Organometallic Reaction Mechanisms. 16. Use of 2,2,6,6-Tetramethylhept-4-en-3-one as a Probe for Detection of Single-Electron Transfer in Grignard Reactions with Ketones

E. C. Ashby* and T. L. Wiesemann

Contribution from the School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332. Received June 20, 1977

Abstract: The reactions of *cis-* and *trans-*2,2,6,6-tetramethylhept-4-en-3-one with various Grignard reagents, dialkylmagnesium compounds, magnesium halides, as well as organolithium, aluminum, and copper compounds have been investigated. The scope and limitations of the use of this enone system for detection of single-electron transfer (SET) in main group metal reactions is discussed. Subject to certain limitations, it appears that the reactions of *t*-BuMgCl with the cis or trans enone (and therefore any ketone of lower reduction potential) is proceeding via a single-electron transfer pathway. Allyl Grignard reactions appear to be proceeding via a polar pathway. Methyl Grignard reactions with these enones are more complicated; however, trends indicate that these reagents are reacting via a polar pathway complicated by a side reaction involving transition metal impurities in the magnesium (from which the Grignard reagent was made) that leads to SET isomerization of the enone. The addition of *p*-dinitrobenzene to reactions of CH₃MgBr with "cis enone" retards isomerization of the "enone". The use of the enone probe for detection of SET pathways involving organolithium, aluminum, and copper reagents is also discussed.

Introduction

The importance of the Grignard reaction in synthetic organic chemistry is well recognized. The mechanism of this reaction has been under investigation for many years by numerous investigators. In recent years the major lack of understanding concerning the reactions of Grignard reagents with ketones has centered on the nature of the alkyl transfer from the reagent to the carbonyl carbon atom. Whether this step occurs by a polar or single-electron transfer mechanism has been the source of considerable speculation.[1-11]

As part of a continuing investigation into the nature of the alkyl transfer step in main group metal addition reactions, 2,2,6,6-tetramethylhept-4-en-3-one was employed as a probe to detect single-electron transfer (SET). This study is primarily directed toward a deeper understanding of the nature and extent (if any) of a SET pathway operating in Grignard reactions with ketones, especially when transition metal catalysts are rigorously excluded, as well as toward gaining insight into the conditions which determine the extent of SET reaction. This study also includes a variety of other metal and mixed metal alkyls in order to gain better perspective regarding the scope and nature of this probe.

The idea underlying the use of 2,2,6,6-tetramethylhept-4-en-3-one as a probe is that the cis isomer is rapidly converted to the trans isomer in any reaction involving the transfer of an electron to the enone.[12] A polar reaction, however, involving the cis isomer would be expected to give only cis products (eq 1). In this way the enone was used as a probe in an attempt to detect SET when allowed to react with Grignard reagents. The experiments generally involve 2 equiv of enone per equivalent of organometallic reagent. This allows observation of "unreacted enone" which, presumably, has been involved in the SET and will reflect the degree of SET occurring in the reaction. Presumably the sequence of events involves electron transfer from the Grignard to cis enone followed by rapid isomerization of the cis radical anion to the trans radical anion followed by electron transfer from the trans radical anion to the cis enone. Thus cis enone is converted to trans enone by an electron-transfer chain process involving a very rapid isomerization step.

The major drawback to the use of this enone as a probe involves the isomerization of the starting "cis enone" through

a SET pathway not necessarily along the main reaction pathway, followed by a polar reaction to give what appears to be products of a SET reaction (see eq 1). Based on information concerning the reactions of Grignard reagents with benzophenones in the presence of *p*-dinitrobenzene (*p*-DNB),[11] it may be possible to inhibit isomerization of cis to trans enone by the addition of *p*-DNB to the enone reactions (eq 2).

There are other subtleties concerning this probe which must also be considered. If the reaction of a Grignard reagent with cis enone proceeds via a polar pathway, only cis-addition product will be observed. If, however, the reaction pathway involves SET, there are three possible observations. If the rate of isomerization of the "cis ketyl" to the "trans ketyl" is faster than the rate of collapse of the SET intermediate (such as the radical cation–radical anion pair) to give products (see eq 1), trans-addition products will be observed. If, on the other hand, the rate of collapse to give products is faster than the rate of isomerization of cis to trans ketyl, then only cis-addition products will be observed, in spite of the SET pathway. If the rate of collapse to give products and the rate of isomerization of cis to trans ketyl are comparable in rate, a mixture of cis- and trans-addition products will be observed. For this reason, then, it would not be possible to observe any difference between a polar reaction and a SET reaction in which collapse to give addition products is faster than ketyl isomerization. Thus isomerization of the probe is a good indication of the SET process; however, lack of isomerization is not incontrovertible evidence that a SET process is not in operation.

In spite of the potential drawbacks of this system, a study of the reaction of *cis-* and *trans-*2,2,6,6-tetramethylhept-4-en-3-one with various Grignard reagents and other organometallic compounds was carried out. The hope was that, by careful comparison of the various reactions, insight could be gained into the mechanism of Grignard reactions with ketones, especially with respect to the mechanism of formation of the 1,2-addition product.

Results and Discussion

Reaction of Various Magnesium Compounds with Cis Enone. The initial study (Table I) was designed to discover the optimum reaction conditions for the reaction of the enone probe with various magnesium compounds. It was observed (entries 7–10) that MgBr₂ itself (which is a component of the Schlenk

(1)

(2)

$$RMgX + p\text{-DNB} \xrightarrow{c} p\text{-DNB}^{-}\cdot + RMgX^{+}\cdot$$
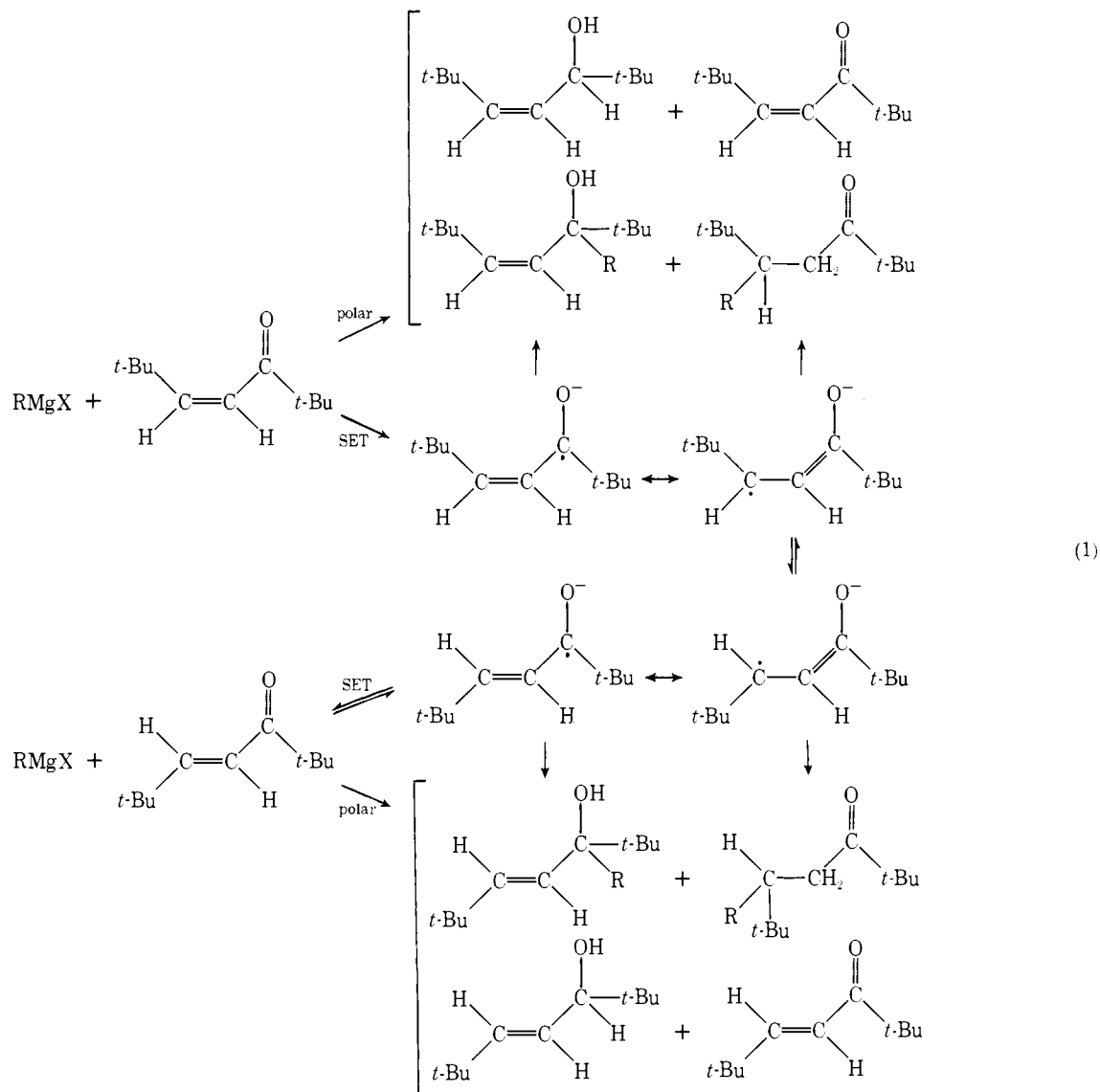
equilibrium describing the Grignard reagent) is capable of isomerizing the cis enone. This would tend to invalidate the probe; however, a comparison of entries 1, 4, and 7 shows that the reaction of the Grignard with enone is completely over before 4% isomerization due to $MgBr_2$ is observed. Therefore the $MgBr_2$ should have no significant effect on the results of the Grignard reaction with the enone. The reaction of $(CH_3)_2Mg$ with cis enone shows some isomerization in this time period (this result will be discussed in more detail later, with respect to Table V). A 20-min reaction time was chosen as the best time period for the experiments reported in this section.

