(4) A. G. Davies, "Organic Peroxides," Butterworths, London, 1961, p 164; see also references therein.
(5) C. A. Bunton in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Wiley-Interscience, New York, N.Y., 1962, pp 16–18, and references therein.
(6) R. Curci and J. O. Edwards in "Organic Peroxides," Vol. I, D. Swern, Ed., Wiley-Interscience, New York, N.Y., 1970, Chapter 4.
(7) P. Yates and R. J. Crawford, *J. Amer. Chem. Soc.*, **88,** 1561 (1966).
(8) A. T. Blomquist and F. W. Schlaefer, *J. Amer. Chem. Soc.*, **83,** 4547 (1961).
(9) J. Ciabattoni, R. A. Campbell, P. W. Concannon, and C. A. Renner, *J. Amer. Chem. Soc.*, **92,** 3826 (1970).
(10) R. Curci, F. DiFuria, and V. Lucchini, *Spectrosc. Lett.*, **7,** 211 (1974).
(11) S. Sorriso and A. Foffani, *J. Chem. Soc., Perkin Trans. 2,* 2124 (1973).
(12) I. G. Csizmadia, S. A. Houlden, O. Meresz, and P. Yates, *Tetrahedron,* **25,** 2121 (1969).
(13) H. C. Brown and K. Ichikawa, *Tetrahedron,* **1,** 221 (1957).
(14) A. Streitwieser and W. R. Young, *J. Amer. Chem. Soc.*, **91,** 529 (1969).
(15) As pointed out by a referee, the similarity in the log relative rates *vs.* number of ring carbons profile observed for reactions III and IV might be partly fortuitous since tritio deprotonation of cycloalkanes catalyzed by cesium cyclohexylamide (CsCHA) is an $sp^3 \rightarrow sp^3$ case, whereas MCPBA oxidation of α-diazo ketones appears to be $sp^2 \rightarrow sp^2$ from reactants to products. For the latter reactions, however, an $sp^3 \rightarrow sp^3$ case can also be envisaged. In fact, the reaction center should be close to an sp^3 hybrid in the transition state according to the mechanism proposed (eq 1), and for the $>\bar{C}-\overset{+}{N}\equiv N$ group in the ground state there should be structures with sp^3 hybridized carbon only little different in energy than sp^2 hybrids (ref 3).
(16) G. Hedestrand, *Z. Phys. Chem., Abt. B,* **2,** 428 (1929); D. P. Shoemaker and C. W. Garland, "Experiments in Physical Chemistry," McGraw-Hill, New York, N. Y., 1967, Chapter 12.
(17) M. Regitz and J. Ruter, *Chem. Ber.*, **101,** 1263, 2622 (1968).
(18) G. Wittig and A. Krebs, *Chem. Ber.*, **94,** 3260 (1961).
(19) A. T. Blomquist, L. H. Liu, and J. C. Bohrer, *J. Amer. Chem. Soc.*, **74,** 3643 (1952).
(20) J. Fenwick, G. Frater, K. Ogi, and O. P. Strauz, *J. Amer. Chem. Soc.*, **95,** 124 (1973).
(21) N. N. Schwartz and J. H. Blumbergs, *J. Org. Chem.*, **29,** 1976 (1964).

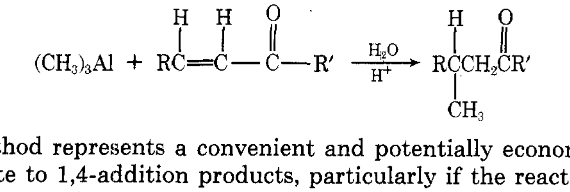
Transition Metal Catalyzed Conjugate Methylation of α,β-Unsaturated Ketones by Trimethylaluminum and Lithium Tetramethylaluminate

Eugene C. Ashby* and George Heinsohn

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

Received June 18, 1974

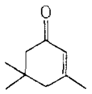
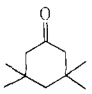
Recently there has been an increased interest in methods for effecting 1,4 addition to α,β-unsaturated systems.[1] In addition to lithium alkylcuprate and copper-catalyzed Grignard reagent addition to α,β-unsaturated compounds, more recent methods show great promise. Brown and Kabalka[2,3] have found that trialkylboranes undergo 1,4 addition to a variety of α,β-unsaturated substrates *via* a free radical chain process. More recently Kabalka and Daley[4] found that trialkylaluminum compounds exhibit analogous behavior when photolyzed at −78° or in the presence of catalytic amounts of oxygen, and were able to demonstrate the intermediacy of free radical species. Because of our interest in the area of transition metal catalyzed reactions of main group organometallic reagents, we were particularly interested in the recent report by Mole, *et al.*,[5] concerning nickel catalyzed conjugate addition of trimethylaluminum to α,β-unsaturated ketones. It would appear that this



