⁻¹; NMR (CDCl₃) $\delta$ 3.01 (1 H, m, C*H*COCH₃), 2.15 (3 H, CH₃CO), 1.67 (3 H, s, CH₃C=C), 2.3-1.3 (6 H, m, aliphatic); MS (70 eV) *m/e* (rel intensity) 152 M⁺ (14.4), 109 (100), 67 (39.5).

Anal. Calcd for C₁₀H₁₆O: C, 78.90; H, 10.59. Found: C, 78.51; H, 10.46.

**Reaction of 1-Methylcyclopentene.** Methods A and B were used at 10-15°C for 10 h for the conversion of the olefin to a 10:1 mixture of 5-acetyl-1-methylcyclopentene[30] and 2-acetyl-1-methylcyclopentene[30] in 90% total yield (NMR). If the reaction temperature was held at 0 °C for 5 h, only the $\beta,\gamma$ isomer was detectable by IR analysis of the crude product and this compound was produced in 90% yield (NMR).

**Reaction of 1-Ethylcyclopentene (15).** Methods A and B, and those of Groves and Jones, were used for the conversion of 15 to 5-acetyl-1-ethylcyclopentene (16) in 80% yield (GLC).[3] If the ketone is allowed to stand at room temperature for extended periods, the $\alpha,\beta$ isomer, 2-acetyl-1-ethylcyclopentene, begins to appear as judged by IR.

**Reaction of Ethylidenecyclopentane (17).** Methods A and B, and the method of Groves and Jones, were used for the conversion of 17 to 3-(1-cyclopentenyl)-2-butanone (18) in 95% yield (GLC). IR and MS spectral data for ketone agree with the expected values and those previously assigned to 2-acetylethylidenecyclopentane.[3]

**Reaction of 1-Methylcycloheptene.** Method B was used for the conversion of 1-methylcycloheptene, which contained 10% methylenecycloheptane, to 1-acetyl-2-methylenecycloheptane, 7-acetyl-1-methylcycloheptene, and 1-(cycloheptenyl)acetone in a ratio of 4:3:3, respectively, and 100% yield (NMR). The reaction was carried out at 20°C for 3 h and monitoring by NMR indicated that olefin is partially isomerized to methylenecycloheptane under the reaction conditions.

Purification of these $\beta,\gamma$ products by GLC or LC resulted in partial

**Table III.** Molecular Ions from Field Ionization Mass Spectroscopy for Determination of the Kinetic Isotope Effect for Reactions of **3**, **3**-$d_4$, **9**, and **9**-$d_4$ with Acetic Anhydride and $ZnCl_2$

| | olefins[a] m/e | | | | | | | ketone[a] m/e | | | | | | | reaction |
| substrate | 96 | 97 | 98 | 99 | 100 | 101 | 102 | 137 | 138 | 139 | 140 | 141 | 142 | 143 | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **3**-3-$d_3$ | 100 | 14.79 | 19.44 | 97.75 | 11.68 | | | | | | | | | | 0 |
| **3**-3-$d_3$ | 100 | 12.33 | 17.69 | 92.47 | 10.84 | | | 3.56 | 100 | 24.72 | 92.54 | 35.08 | | | 20 |
| **3**-3-$d_3$ | 100 | 13.51 | 20.52 | 95.71 | 12.08 | | | 6.24 | 99.47 | 27.30 | 100 | 41.27 | | | 30 |
| **9**-9-$d_4$ | 7.59 | 0.60 | 0.09 | 1.40 | 10.0 | 1.68 | 0.15 | | | | | | | | 0 |
| **9**-9-$d_4$ | 6.97 | 0.52 | 0.10 | 0.57 | 10.0 | 1.56 | 11.1 | | 5.41 | 0.70 | 0.98 | 10.0 | 5.16 | 0.68 | 35 |

[a] Matrix correction for heavy isotopes not applied.

**Table IV.** Molecular Ions from Normalized Mass Spectra of Deuterated 1-Cyclohexenylacetones (**10**-$d_1$ and **10**-$d_2$) Produced from the Reaction of 2,2-Dideuteriomethylenecyclohexane (**9**-$d_2$) with Acetic Anhydride and $ZnCl_2$[a]

| m/e (rel intensities) | | | |
|---|---|---|---|
| 138 | 139 | 140 | 141 |
| 5.1 ± 3.3 | 23.4 ± 2.7 | 65.1 | 6.3 ± 3.8 |

[a] Percent deuterium determined by summation of all m/e intensity terms from average intensities for four runs.

isomerization to the corresponding α,β isomer. Separation of the α,β isomer from the β,γ isomers was successful by medium-pressure liquid chromatography on a 1-m silica gel column using $CH_2Cl_2$ as the elution solvent. However, the β,γ isomers could not be separated and were analyzed as a three-component mixture.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.00; H, 10.52.