The reaction of CH_3MgBr with excess cis enone is shown to result in both 1,2 and 1,4 addition to the enone with various amounts of isomerization depending upon the grade of magnesium from which the Grignard reagent was prepared (Table II, entries 1, 2, and 4). Addition of increasing amounts of $FeCl_3$ to the reaction results in increasing amounts of isomerization observed in the products, as well as in the unreacted enone (entries 4–7). The reaction of CH_3MgBr with trans enone (entry 3) yields only 1,4 and 1,2-trans addition, as may have been expected. It is interesting to note, however, that whether one begins with the cis or trans enone, the ratio of percent 1,4 addition to 1,2-trans addition is about the same, regardless of the amount of 1,2-cis addition produced in the reaction. The suggestion is that two separate processes are involved: the addition of the Grignard reagent to the cis enone to form
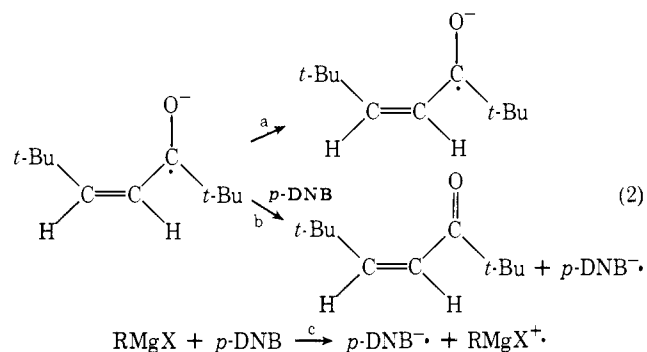
1,2-cis-addition product (path A) and the isomerization of the enone followed by Grignard addition to form 1,2-trans addition and 1,4 addition in ~50:50 ratio (path B) (eq 3). An analogy to the situation existing in Grignard reactions with benzophenones seems obvious (eq 4). In eq 4 it was shown that the pathway leading to pinacol formation is an iron-catalyzed side reaction unrelated to the normal Grignard addition pathway.[10-11] In light of this observation, it seems likely that the isomerization of the enone in the present reaction (eq 3) is also due to transition metal impurities in the magnesium. What can be said about the mechanism of the addition reaction is not as obvious. This topic will be discussed further a little later.

On the other hand, reaction of *t*-BuMgCl with excess cis enone (Table II, entries 8 and 9) shows almost complete

Table I. Products from the Reactions of Various Magnesium Compounds (0.050 M) with Cis Enone (0.10 M) in Diethyl Ether at Room Temperature: a Qualitative Rate Study

Expt	RMgX	Rxn time, min	Starting enone[a] % cis	% trans	% 1,4 addn	% 1,2-addn trans product	% 1,2-addn cis product	% 1,2 redn	% rxn
1	CH_3MgBr^c	10	85.2	14.8	41.2	40.0	18.8	0	100
2	CH_3MgBr	20	83.7	16.3	45.7	40.7	13.6	0	100
3	CH_3MgBr	30	81.3	18.7	51.2	40.3	8.4	0	100
4	$t\text{-BuMgCl}^d$	10	2.8	97.2	9.2	30.5	3.7	56.6	100
5	$t\text{-BuMgCl}$	20	3.7	96.3	8.8	26.5	1.6	63.1	100
6	$t\text{-BuMgCl}$	30	3.7	96.3	10.5	25.5	0.8	63.2	100
7	$MgBr_2{}^d$	10	96.3	3.7					3.7
8	$MgBr_2$	20	93.0	7.0					7.0
9	$MgBr_2$	30	88.7	11.3					11.3
10	$MgBr_2$	100	80.9	19.1					19.1
11	$(CH_3)_2Mg^d$	10	98.4	1.6	9.4	15.0	75.6	0	100
12	$(CH_3)_2Mg$	20	98.5	1.5	13.2	26.7	60.0	0	100
13	$(CH_3)_2Mg$	30	98.7	1.3	16.5	31.4	52.2	0	100
14	Blank	30	99.7	0.3					

[a] Normalized: 100% = % cis enone + % trans enone. [b] Normalized: 100% = % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition + % 1,2 reduction. [c] Made from Dow doubly sublimed magnesium using excess CH_3Br. [d] Made from Dow doubly sublimed magnesium.

Table II. Products of the Reactions of Grignard Reagents (0.033 M) with Cis and Trans Enone (0.0667 M) in Diethyl Ether at Room Temperature

Expt	Grignard reagent	Grade[a] of Mg	$FeCl_3$, ppm	Enone[b] (% purity)	Starting enone[b] % cis	% trans	% 1,4 addn	% 1,2-trans addn	% 1,2-cis addn	% 1,2 redn
1	CH_3MgBr	Stork	0	Cis (99.5)	88.8	11.2	55.0	35.2	9.0	0
2	CH_3MgBr	GGT	0	Cis (99.2)	83.8	16.2	47.7	40.2	12.0	0
3	CH_3MgBr	D.S.	0	Trans (100)	0	100.0	51.4	48.6	0	0
4	CH_3MgBr	D.S.	0	Cis (99.2)	83.1	16.7	40.9	40.2	18.9	0
5	CH_3MgBr	D.S.	400	Cis (99.2)	73.7	26.3	48.4	44.6	6.9	0
6	CH_3MgBr	D.S.	4 000	Cis (99.2)	39.3	60.7	48.4	50.4	1.2	0
7	CH_3MgBr	D.S.	40 000	Cis (99.2)	12.4	87.6	46.7	53.2	0.1	0
8	$t\text{-BuMgCl}$	GGT	0	Cis (99.2)	6.2	93.8	10.2	26.5	3.7	59.7
9	$t\text{-BuMgCl}$	D.S.	0	Cis (99.2)	4.0	96.0	11.9	25.3	3.1	59.7[d]
10	$t\text{-BuMgCl}$	D.S.	40 000	Cis (99.2)	6.5	93.5	9.1	24.4	0.5	66.0
11	$t\text{-BuMgCl}$	D.S.	0	Trans (100)	2.3	97.7	15.9	33.9	0	50.2[d]
12	Allyl-MgBr	D.S.	0	Cis (99.7)	99.2	0.8	0	0.7	99.3	Trace
13	Allyl-MgBr	D.S.	40 000	Cis (99.6)	24.5	75.5	0	4.0	96.0	Trace
14	Allyl-MgBr	D.S.	0	Trans (100)	0	100.0	0	100.0	0	Trace
15	$MgBr_2$	D.S.	0	Cis (99.7)	93.0	7.0				
16			40 000	Cis (99.7)	99.7	0.3				

[a] GGT, Grignard grade turnings; D.S., Dow doubly sublimed magnesium. [b] Normalized: 100% = % cis enone + % trans enone. [c] Normalized: 100% = % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition + % 1,2 reduction. [d] Shown to be 100% trans by GLC on TCEP.