$$(CH_3)_3Al + R\overset{H}{C}=\overset{H}{C}-\overset{O}{\overset{\|}{C}}-R' \xrightarrow[H^+]{H_2O} R\underset{CH_3}{\overset{H}{C}}CH_2\overset{O}{\overset{\|}{C}}R' \qquad (1)$$

method represents a convenient and potentially economic route to 1,4-addition products, particularly if the reaction is stereoselective. In an attempt to determine the stereoselectivity of this reaction and in addition to determine the applicability of this method to 1,4-conjugate addition to prostaglandin precursors, we synthesized 4-methyl-2-cyclopentenone, 4-acetoxy-2-cyclopentenone, and 4-methyl-2-cyclohexenone. We wish now to report the results of not only $(CH_3)_3Al$ addition, but also $LiAl(CH_3)_4$ addition to a variety of α,β-unsaturated ketones in order to provide information concerning the scope and stereochemistry of these reactions.

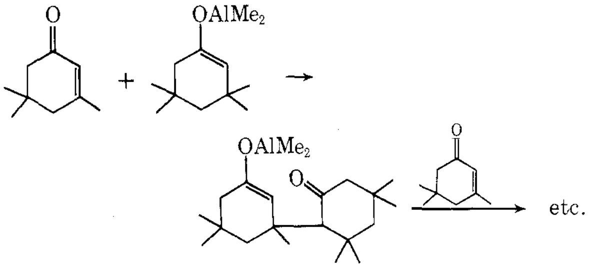
Table I
Reaction of Trimethylaluminum with Isophorone in the Presence of Nickel Acetylacetonate

Time, min	 (mmol)	 (mmol)	Material balance, %
0	1.000	0.000	100
1	0.300	0.680	98
5	0.075	0.838	91
30	0.000	0.845	85
60	0.000	0.863	86
120	0.000	0.850	84

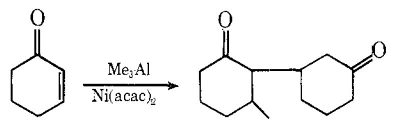
Results and Discussion

Table I presents data obtained by sequential quenching of aliquots from the reaction of trimethylaluminum with 3,5,5-trimethyl-2-cyclohexenone (isophorone) in the presence of 3.0 mol % nickel acetylacetonate [$Ni(acac)_2$].

Several features of Table I are striking. While Mole, *et al.*,[5] suggest typical reaction times of 18 hr for the reaction of α,β-unsaturated ketones with trimethylaluminum in the presence of $Ni(acac)_2$, our data indicate that methylation is essentially complete in less than 30 min. The only other product formed is polymer and its formation seems to occur only while unreacted isophorone is present. This suggests that the polymer is formed by Michael addition to the aluminum enolate of the product to the α,β-unsaturated ketone according to eq 2. The isolation of 1 after nickel acetylacetonate catalyzed addition of trimethylaluminum to 2-cyclohexenone provides additional support for this suggestion.



(2)



(3)

1

In Table II are listed the results obtained for the catalyzed reaction of trimethylaluminum with isophorone and 2-cyclohexenone. In all cases the starting material was entirely consumed and no other volatile products were formed. It is apparent from the data that ether is the solvent of choice and that cupric acetylacetonate is an effective catalyst. Although Mole[5] suggests that cobalt acetylacetonate was an effective catalyst, in our hands only starting material was recovered after attempted reaction of isophorone with trimethylaluminum in the presence of 3 mol % cobalt acetylacetonate. This result, however, suggests partici-

Table II
Transition Metal Catalyzed Reaction of Isophorone (2) and 2-Cyclohexenone (3) with Trimethylaluminum[a]

Run	Ketone	Catalyst[b]	Solvent	Time, hr	Temp, °C	% 1,4 addition	% 1,2 addition
1	2	Ni(acac)$_2$	Et$_2$O	1	0	86	
2	2	Ni(acac)$_2$	Et$_2$O	2	22	86	
3	2	Ni(acac)$_2$	THF	1	0	58	
4	2	Cu(acac)$_2$	Et$_2$O	2	22	85	
5	3	Ni(acac)$_2$	Et$_2$O	1	0	44	7
6	3	Ni(acac)$_2$	Et$_2$O	2	−30	29	6
7	3	Ni(acac)$_2$	THF	2	0	41	6
8	3	Ni(acac)$_2$	PhH	2	0	35	8

[a] Each run employed 1.0 mmol of Me$_3$Al, 1.0 mmol of ketone, and 0.03 mmol of metal acetylacetonate in 10 ml of solvent. [b] Added as *ca.* 0.03 *M* solution in THF.