1-Acetylmethylenecycloheptane: NMR (CDCl₃) δ 4.96 (1 H, s, $J \simeq$ 1 Hz, vinyl), 4.84 (1 H, s, $J \simeq$ 1 Hz, vinyl), 3.32 (1 H, t, $J$ = 6 Hz, CHCOCH₃), 2.15 (3 H, s, CH₃CO).

7-Acetyl-1-methylcycloheptene: NMR (CDCl₃) δ 5.72 (1 H, triplet, $J$ = 6 Hz, vinyl) 3.10 (1 H, m, CHCOCH₃), 2.12 (3 H, s, CH₃CO).

(1-Cycloheptenyl)acetone: NMR (CDCl₃) δ 5.70 (1 H, t, $J$ = 6 Hz, vinyl), 3.05 (2 H, s, CH₂COCH₃), 2.12 (3 H, s, CH₃CO).

**Reaction of 1-Methylcyclooctene.** Method B was used for the conversion of 1-methylcyclooctene to 2-acetyl-1-methylenecyclooctane, 8-acetyl-1-methylenecyclooctene, and (1-cyclooctenyl)acetone in a 4:3:3 ratio and 90% yield (NMR). Spectral data for the mixture of β,γ isomers: IR (neat) 1710 cm⁻¹; MS (70 eV) m/e (rel intensity) 166 (15.1).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.47; H, 10.79.

2-Acetyl-1-methylenecyclooctane: NMR (CDCl₃) δ 5.01 (1 H, s, vinyl), 4.89 (1 H, s, vinyl), ca. 3.1 (1 H, m, CHCOCH₃), 2.13 (3 H, s, CH₃CO).

8-Acetyl-1-methylcyclooctene: NMR (CDCl₃) δ 5.5 (H, m, vinyl), 3.17 (H, double doublet, $J$ = 4.5 Hz, $J$ = 1.5 Hz, CHCOCH₃), 2.13 (3H, s, CH₃CO), 1.48 (3H, s, CH₃C═C).

(1-Cyclooctenyl)-acetone: NMR (CDCl₃) δ 5.5 (H, m, vinyl), 3.00 (2H, s, CH₂COCH₃), 2.13 (s, CH₃CO).

**Reaction of 2-Ethyl-1-butene.** Methods A and B were used for the conversion of the olefin at 20 °C for 10 h to (Z)- and (E)-4-ethyl-4-hexen-2-one in 90% yield (GLC). The Z and E ketones could be separated by GLC or MPLC; however, use of europium tris(6,6,7,7,8,8-heptafluoro-2,2-dimethyl-3,5-octanedione)[31] and investigation of the LIS of the vinyl protons of (1-cyclohexenyl)acetone (LIS, 7.4), 6-acetyl-1-ethylcyclohexene (LIS, 2.7), and 3-(1-cyclohexenyl)-2-butanone (LIS, 6.0) as models allowed assignments of the LIS in the NMR spectrum of the mixture to Z (LIS, 4.6) and E (LIS, 11.6) and determination of the Z/E ratio of 2.3 ± 0.3.

Spectral data for (Z)-4-ethyl-4-hexen-2-one and (E)-4-ethyl-4-hexen-2-one mixture: IR (neat) 1710 cm⁻¹; NMR (CDCl₃) δ 5.42 (1 H, q, $J$ = 7 Hz, vinyl of Z), 5.31 (1 H, q, $J$ = Hz, vinyl of E), 3.10 (2 H, s, CH₂COCH₃ of Z), 3.02 (2 H, s, CH₂COCH₃ of E), 2.04 (3 H, s, CH₃CO), 2.0 (2 H, q, $J$ = 7 Hz, CH₂C═C), 1.60 (3 H, d, $J$ = 7 Hz, CH₃CH═C), 0.93 (3 H, t, $J$ = 7 Hz, CH₃CH₂).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H 11.18. Found: C, 76.19; H 11.14.

**Reaction of 2-Ethyl-1-butene with a Stable Acetylium Salt.** With diisopropylethylamine as the base, the procedure of Hoffmann was followed for the reaction of 2-ethyl-1-butene with commercially available acetylium hexachloroantimonate.[9] The ketonic products found in 90% yield (GLC) had a Z:E ratio of 1.5 ± 0.1.