$$CH_3MgBr + Ph_2C{=}O \longrightarrow Ph_2COMgBr \quad (4)$$
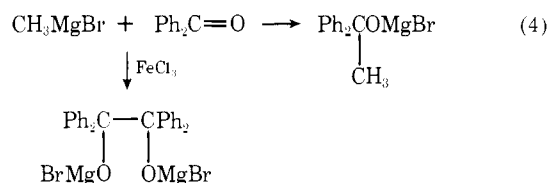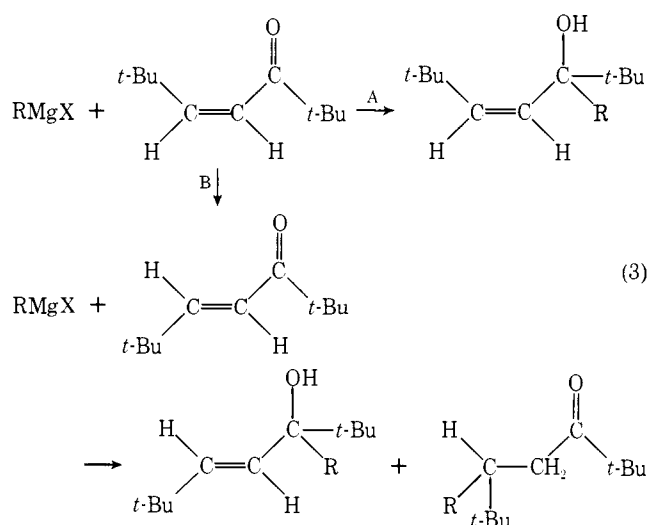
isomerization of both starting materials and products, indicative of a SET reaction. The observation made previously (eq 3) again seems to be true; i.e., the 1,4-addition to 1,2-trans-addition ratio is constant (30:70) even when the reaction is carried out with trans enone (entry 11). However, there is never really enough 1,2-cis-addition product produced to make the comparison as compelling in this case as in the methyl Grignard case. It is interesting to note that the addition of 40 000 ppm of $FeCl_3$ to the reaction of t-BuMgCl with cis enone (entry 10) results in a 6% increase in the amount of 1,2 reduction observed, reminiscent of the unusual increase in reduction product observed with acetone in the presence of

Table III. Rate Studies of the Reactions of CH_3MgBr (0.025 M) with Cis and Trans Enone (0.025 M) in Diethyl Ether at Room Temperature

Expt	Enone	Rxn time, s	Starting[a] enone[a] % cis	% trans	Products % 1,4 addition	% 1,2-addn trans product	% 1,2-addn cis product
1	Cis[b]	10	99.7	0	0.02	0.2	0.01
2	Cis	29	98.2	0	0.4	0.9	0.4
3	Cis	60	97.9	0	0.7	0.7	0.7
4	Cis	120	89.2	0	4.2	3.1	3.5
5	Cis	240	78.5	0	8.1	5.3	8.1
6	Cis	300	63.4	0	17.1	13.0	6.5
7	Cis	600	40.1	0	27.8	22.5	9.6
8	Cis	1200	22.7	0	35.6	30.2	11.5
9	Trans	10	0	51.9	25.3	23.0	0
10	Trans	34	0	22.6	41.0	36.3	0
11	Trans	60	0	16.8	43.6	39.8	0
12	Trans	120	0	6.8	47.8	45.3	0
13	Trans	240	0	2.0	49.7	48.4	0

[a] Normalized: 100% = % cis enone + % trans enone + % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition. [b] Blank run demonstrated cis enone to be 99.3% cis and 0.7% trans isomer.
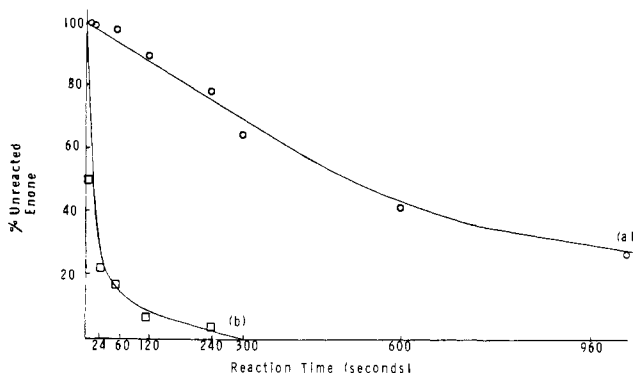

Figure 1. (a) Reaction of CH_3MgBr (0.0250 M) with cis enone (0.0250 M) in diethyl ether at room temperature. (b) Reaction of CH_3MgBr (0.0250 M) with trans enone (0.0250 M) in diethyl ether at room temperature.

$FeCl_3$.[13] The increase in enone reduction product observed in the *t*-BuMgCl case is considerably smaller than the increase in reduction product observed in the *t*-BuMgCl reaction with acetone, especially considering the tenfold increase in $FeCl_3$ used in the enone experiments. These data indicate that the reaction competing with the reduction is faster (relatively) in the enone reaction than in the reaction with acetone. It is also interesting to note that the reaction of *t*-BuMgCl with trans enone (100%) yields 2.3% cis enone in the product mixture (entry 11), indicating a cis–trans-ketyl equilibration which, of course, lies far to the side of the trans ketyl. All of the data concerning reaction of the cis enone with *t*-BuMgCl lends credence to the theory that the reaction proceeds predominantly through a SET pathway.

The reaction of allyl-MgBr with excess cis enone seems less complicated. It produces almost all 1,2-cis-addition product and does not significantly isomerize the remaining cis enone starting material (Table II, entry 12). The addition of 40 000 ppm of $FeCl_3$ (entry 13) isomerizes the starting enone somewhat, but has only a small effect on the isomerization of the 1,2-addition product. This isomerization may be occurring via a route not related to the major reaction pathway (such as B in eq 3), after the addition of allyl-MgBr to the cis enone has already occurred, since only the excess starting enone is affected (and not the addition products). In any case, the addition reaction is probably occurring too rapidly for the iron to have much effect. Reaction of the allyl-MgBr with trans enone produces only 1,2-trans addition. In no case is any 1,4 addition

observed. The allyl Grignard reaction, therefore appears to be a straightforward case of polar addition to the enone. There remains the possibility, however, that the reaction proceeds by SET owing to the fact that 1,2-addition proceeds more rapidly than the isomerization of the ketyl from cis to trans. However, since allyl magnesium bromide reacts with benzophenone only three times faster than does *t*-BuMgCl and the latter shows essentially complete isomerization when allowed to react with the enones, it is clear that the allyl Grignard reagent should exhibit significant isomerization when allowed to react with the same enone if indeed SET is the reaction pathway. Since the allyl Grignard exhibits not more than a trace of isomerized enone or 1,2-addition product, one must conclude that the allyl Grignard reagent most probably reacts via a polar pathway.

It is important to note that a control experiment in which $FeCl_3$ equivalent to 40 000 ppm used in the Grignard reactions with cis enone was carried out (entry 16). No isomerization of the cis enone was observed under these conditions in the absence of Grignard reagent.

Relative Rates of Methyl Grignard Reactions with Cis and Trans Enones. In order to help elucidate the nature of the reaction of CH_3MgBr with cis enone, a qualitative rate comparison was made between the reaction of methyl Grignard with cis vs. trans enone (Table III, Figure 1). It is readily apparent that CH_3MgBr reacts much more rapidly with the trans than the cis isomer. This fact, along with a pathway involving isomerization of the cis enone, such as path B, eq 3, would easily explain the predominance of isomerized 1,2-addition product. Note in Table III, entries 1–8, that, when Grignard reagent and cis enone are allowed to react in 1:1 ratio, no isomerized enone was ever detected. It is apparent that the trans enone formed by isomerization reacts with the Grignard reagent as soon as isomerization occurs. There is never any chance for the trans enone to build up as in the reactions using excess enone. This difference in rate emphasizes the point that there are two separate pathways involved in the reaction of CH_3MgBr with cis enone. It is possible, but not necessary, that these pathways involve different mechanisms (e.g., 1,2-cis addition via polar pathway; 1,4- and 1,2-trans addition via SET).

Reaction of Other Organometallic Compounds with Cis Enone. The reaction of MeLi with cis and trans enone (Table IV, entries 1–4) gave much the same results as the reaction of allyl-MgBr. The only product observed was 1,2 addition, although a small amount of isomerization was observed in the presence of $FeCl_3$. It is interesting to note (entry 4) that MeLi

Table IV. Products of the Reactions of Various Organolithium Compounds (0.0333 M) with Cis and Trans Enone (0.0667 M) in Diethyl Ether at Room Temperature[a]

Expt	RM	Enone[b] (% purity)	FeCl$_3$, ppm	Starting enone[a] % cis	% trans	Products[c] % 1,4 addn	% 1,2-addn trans product	% 1,2-addn cis product	% 1,2 redn
1	MeLi	Cis (99.5)	0	98.7	1.3	0	1.3	98.7	0
2	MeLi	Cis (99.5)	40 000	60.3	39.7	0	25.0	75.0	0
3	MeLi	Trans (100)	0	0	100.0	0	100.0	0	0
4	MeLi	Cis (87.0)	0	89.0	11.0	0	17.7	82.3	0
5	LiCuMe$_2$	Cis (99.7)	0	0.2	99.8	100	0	0	0
6	LiCuMe$_2$	Cis (99.7)	40 000	0	100.0	100	0	0	0
7	LiCuMe$_2$	Trans (100)	0	0	100.0	100	0	0	0
8	(4MeLi + CuI)[d]	Cis (99.7)	0	2.2	97.8	31.3	10.1	58.5	0
9	(4MeLi + CuI)[d]	Trans (100)	0	0	100.0	40.1	59.9	0	0
10	LiCu$_2$Me$_3$[e]	Cis (99.3)	0	0	100.0	100	0	0	0
11	LiCu$_2$Me$_3$[e]	Trans (100)	0	0	100.0	100	0	0	0
12	*t*-BuLi[f]	Cis (99.3)	0	63.2	36.8	7.0	6.8	85.6	0.7
13	*t*-BuLi	Cis (99.5)	40 000	40.6	59.4	2.0	5.4	92.0	0.6
14	*t*-BuLi	Trans (100)	0	3.9	96.1	46.9	51.2	0	1.9

[a] Reaction time, 20 min. [b] Normalized 100% = % cis + % trans. [c] Normalized 100% = % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition + % 1,2 reduction. [d] 0.013 M. [e] 0.020 M in THF. [f] 0.0667 M.

reacts at a similar rate with both the cis and trans enone. In this reaction an 87:13 mixture of cis–trans enone is converted to an 82:18 mixture of cis–trans-1,2-addition products leaving an 89:11 mixture of starting materials. The MeLi apparently reacts ~1.4 times faster with the trans enone than with the cis enone. As with the allyl Grignard reagents, the conclusion is that the reaction of MeLi with cis enone is either polar or that the SET reaction proceeds to products too quickly for isomerization of an intermediate ketyl to be observed.

The reaction of LiCuMe$_2$ with the enone (entries 5–7) shows only 1,4-addition product and complete isomerization of the starting enone. The reactions of LiCu$_2$Me$_3$[13,14] gave similar results (entries 11 and 10). The total isomerization of the starting cis enone is, of course, indicative of SET. The reaction of cuprates with enones is thought to proceed through a SET pathway. The mixture of 4 equiv of MeLi with 1 equiv of CuI in THF has been shown to give an equilibrium mixture of Li$_2$CuMe$_3$ ⇌ LiCuMe$_2$ + MeLi.[13,14] The reaction of this reagent with cis enone (entry 8) gave 31% 1,4 addition and 69% 1,2 addition. Although almost all of the starting cis enone was isomerized during the reaction, 85% of the 1,2-addition product is cis. Under these reaction conditions, it seems that the MeLi in the equilibrium mixture is reacting rapidly to give 1,2 addition (predominantly cis in the early stages). The Li$_2$CuMe$_3$ and the LiCuMe$_2$ are probably reacting more slowly but through a SET pathway to yield 1,4-addition product and isomerized enone. The 1,2-trans-addition product then comes about by reaction of MeLi with the isomerized enone. These results may also be taken to indicate that the reaction of MeLi with cis enone to form 1,2-addition product is faster than isomerization of the enone.

The reaction of *tert*-butyllithium with cis and trans enone, provide another interesting case (entries 12–14). With excess cis enone, *tert*-butyllithium gives mostly (85.6%) unisomerized 1,2-addition product (possibly indicative of polar addition). However, this reaction also yields 1,4- (7.0%) and 1,2-trans addition (6.8%) as well as 36.8% isomerization of the starting cis enone. This may be more indicative of a SET reaction which proceeds to products somewhat more rapidly than the rate of isomerization occurs. The addition of 40 000 ppm of FeCl$_3$ causes a somewhat greater amount of isomerization of the remaining enone, but slightly less isomerization of the products. This probably indicates no effect of iron on the main reaction pathway. (The iron, however, probably is involved in the isomerization of the enone via route B, eq 3.) The significant result, once again is seen in the reaction with trans enone. The

only products are 1,4- and 1,2-trans addition, but more importantly the ratio of percent 1,4 addition to percent 1,2-trans addition (~47:53) once again turns out to be the same starting with either the cis or trans enone, regardless of how much 1,2-cis-addition product is produced in the reaction. In this reaction, the observation is dramatic because 1,2-cis addition is the predominant product in the reaction with cis enone and is not observed at all in the reaction with trans enone. Apparently (as in eq 3) again two pathways are involved: the reaction of *tert*-butyllithium with cis enone to produce 1,2-cis-addition product and the reaction of *tert*-butyllithium with trans enone to produce a ~47:53 mixture of 1,4- and 1,2-trans-addition products.

The reaction of Me$_2$Mg with cis and trans enones gives results very similar to those observed with *tert*-butyllithium (except for the effect of iron on the reaction) (Table V, entries 1–3). The reaction with cis enone gives mostly 1,2-cis addition with a small amount of 1,4 and 1,2-trans addition. Very little isomerization of the starting enone is observed. The same reaction in the presence of 40 000 ppm of FeCl$_3$ gives predominantly 1,4 and 1,2-trans addition, but with only ~25% isomerization of the remaining cis enone. This probably indicates that Me$_2$Mg reacts much more rapidly with the trans enone than with the cis isomer (similar to the observation in the case of CH$_3$MgBr). The reaction of Me$_2$Mg with trans enone shows only 1,4 and 1,2-trans addition. As noted with CH$_3$MgBr and *tert*-butyllithium, the ratio of percent 1,4 addition to 1,2-trans addition (~49:51) remains nearly constant throughout these reactions, in spite of the dramatic change in 1,2-cis addition produced. Again, the suggestion is that, in the reaction with cis enone, the 1,2-trans-addition product results from Me$_2$Mg addition to the trans enone after isomerization (eq 3).

The reactions of various organoaluminum and zinc compounds with cis and trans enone were studied in diethyl ether and benzene. Much less reaction was observed with these compounds than with the corresponding magnesium compounds. When Me$_3$Al was allowed to react with cis enone for 46 h in diethyl ether (Table V, entry 4), almost no reaction occurred; the only product observed was a trace amount of 1,2-trans addition. The same reaction with 40 000 ppm of FeCl$_3$ added (entry 5) gave 17% reaction to yield a 15:85 ratio of 1,4 addition to 1,2-trans addition as well as 27% isomerization of the starting cis enone. It appears that Me$_3$Al is unable to react with the cis enone, but, in the presence of FeCl$_3$, some isomerization of the enone takes place. Reaction of this isomerized enone with Me$_3$Al then leads to the mixture of 1,4

Table V. Products of the Reactions of Organometallic Compounds (0.033 M) with Cis and Trans Enone (0.0667 M) at Room Temperature[a]

Expt	RM	Enone[b] (% purity)	Solvent	FeCl$_3$, ppm	Starting enone[b] % cis	Starting enone[b] % trans	% 1,4 addn	% 1,2-trans-addn product	% 1,2-cis-addn product	% 1,2 redn	%[d] rxn
1	Me$_2$Mg[f]	Cis (99.8)	Ether	0	98.9	1.1	5.0	6.5	88.5	0	100
2	Me$_2$Mg[e]	Cis (87.3)	Ether	40 000	75.0	25.0	47.3	52.3	0.4	0	100
3	Me$_2$Mg[e]	Trans (98)	Ether	0	1.4	98.6	50.3	49.7	0	0	100
4	Me$_3$Al	Cis (99.7)	Ether	0	98.8	1.2	0	100	0	0	0.3
5	Me$_3$Al	Cis (99.7)	Ether	40 000	73.0	27.0	15.3	84.7	0	0	17.0
6	Me$_3$Al	Trans (100)	Ether	0	0	100	12.2	87.8	0	0	45.8
7	Me$_3$Al	Trans (100)	Ether	40 000	0	100	20.4	79.6	0	0	45.0
8	Me$_3$Al	Cis (75.0)	Benzene	0	64.7	35.3	28.5	38.5	33.1	0	47.8
9	Me$_3$Al	Cis (75.0	Benzene	40 000	36.0	64.0	41.0	46.5	12.5	0	66.0
10	Me$_3$Al	Trans (98)	Benzene	0	2.7	97.3	29.4	70.6	0	0	59.8
11	Me$_3$Al	Trans (98)	Benzene	40 000	0	100	34.3	65.7	0	0	76.6
12	Me$_2$AlCl	Cis (75.0)	Benzene	0	0	100	48.8	41.5	9.8	0	8.2
13	Me$_2$AlCl	Cis (75.0)	Benzene	40 000	0	100	58.3	41.7	0	0	4.8

[a] The following compounds failed to effect any changes in the starting enone (cis or trans) after 46 h in either ether or benzene in the presence or absence of 40 000 ppm of FeCl$_3$: Me$_2$Zn, MeZnBr, t-Bu$_2$Zn. Reaction times: 46 h in ether; 44 h in benzene; 20 min for Me$_2$Mg reactions. [b] Normalized: 100% = cis enone + % trans enone. [c] Normalized: 100% = % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition + % 1,2 reduction. [d] Based on organometallic. [e] 0.0167 M. [f] 0.103 M.

and 1,2-trans addition. It is apparent by comparison of entries 6 and 7, however, that the rate of reaction of Me$_3$Al with trans enone is not affected by the presence of FeCl$_3$. Both the reaction of Me$_3$Al with trans enone in ether and the same reaction in the presence of 40 000 ppm of FeCl$_3$ show the same amount of reaction (45%) after 46 h at room temperature. The product distribution is slightly affected by the FeCl$_3$; somewhat more 1,4 addition is seen in the presence of FeCl$_3$. That there are two distinct pathways involved in this reaction (as in eq 3) is quite obvious, since the Me$_3$Al reacts with the trans enone to generate 1,4- and 1,2-trans-addition products, but does not react at all with the cis enone.