Product mixtures from previous reactions of 2-ethyl-1-butene were resubmitted to the conditions of method B. The Z/E product ratios of 2.3 ± 0.3 and 1.4 ± 0.1 remained unchanged.

**Reaction of 1-Hexene.** Method B was used for the conversion of 1-hexene to 4-octen-2-one in 50% yield (NMR). The ketone could be isolated in 30% yield.[32] Spectra of the crude reaction mixture indicated that β,γ and α,β isomers are present.

**Reaction of 2-Methyl-2-butene.** Method B was used for conversion of 2-methyl-2-butene, in 38% yield (NMR), to 3,4-dimethyl-4-penten-2-one: IR (neat) 1710 (C═O), 900 cm⁻¹; NMR (CCl₄) δ 4.83 (2 H, s, $J$ = 1 Hz, C═CH₂), 3.16 (1 H, q, $J$ = 7 Hz, CHCH₃), 2.13 (3 H, s, CH₃CO), 1.68 (3 H, s, $J$ = 11 Hz, CH₃C═C), 1.17 (3 H, d, $J$ = 7 Hz, CH₃CH); MS (70 eV) m/e (rel intensity) 112 M⁺ (4.6), 43 (100), 41 (34.7).

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.66; H, 10.59.

**Reaction of (Z)- and (E)-3-Hexene.** Method B was used for the reactions of (Z)-3-hexene and of (E)-3-hexene with reaction times of 48 h. For the E isomer, no reaction occurred as judged by NMR. The Z isomer was converted in 10% yield to 3-ethyl-4-hexen-2-one: IR (neat) 1710 cm⁻¹; NMR (CDCl₃) δ 5.8–5.0 (2 H, m, vinyl), 2.9 (1 H, m, CHCOCH₃), 2.07 (3 H, s, CH₃CO), 1.64 (2 H, d, $J$ = 6 Hz, CH₂CH₃), 0.81 (3 H, t, $J$ = 6 Hz, CH₃CH₂); MS (70 eV) m/e (rel intensity) 126 M⁺ (9.4), 97 (19.3), 83 (38.9), 55 (100), 43 (82.2), 41 (28.5).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.18; H, 10.98.

**Relative Rates of Acetylation of Substituted 1-Phenylcyclohexenes.** Vials were prepared for each of substituted 1-phenylcyclohexenes and the reaction allowed to proceed to ca. 50% completion. The samples were quenched and worked up, and NMR analysis was performed. The results are listed in Table 11.

**Kinetic Isotope Effect for the Reaction of 1-Methylcyclohexene (3) and 1-Methyl-2,6,6-trideuteriocyclohexene (3-$d_3$).** Methods A and B were used for the reaction of known mixtures of **3** and **3**-$d_3$. The reaction mixtures were worked up in the usual manner, except that the pentane solution of the crude reaction mixture was not concentrated. The percent conversion was determined by GLC of the pentane solution. The deuterium distribution in the remaining olefin and in the products formed, 6-acetyl-1-methylcyclohexene and 6-acetyl-2,6-dideuterio-1-methylcyclohexene, was determined by FIMS analysis of the pentane solution of the crude reaction mixture. Typical data appears in Table III.[12]

The kinetic isotope effects calculated using eq 1 and 2 are 1.0 ± 0.3. The error limit is derived from one standard deviation of the FIMS data. The range expressed in 1.0 ± 0.3 results from using the high and low values of the FIMS data.

**Kinetic Isotope Effect for the Reaction of 1-Methylenecyclohexane (9) and 1-Methylene-2,2,6,6-tetradeuteriocyclohexane (9-$d_4$).** Method B was used for the reaction of a mixture of **9** and **9**-$d_4$. The reaction mixture was worked up in the usual manner and the pentane solution of the reaction mixture was analyzed by GLC and FIMS to produce the data in Table III. The kinetic isotope effect calculated was 1.0 ± 0.3.

**Product Isotope Effect for the Reaction of 2,2-Dideuteriomethylenecyclohexane (9-$d_2$).** Method B was used for the reaction of CCl₄ solution of olefin **9**-$d_2$. The reaction mixture was worked up in the usual manner. The pentane solution of the crude reaction mixture was analyzed by FIMS to provide the data listed in Table IV. The product isotope effect was calculated to be 3.2 ± 0.7.[12]

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(12) Details of the calculations, data, and full discussion are available. K. R. Berger, Ph.D. Thesis, University of Illinois, 1979; available from University Microfilms, Ann Arbor, Mich.