The reaction of Me$_3$Al with cis and trans enone in benzene, however, is a different matter entirely. When Me$_3$Al was allowed to react with cis enone in benzene for 44 h, almost 50% reaction occurred (Table V, entry 8). The product mixture includes 28.5% 1,4 addition, 38.5% 1,2-trans addition and 33.1% 1,2-cis addition. Some isomerization of the starting cis enone was also observed. The same reaction in the presence of 40 000 ppm of FeCl$_3$ (entry 8) showed a marked increase in the amount of 1,4 addition observed, as well as an increase in the percent isomerization of both the 1,2-addition product and the starting cis-enone. It appears in this case that iron catalyzes the formation of 1,4-addition product possibly via a SET pathway. The reaction of Me$_3$Al with trans enone (entry 10) in benzene gives ∼60% conversion to a mixture containing 29.4% 1,4 addition and 70.6% 1,2-trans addition. Addition of 40 000 ppm of FeCl$_3$ under these conditions has little effect on the reaction. (The percent 1,4-addition product increases by ∼5% and the percent conversion increases to ∼77%, but these changes are not so significant.) A comparison of entries 8 and 10, however, shows a significant change from the trend observed in diethyl ether. The amount of 1,4 addition observed in the reaction of Me$_3$Al with cis enone and that observed in the reaction with trans enone is the same when the solvent is benzene. The reaction with cis enone gives a mixture of cis- and trans-1,2 addition while the reaction with trans enone gives only trans-1,2 addition, but in each case the relative percent 1,2 addition is the same. This is not at all indicative of the two-pathway reaction indicated in eq 3. The data is much more consistent with a mechanism involving a single pathway leading to all products (such as eq 5) or a pair of pathways (such as 6) in which one pathway leads to 1,4 addition (path
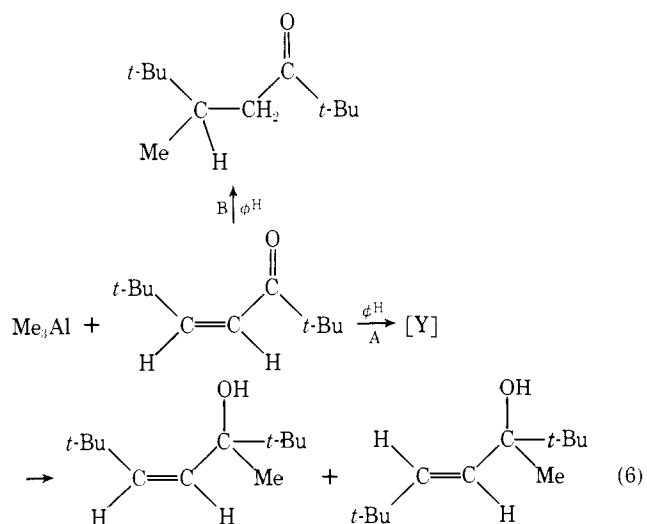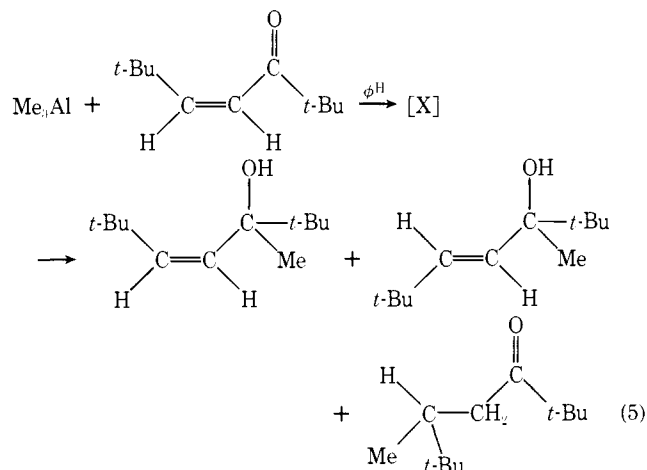
B) and the other leads to both cis- and trans-1,2 addition (path A). It is probable that either mechanism would have to involve some intermediate ([X] or [Y]) which provides for the isomerization of enone. It is clear, in any event, that the mechanism of this reaction in benzene is different than the one in diethyl ether and is different from those proposed to involve the two

Table VI. Products of the Reactions of Organometallic Reagents (0.0333 M) with Cis and Trans Enone (0.0667 M) in the Presence of p-DNB in Diethyl Ether at Room Temperature

Expt	RM	% p-DNB	Rxn time, min[c]	Enone (% purity)	Starting enone[a] % cis	% trans	% 1,4 addn	% 1,2-trans-addn product	% 1,2-cis-addn product	% 1,2 redn	%[d] rxn
1	CH₃MgBr	20	20	Cis (98.7)	96.4	3.6	44.8	37.2	17.9	0	45
2	CH₃MgBr	20	3 h	Cis (98.7)	95.3	4.7	47.3	38.6	14.0	0	41
3	CH₃MgBr	20	19 h	Cis (98.7)	93.9	6.1	48.2	40.6	11.2	0	56
4	CH₃MgBr	30	20	Cis (99.3)	100	0.04	16.1	13.3	70.6	0	42
5	CH₃MgBr	100	20	Cis (99.2)	98.7	1.3	Trace	Trace	Trace	0	0.1
6	t-BuMgCl	5	20	Cis (98.7)	3.5	96.5	13.7	14.0	1.3	71.1	60
7	t-BuMgCl	20	20	Cis (87.3)	84.2	15.8	0	0	0	0.2	0.2
8	t-BuMgCl	100	20	Cis (87.3)	86.0	14.0	0	0	0	0	0
9	Allyl-MgBr	20	20	Cis (99.6)	97.9	2.1	0	2.5	97.5	Trace	100
10	Allyl-MgBr	100	20	Cis (99.6)	98.0	2.0	0	2.4	97.6	Trace	100
11	LiCuMe₂	20	15	Trans (100)	0	100	100	0	0	0	7.1
12	LiCuMe₂	100	15	Trans (100)	0	100	100	0	0	0	40

[a] Normalized % cis enone + % trans enone = 100%. [b] Normalized % 1,4 addition + % 1,2-trans addition + % 1,2-cis addition + % 1,2 reduction = 100%. [c] Except as noted. [d] Based on organometallic reagent.

pathways depicted in eq 3. It is difficult to make any statements concerning the polar or SET nature of these reactions in ether or in benzene based on these data. However, in ether it appears as if the reaction is proceeding by a polar pathway (results similar to those of CH₃MgBr in ether), whereas in benzene it appears as if the reaction is SET in nature or SET in conjunction with a polar pathway.

The reaction of Me₂AlCl with cis enone for 44 h in benzene gives only 8% conversion to a mixture containing 48.8% 1,4 addition, 41.5% 1,2-trans addition, and 9.8% 1,2-cis addition. All of the enone that remains, however, is isomerized to the trans isomer. The same reaction in the presence of 40 000 ppm of FeCl₃ yields 5% conversion to a mixture that is 58.3% 1,4-addition product and 41.7% 1,2-trans-addition product. The reagents Me₂Zn, MeZnBr, and t-Bu₂Zn all failed to give any reaction with either cis or trans enone in the presence or absence of 40 000 ppm of FeCl₃ after 44 h of contact in benzene or 46 h of contact in diethyl ether at room temperature. The starting material was not isomerized in any of these reactions. The lack of reactivity of these reagents makes conclusions somewhat hazardous; however, comparison of the results of experiments 4 and 12 tend to indicate that Me₂AlCl is reacting with enone by a SET pathway.

Effect of p-DNB on Enone Reactions. The reaction of CH₃MgBr with cis enone in the presence of 20% p-DNB

(Table VI, entry 1) shows about the same product mixture as the reaction in the absence of p-DNB (Table II, entry 4), however, without the isomerization of the starting cis enone observed in that reaction. This is the best single piece of data supporting the case for a SET mechanism for the reaction of CH₃MgBr with ketones. If the p-DNB is indeed able to eliminate isomerization of the cis enone by removing an electron at a faster rate than cis- to trans-ketyl isomerization (see eq 2), the isomerized addition products could then come about only through a SET process in the product formation step of the mechanism. It is possible that the p-DNB intercepts the "free" ketyl radical anion, and yet is unable to intercept a bound radical anion–radical cation pair. It appears, then, that isomerization of the starting cis enone is occurring exclusively through a process involving the free ketyl, a process that could be stopped by p-DNB in the reactions. SET formation of radical anion–radical cation pairs involving Grignard reagent and enone which would presumably be unaffected by the p-DNB could then collapse to form the observed addition. products.

It is more likely, however, that the Grignard reaction with the enone involves the two pathways postulated in eq 3. It is likely that the isomerization step (path B) involves SET to give the "free" ketyl and that p-DNB reverses this step by interception of the ketyl radical anion to regenerate the cis enone

(7)
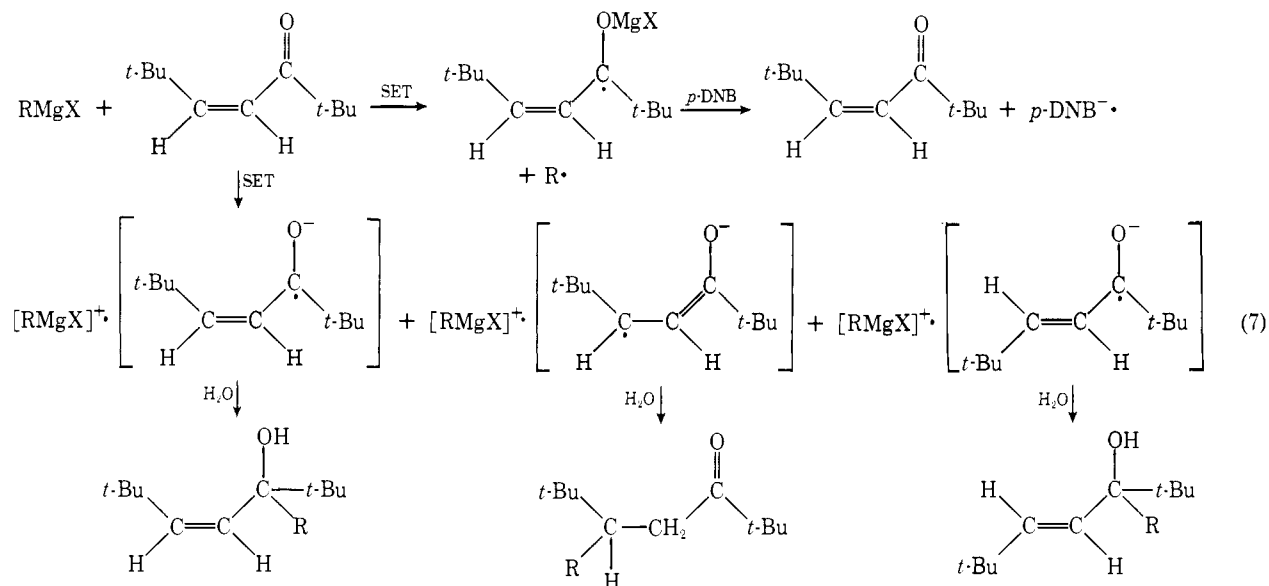
in the presence of 30% *p*-DNB (Table VI, entry 4). This shows that the more *p*-DNB present in the reaction, the less isomerization occurs. While this result is not irreconcilably inconsistent with the mechanism proposed in eq 7, it certainly seems to be more consistent with the pathway proposed in eq 3. The role of the *p*-DNB apparently is only to inhibit isomerization of the cis enone. It appears, from the trend observed in Table VI (entries 1 and 4) that, in the (hypothetical) reaction of CH₃MgBr with cis enone where enough *p*-DNB has been added such that no isomerization of the enone would occur, the only product would be 1,2-cis addition. Unfortunately, it is impossible to test this hypothesis (other than by extrapolation of these results) because larger concentrations of *p*-DNB destroy all of the CH₃MgBr in a side reaction and no reaction with the cis enone is observed. This trend, however, does seem to enhance the argument that the reaction of methyl Grignard reagents with ketones proceeds (at least predominantly) through a polar mechanism (in the absence of transition metal impurities). The alternative argument that the 1,2-cis-addition product is the result of addition to the cis enone via a SET pathway too rapid for the reaction to be "short circuited" by the *p*-DNB is not refutable, however.

Table VI (entries 6–8) shows that the reaction of *t*-BuMgCl with cis enone is not significantly affected by *p*-DNB, except for the destruction of the Grignard reagent in a side reaction which renders it useless for reactions with the enone. Allyl-MgBr reactions with cis enone (entries 9 and 10) are entirely unaffected by *p*-DNB. Presumably this Grignard reagent reacts with the ketone faster than it does with the *p*-DNB. This, in itself, points to a polar reaction pathway, since the reduction potential of *p*-DNB is much lower than that of cis enone and a SET reaction would be expected to occur predominantly with the substrate of lower reduction potential. The reactions of LiMe₂Cu with trans enone in the presence of *p*-DNB (entries 11 and 12) like those of *t*-BuMgCl are only affected to the extent that the cuprate reacts with the *p*-DNB in a side reaction which prevents addition to the enone.

Conclusion

In spite of certain difficulties, it has been possible to use *cis*-2,2,6,6-tetramethylhept-4-en-3-one as a probe to gain insight into the nature of Grignard reactions with ketones.

Almost all of the organometallic reagents tested isomerized the cis enone at least to some extent. It seems likely that in most cases this is due to the production of an intermediate (likely a reduced transition metal species) which is capable of electron transfer to the enone. As in the reaction of CH₃MgBr with benzophenones,[10] it is likely that this is a side reaction and not the main reaction pathway.

It seems apparent that *tert*-butylmagnesium chloride reacts with cis and trans enones at least predominantly via a SET pathway. Almost complete isomerization of both excess starting materials and products are observed in reactions with cis enone. Equally convincing is the observation of small amounts of cis enone produced in the reaction of *t*-BuMgCl with excess trans enone. This indicates that an equilibrium amount of cis ketyl was produced in the reaction. The reaction of *t*-BuMgCl with trace amounts of FeCl₃ apparently produces an iron hydride species (previously described)[10] which is capable of reducing the enone. This reduction pathway is slow, however, compared with the normal *tert*-butyl Grignard addition reaction with the enone.

The reactions of allyl Grignard reagents with these enones are very rapid and give indications of only a polar mechanism. Cis enone reacts with allyl-MgBr to give only cis-1,2 addition and trans enone reacts to give only trans-1,2 addition. A SET pathway in which the addition step is much more rapid than the rate of isomerization is also a possibility; however, consideration of all of the evidence available indicates that the

reaction is polar in nature. The reaction of allyl-MgBr with enone is not affected by the addition of FeCl₃. This is a good indication that polar and SET pathways are not competing in this case.

The reactions of methyl Grignard reagents with cis and trans enone are not as easily interpreted in terms of the nature of the alkyl transfer. They show some characteristic of both polar and SET reactions. The main complicating factor is that the reaction of CH₃MgBr with FeCl₃ (or other transition metal impurities, even in trace amounts) produces a species which is capable of SET to ketones by an apparently catalytic process involving the Grignard reagent. This SET leads to isomerization of the cis enone. Although Grignard reagents have been shown to react with *p*-dinitrobenzene, small amounts of *p*-DNB have been demonstrated to be capable of inhibiting the formation of free ketyls in solutions.[11] Methyl Grignard reactions with cis enone show significantly reduced amounts of isomerization. Trends in these data seem to indicate that the reaction of methyl Grignard reagents with cis and trans enone is polar. As has been previously indicated, a SET reaction followed rapidly by collapse to give addition products cannot be completely ruled out.

Methyllithium reacts much like allyl-MgBr, apparently via a polar pathway. The reaction of cis enone with MeLi yields only cis-1,2-addition product. Lithium alkyl cuprates apparently react predominantly via SET to give exclusively 1,4-addition products and almost complete isomerization of the starting cis enone. These observations make the reagent obtained by mixing 4 equiv of MeLi with 1 equiv of CuI (Li₂CuMe₃ ⇌ LiCuMe₃ + MeLi) very interesting indeed. This combines a SET and a polar reagent in the same mixture and the product analysis bears the appearance of both, apparently reacting at relatively similar rates (MeLi reacts only about twice as fast as cuprate according to the 1,2- to 1,4-addition ratio). It is apparent from these results that the reaction of MeLi with cis enone is faster than isomerization of the enone. The reaction of *tert*-butyllithium with cis enone may be an example of a SET reaction which proceeds to products at a rate somewhat more rapidly than the rate of isomerization of cis to trans ketyl, but not so much more rapidly that no isomerization occurs. The reaction of Me₂Mg with cis enone may also fit into this category.

Although the reactions of cis and trans enone with organozinc and organoaluminum reagents were inconclusive from a mechanistic point of view, they led to the observation that many organometallic reagents react much more rapidly with the trans enone than with the cis isomer. This point has undoubtedly caused much of the confusion in interpretation of the Grignard reactions with cis enone (especially in the case of CH₃MgBr).