(13) A difference in kinetic and product isotope effects is well recognized as unambiguous evidence for a reaction intermediate. This mechanistic test has been developed and nicely used by Stephenson and co-workers to establish the presence of a reaction intermediate in the reaction of singlet oxygen with olefins, a process which is also a formal ene reaction. L. M. Stephenson, D. E. McClure, and P. K. Sysak, *J. Am. Chem. Soc.*, **95**, 7888 (1973); D. J. Crieghton, J. Hajdu, and D. S. Sigman, *ibid.*, **98**, 4619 (1976);

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(15) This species could alternatively be represented by an oriented ion pair in which the acetate ion takes the position shown for the zinc complexed oxygen.

(16) In **21**, and the following representations, the solid p orbital represents the locus of the positive charge while the dotted p orbital represents the alignment of the new orbital which would develop as proton transfer occurs.

(17) Melting points were determined in open capillaries and are uncorrected. Boiling points, taken from distillations, are likewise uncorrected. Infrared (IR) spectra were calibrated with a polystyrene standard. Chemical shifts of magnetic resonance spectra are reported in $\delta$ (ppm) relative to an internal tetramethylsilane standard. Mass spectral (MS) data were obtained by C. Cook and associates using a Varian MAT CH-5, gas chromatography MAT 112 spectrometer (GC/MS), and high-resolution (HRMS) and field ionization mass spectral (FIMS) data were obtained with a Varian MAT 731 spectrometer.

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# Mechanism of Anodic Cleavage of Benzyl Ethers

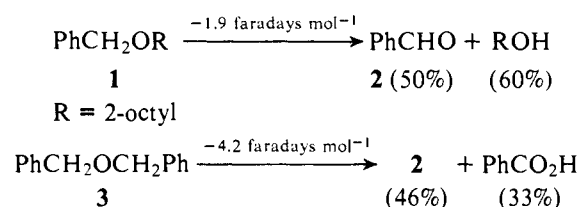**Jean W. Boyd, Paul W. Schmalzl, and Larry L. Miller\***

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**Abstract:** Kinetic isotope effects and substituent effects are utilized to elucidate the mechanism of the anodic oxidation of benzyl ethers at platinum in acetonitrile. All of the data, including some previously published results, are consistent with a mechanism involving phenylalkoxy carbonium ions. Much of the data is incompatible with a previous mechanistic proposal involving initial oxidative cleavage of the benzylic carbon–oxygen bond.

In 1972 Mayeda, Miller, and Wolf (MMW) published a study of the electrochemical oxidation of several benzyl ethers.[1] The reaction products were of primary interest, but a mechanism was also proposed, based upon several pertinent observations and literature analogies. In 1977 Lines and Utley (LU) studied the oxidation of dibenzyl ether, using similar conditions, and proposed an alternative mechanism.[2] It is the objective of the present work to resolve the mechanistic question raised by these papers.

Because the MMW and LU studies involved similar conditions, but produced some dissimilar results and quite different mechanistic conclusions, it is important to review these papers. Other studies of anodic benzyl ether oxidations have been reported, but these contain little mechanistic information and the results of interest are cited later. In the MMW study, preparative electrolyses employed a platinum foil anode, divided cell, acetonitrile solvent, Ag/0.1 M AgNO$_3$ reference electrode, and potentiostatic conditions. The electrolyte was

0.1 M lithium perchlorate and sodium carbonate was generally added to the anolyte. Oxidations were carried nearly to completion and the products were isolated and quantitated.[3] Two representative and apposite samples are

$$\text{PhCH}_2\text{OR} \xrightarrow{-1.9 \text{ faradays mol}^{-1}} \text{PhCHO} + \text{ROH}$$

$$\begin{array}{ccc} \mathbf{1} & \mathbf{2}\,(50\%) & (60\%) \\ \text{R} = \text{2-octyl} & & \end{array}$$

$$\text{PhCH}_2\text{OCH}_2\text{Ph} \xrightarrow{-4.2 \text{ faradays mol}^{-1}} \mathbf{2} + \text{PhCO}_2\text{H}$$

$$\begin{array}{ccc} \mathbf{3} & (46\%) & (33\%) \end{array}$$

This study also established that benzyl alcohol oxidized to benzaldehyde at the potential used for preparative oxidations of benzyl ethers, but that aliphatic alcohols were stable. Because this potential, 1.9 V, corresponded to the potential for oxidation of toluene it was proposed that the initial step in the