It appears, at least in ether solvent, that reactions leading to 1,4-addition products come about only by attack of the reagent upon the trans isomer of the enone. It seems apparent, in the cases of Me₂Mg, *t*-BuLi, Me₃Al, and CH₃MgBr, that 1,4 and 1,2-trans addition come about via one pathway and that 1,2-cis addition comes about through another. The logical explanation is that the 1,4- and 1,2-trans-addition products come about via attack of the reagent upon the trans enone and that 1,2-cis addition comes about via attack on the cis enone. It is further possible that 1,2-cis addition is the result of polar attack on the enone and that 1,4 and 1,2-trans addition are the result of SET reaction. The latter does not appear to be the case since the 1,4- to 1,2-trans-addition product ratio for reaction with cis enone is the same as that for the reactions with trans enone in spite of the presence or absence of cis-addition product. One could expect that polar addition to the trans enone would give an amount of 1,2-trans-addition product equal to that amount of 1,2-cis-addition product observed in the case of addition to the cis enone. This would, of course, change the

observed ratio of 1,4- to 1,2-trans-addition product since some of the 1,2-trans product would come about through each mechanism. It seems likely that there is some other reason, probably steric in nature, to explain why 1,4 addition comes about only by attack of the reagent upon the trans enone. Further investigations into the implication of this conclusion are being presently conducted in our laboratories.

Experimental Section

Materials. Solvents. Fisher reagent grade anhydrous diethyl ether was stored over sodium and then distilled under nitrogen from LiAlH$_4$ and/or sodium benzophenone ketyl just prior to use. Fisher reagent grade tetrahydrofuran (THF), benzene, and toluene were dried over NaAlH$_4$ and distilled under nitrogen just prior to use.

Alkyl Halides. Methyl bromide (Matheson 99.5% purity) was dried and purified by passing through a 30-cm tube of NaOH pellets and then through a 70-cm tube of Linde 4A Molecular Sieve. Fisher reagent grade *tert*-butyl chloride and allyl bromide were distilled through an 18-inch glass-helix-packed column.

Transition Metals. FeCl$_3$ (Fisher sublimed) was opened only in the glove box and used without further purification.

Organometallic Compounds. Grignard reagent solutions were prepared as previously described.[3] Grignard reagents were analyzed by hydrolyzing an aliquot with distilled water, adding excess standard H$_2$SO$_4$, and back-titrating with standard NaOH to a phenolphthalein end point. Magnesium was determined by titrating hydrolyzed samples with standard EDTA solution at pH 10 using Eriochrome Black T as an indicator. In some cases halide was determined by titration with AgNO$_3$ and back-titration by KCNS with ferric alum indicator. In some cases the amount of active C–Mg was determined by titrating active Grignard reagent with dry 2-butanol in xylene using 2,2'-biquinoline as an indicator. In those cases where all four types of analysis were carried out, the ratio halide:C–Mg:Mg:total base was within 3% of 1.0:1.0:1.0:1.0. Lithcoa *tert*-butyllithium was analyzed by standard Gilman double-titration method. Methyllithium, LiCuMe$_2$, Li-Cu$_2$Me$_3$, (Li$_2$CuMe $\rightleftharpoons$ LiCuMe$_2$ + MeLi), and LiCu(*t*-Bu)$_2$ were prepared as described elsewhere[13,14] and were stored at −78 °C prior to use.

Others. The preparation of 3-methyl-*cis*-2,2,6,6-tetramethyl-hept-4-en-3-ol, 3-methyl-*trans*-2,2,6,6-tetramethylhept-4-en-3-ol, 5-methyl-2,2,6,6-tetramethyl-3-heptanone, and *cis*- and *trans*-2,2,6,6-tetramethylhept-4-en-3-ol has been previously described.[12,15] Eastman highest purity *p*-dinitrobenzene was used without further purification.

Preparations. Ketones. *trans*-2,2,6,6-Tetramethylhept-4-en-3-one (trans enone) was prepared as previously described.[12]

***cis*-2,2,6,6-Tetramethylhept-4-en-3-one (Cis Enone).** A solution of 11.19 g (66.6 mmol) of trans enone in 250 ml of hexane was photolyzed for 2 h with a high-intensity lamp using a quartz filter. The solution (44% cis) was cooled to −78 °C for 2 h and then filtered. The solid (trans enone) was recycled for further photolysis. The hexane was removed under vacuum and the mixture (72% cis) was further purified by preparative GLC. The product obtained was generally >99% pure by GLC. Upon standing the cis enone slowly isomerized so fresh batches were prepared regularly. NMR (CDCl$_3$, Me$_4$Si); 18 H singlet at δ 1.12, 2 H vinylic ab multiplet centered on 5.97 (J_{ab} = 12 Hz).

Solutions of these ketones were stored in a glove box and shielded from light prior to use.

Miscellaneous. 3-*tert*-Butyl-*trans*-2,2,6,6-tetramethylhept-4-en-3-ol. To 5.0 mmol of trans enone in 12.5 mL of ether at −78 °C was added 7.0 mmol of *t*-BuLi in solution and the mixture was then reacted at −25 °C for 7 h. After hydrolysis with saturated NH$_4$Cl/H$_2$O, GLC showed a mixture which was subsequently separated and identified by preparative GLC and NMR and mass spectroscopy. The products were 1,2-reduction, trans-1,2-addition, and 1,4-addition products. The latter two products predominated. (They have retention times close enough together to make preparative GLC difficult, but the ketone can be moved away by further reaction of the mixture with allylmagnesium bromide.) The trans-1,2-addition product was characterized: NMR (CHCl$_3$, Me$_4$Si) 27 H singlet at 1.03, 1 H broad singlet at 1.57, 2 H vinylic ab pattern centered on 5.60 (J_{ab} = 16 Hz); IR (neat, film) peaks at 3610 (–OH), 3010 (=CH), 2960 (–CH), 1692 (C=C), 1477, 1390, 1365 (CH and –CH$_3$ bending), 972 cm^{-1} (*trans*-CH=CH); mass spectrum, weak molecular

ion peak at *m/e* 226, M − L peak at 225, and abundant fragments at 169, 154, 111, 95, 83, 69, 57, 55, 43, 41, and 29, metastable at 135; bp 61–63 °C (0.2 mm); n^{25}D 1.4583. Anal. Calcd for C$_{15}$H$_{30}$O: C, 79.58; H, 13.36. Found: C, 79.56; H, 13.34.

3-*tert*-Butyl-*cis*-2,2,6,6-tetramethylhept-4-en-3-ol. To 5.0 mmol of cis enone in 12.5 mL of ether at −78 °C was added 7.0 mmol of *t*-BuLi in 3.5 mL of hexane. The mixture was reacted for 7 h at −25 °C and then hydrolyzed with saturated NH$_4$Cl/H$_2$O. GLC of the crude product showed a mixture which was subsequently separated and identified by preparative GLC, and NMR and mass spectroscopy. The products were 1,2-reduction, trans-1,2-addition, 1,4-addition, and cis-1,2-addition products. The latter product predominated. The cis-1,2-addition product was characterized: NMR (CDCl$_3$, Me$_4$Si) 18 H singlet at δ 1.08, 9 H singlet at 1.18, 1 H broad singlet at 1.67, 2 H vinylic pattern at 5.38; IR (neat, film) peaks at 3635 (–OH), 3010 (=CH), 2960 (–CH), 1665 (C=C), 1482, 1373 (–CH and –CH$_3$ bending) 725 cm^{-1} (*cis*-CH=CH); mass spectrum, weak molecular ion peak at *m/e* 226, M − 1 peak at 225, and abundant fragments at 169, 151, 111, 95, 83, 69, 58, 55, 43, 41, and 28, metastable at 135; bp 74 °C (0.2 mm); n^{25}D 1.4701. Anal. Calcd for C$_{15}$H$_{30}$O: C, 79.58; H, 13.36. Found: C, 79.73; H, 13.27.

5-*tert*-Butyl-2,2,6,6-tetramethyl-3-heptanone. To 10.0 mmol of LiCu(*t*-Bu)$_2$ in 5 mL of hexane, 2.5 mL of ether, and 35 mL of Me$_2$Si at −78 °C was added 5.0 mmol of trans enone in 12.5 mL of ether. The mixture was reacted at −55 °C for 2 h, stored at −78 °C for 16 h, and then placed in a −55 °C bath which was allowed to slowly warm to room temperature (3 h). After hydrolysis (with saturated NH$_4$Cl/H$_2$O), the layers were separated and the ether was removed. GLC of the crude product showed a mixture which was subsequently separated and identified by preparative GLC and NMR and mass spectroscopy. The products were 1,2-reduction, 1,2-addition, dimer (probably at the 5 position), and 1,4-addition products. The latter product predominated. The 1,4-addition product was characterized: NMR (CDCl$_3$, Me$_4$Si) 18 H singlet at δ 0.95, 9 H singlet at 1.18, 1 H multiplet at 2.17, 2 H doublet at 2.48; IR (neat, film) peaks at 2965, 1482, 1370 (various C–H vibrations), and 1714 cm^{-1} (C=O); mass spectrum, molecular ion peak at *m/e* 226, with abundant fragments at 169, 113, 85, 71, 57, 43, 41, and 29; bp 57–59 °C (0.1 mm); n^{25}D 1.5409. Anal. Calcd for C$_{15}$H$_{30}$O: C, 79.58; H, 13.36. Found: C, 79.53; H, 13.37.

3-Allyl-*cis*-2,2,6,6-tetramethylhept-4-en-3-ol. To 2.9 mmol of cis enone in 36 mL of ether was added 12.0 mmol of allylmagnesium bromide in 14 mL of ether. After 6 h the reaction was hydrolyzed with NH$_4$Cl/H$_2$O. The ether was dried and removed. GLC of the crude reaction mixture showed it to be ~2% trans-1,2-addition, 1% 1,2-reduction, and 97% cis-1,2-addition products. The cis-1,2-addition product was purified by preparative GLC and characterized: NMR (CDCl$_3$, Me$_4$Si) 9 H singlet at δ 0.98, 9 H singlet at 1.12, 1 H broad singlet at 1.68, 2 H multiplet at 2.27, 2 H vinylic ab pattern (J_{ab} = 7 Hz) centered on 5.12 with an overlapping 3 H vinylic pattern centered on 5.0; IR (neat, film) peaks at 3570 (–OH), 3080, 3010 (=CH), 2960 (–CH), 1640 (C=C), 1475, 1385, 1363 (–CH and –CH$_3$ bending), 997, 912 (–CH=CH$_2$), 754 cm^{-1} (*cis*-CH=CH); mass spectrum, very weak molecular ion peak at *m/e* 210 as well as weak peaks at 195, 192, and 177 corresponding to loss of CH$_3$, H$_2$O, and both, abundant fragments at 169, 153, 83, 69, 57, 55, 43, 41, and 29; bp 68–70 °C (0.15 mm); n^{25}D 1.4645. Anal. Calcd for C$_{14}$H$_{26}$O; C, 79.94; H, 12.46. Found: C, 79.85; H, 12.48.

3-Allyl-*trans*-2,2,6,6-tetramethylhept-4-en-3-ol. To 33.0 mmol of trans enone in 250 mL of ether was added 86.0 mmol of allylmagnesium bromide in 100 mL of ether. After 10 h the reaction was hydrolyzed with NH$_4$Cl/H$_2$O. The ether was dried and removed. GLC of the crude mixture showed it to be ~2% 1,2-reduction and 98% trans-1,2-addition products. The trans-1,2-addition product was purified by preparative GLC and characterized: NMR (CDCl$_3$, Me$_4$Si) 9 H singlet at δ 0.90, 9 H singlet at 1.05, 1 H broad singlet at 1.58, 2 H multiplet at 2.33, 2 H vinylic ab pattern (J_{ab} = 12.5 Hz) centered on 5.47 with an overlapping 3 H vinylic pattern centered on 5.0; IR (neat, film) peaks at 3575 (–OH), 3087, 3025 (=CH), 2968 (–CH), 1642 (C=C), 1480 1395, 1368 (–CH and –CH$_3$ bending), 1012, 925 (–CH=CH$_2$), 990 cm^{-1} (*trans*-CH=CH); mass spectrum, very weak molecular ion peak at *m/e* 210 as well as weak peaks at 195, 192, 177 corresponding to loss of CH$_3$, H$_2$O, and both, abundant fragments at 169, 153, 111, 83, 69, 57, 55, 43, 41, and 29; bp 54–56 °C (0.2 mm); n^{25}D 1.4514. Anal. Calcd for C$_{14}$H$_{26}$O: C, 79.94; H, 12.46. Found: C, 79.82; H, 12.44.

1-(2,4-Dimethylphenyl)-1-phenylethanol. To a solution of 0.325 g (1.15 mmol) of 2,4-dimethylbenzophenone in 10 mL of ether was added 2.86 mmol of CH₃MgBr in 2.6 mL of ether. After 7 h the reaction was hydrolyzed with saturated NH₄Cl/H₂O. The mixture was dried and the ether was removed. The product was shown to be >95% pure by NMR spectroscopy (CDCl₃, Me₄Si): 8 H multiplet at δ 6.8 to 7.7, 3 H singlet at 1.83, 3 H singlet at 1.93, 3 H singlet at 2.28, 1 H singlet at 2.20.

1-(2,5-Dimethylphenyl)-1-phenylethanol. To a solution of 0.0541 g (0.259 mmol) of 2,5-dimethylbenzophenone in 10 mL of ether was added 0.465 mmol of CH₃MgBr in 0.20 mL of ether. After 4 h the reaction was hydrolyzed with saturated NH₄Cl/H₂O. The mixture was dried and the ether removed. The product was shown to be >95% pure by NMR spectroscopy (CDCl₃, Me₄Si: 8 H multiplet at δ 7.0–7.6, two 3 H singlets close together at 1.88 and 1.90, 3 H singlet at 2.38, 1 H broad singlet at 2.17.

Methods. Apparatus and Procedure. A Varian A-60D, 60-MHz spectrometer was used for recording nuclear magnetic resonance spectra. GLC analyses were carried out on F & M Models 700 and 720 gas chromatographs. Materials used in this study were transferred in a glove box described elsewhere[16] or in Schlenk tubes under a blanket of nitrogen.

Calibrated syringes equipped with stainless steel needles were used for transfer of reagents. Ketone and metal salt solutions were prepared by weighing the reagent in a tared volumetric flask and diluting with the appropriate solvent. All metal solutions were used within 24 h of preparation.

Reactions in General. Glassware and syringes were flamed and taken into a glove box under vacuum. The appropriate amounts of solvent and ketone solutions were syringed into a septum capped test tube. An appropriate amount of Grignard solution was added with swirling. In these cases in which the reaction was carried out in the presence of an iron salt, the salt was added immediately prior to addition of the Grignard reagent. In general, these reactions used 0.10 mmol of enone and 0.05 mmol of organometallic reagent in 1.5 mL of ether. The rate studies used 0.05 mmol of enone and 0.05 mmol of Grignard reagent in 2.0 mL of ether. After an appropriate reaction time, usually 20 min, the reactions were hydrolyzed with 50 mL of saturated NH₄Cl solution and dried over MgSO₄.

The identification of all the products from the reactions with cis and trans enone was determined by GLC on a 12-ft 20% Carbowax 20M column at 125 °C: injection port temperature, 180 °C; detector temperature, 240 °C; and helium flow rate, 80 mL/min were generally

used. Retention times varied with conditions, but typically were as follows: dodecane, 10.3, cis enone, 12.6, trans enone, 14.9, methyl 1,4-addition product, 17.4, methyl trans-1,2-addition product, 19.7, cis- and trans-1,2-reduction product, 24.8, allyl trans-1,2-addition product, 34.0, allyl cis-1,2-addition product, 50.8, *tert*-butyl trans-1,2-addition product, 38.9, *tert*-butyl 1,4-addition product, 42.9, *tert*-butyl *cis*-1,2-addition product, 68.6 min. Dodecane was employed as internal standard and relative response factors were determined regularly. In some cases cis- and trans-1,2-reduction products were separated on a 12-ft 10% TCEP column at 115 °C, but generally they were analyzed together and identified as "1,2-reduction products".

In general, these reactions had essentially 100% material balances.

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Mechanistic Aspects of Transition Metal and Trichloroacetic Acid Catalyzed Reactions of 3-Oxaquadricyclanes

H. Hogeveen* and B. J. Nusse

Contribution from the Department of Organic Chemistry, University of Groningen, Nijenborgh, Groningen, The Netherlands. Received November 10, 1977

Abstract: The reactivity of 1,5-dicarbomethoxy-3-oxaquadricyclanes toward different catalysts has been found to vary strongly with the type of catalyst used. The various reactions initiate at different sites in the substrates: CCl₃COOH reacts at a cyclopropyl ring atom with inversion of configuration; Rh₂(CO)₄Cl₂ reacts preferentially as a Lewis acid at the C–O–C fragment; to a minor extent oxidative addition of a cyclopropyl ring to the rhodium(1) complex occurs as in the case of the Pd(C₆H₅CN)₂-Cl₂ catalyzed reaction; a kinetic analysis shows that the AgClO₄ catalyzed reaction initiates at two sites (at the C–O–C fragment and at a cyclopropyl ring), both leading to the same reaction product. Compound **1b** reacts much faster than **1a** in the thermal and CCl₃COOH catalyzed reactions in contrast to the metal catalyzed processes.

Introduction

For more than a decade there has been much interest in the interconversion between two ethylene units and a cyclobutane unit catalyzed by transition metal complexes. In 1964 the first report on olefin disproportionation (metathesis) ap-

peared (the conversion of propylene into ethylene and 2-butene over a molybdenum hexacarbonyl–alumina catalyst)[1] and in 1967 the valence isomerization of quadricyclane into norbornadiene was reported[2] (Scheme I).

Much experimental and theoretical work has been carried out, as a result of which the original idea of a common under-