Table III
Transition Metal Catalyzed Reaction of Isophorone with Lithium Tetramethylaluminate[a]

Run	Catalyst	Time, hr	Temp, °C	% 1,4 addition	% 1,2 addition	% recovered ketone
9	Ni(acac)$_2$	2	22	80		
10	Ni(acac)$_2$	112	22	8	27	61
11	Cu(acac)$_2$	2	22	73		
12	Ni(acac)$_2$	1	0	58		18
13[b]	Ni(acac)$_2$	1	0	29		48

[a] Each run employed 1.0 mmol of lithium tetramethylaluminate, 1.0 mmol of isophorone, 0.03 mml of metal acetylacetonate added as a *ca.* 0.03 *M* solution in THF, and 10 ml of ether as solvent. [b] Lithium tetramethylaluminate solution stored for 24 hr and clear supernate employed in this run.

Table IV
Stereochemistry of Conjugate Methylation of 4-Methyl-2-cyclohexenone

Run	Catalyst	Reagent	Time, hr	Temp, °C	% 1,4 addition	% trans	% cis
14	Ni(acac)$_2$	Me$_3$Al	1	0	66	84	16
15	Ni(acac)$_2$	LTA	2	22	62	87	13

pation by the transition metal since 1,2 addition would have been observed in its absence.[6] As would be expected, polymer formation occurs to a greater extent with 2-cyclohexenone than with isophorone presumably due to less steric hindrance at the terminal carbon atom of the α,β-unsaturated system. It is noteworthy that reaction of a twofold molar excess of isophorone with trimethylaluminum under conditions otherwise identical with those of entry 2 leads to isolation of 43% of the 1,4 product (based on isophorone) showing that only one methyl group of the organometallic compound is available for reaction.

Table III reports results obtained from transition metal catalyzed reaction of isophorone with lithium tetramethylaluminate (LTA). Except for recovery of starting material from runs 10, 12, and 13, no other volatile products were observed. Conjugate addition with LTA is considerably slower than with trimethylaluminum, the former reaction requiring 2 hr at 22° before all starting material was consumed. Unlike the reactions with trimethylaluminum, cupric acetylacetonate is a less efficient catalyst than the corresponding nickel salt. For optimum results, it is essential that the LTA be used as quickly as possible after preparation from methyllithium and trimethylaluminum. Upon standing, the initially clear solution becomes cloudy and within several hours precipitation is apparent. Although analysis of the clear supernatant solution after precipitation gives a ratio of lithium/aluminum/methyl of 1.00:0.97:3.98, comparison of runs 12 and 13 show that the efficiency of conjugate addition is seriously impaired using this solution. In an experiment employing a twofold molar excess of isophorone under conditions otherwise identical with run 9, 3,3,5,5-tetramethylcyclohexanone was isolated in 41% yield (based on isophorone) demonstrating that only one methyl group per LTA is available for reaction.

Table IV provides data that demonstrate the stereochemistry of the reaction of the catalyzed conjugate methylation of 4-methyl-2-cyclohexenone by trimethylaluminum and LTA. By way of comparison, Riviere and coworkers[7,8] report formation of 3,4-dimethylcyclohexanone with trans/cis ratio of 72:28 for cuprous chloride catalyzed addition of methylmagnesium bromide to 4-methyl-2-cyclohexenone and trans/cis ratio of 91:9 using LiCu(CH$_3$)$_2$.[7]

Synthesis of 4-acetoxy- and 4-methyl-2-cyclopentenone provided model prostaglandin systems for the determination of the stereochemistry of transition metal catalyzed 1,4 addition by reaction with (CH$_3$)$_3$Al or LiAl(CH$_3$)$_4$. Unfortunately, under a variety of conditions both of the above ketones produced only polymer.

Experimental Section

General. The metal acetylacetonates used in this study were prepared by refluxing the appropriate metal acetate with 1.5 equiv of 2,4-pentanedione in methanol for 2 hr. The product was isolated by crystallization from methanol. Ether and THF were freshly distilled from LiAlH$_4$. Reaction vessels were flash flamed under nitrogen. Product analyses were performed on an F and M Model 720 gas chromatograph using a 20 ft column of 5% Carbowax 20M on Chromosorb W at a flow rate of 55 ml of He/min.

Conjugate Methylation with Trimethylaluminum. To a 50-ml reaction vessel was added sufficient solvent to bring the final volume to 10 ml, substrate ketone (1.0 mmol), and the appropriate metal acetylacetonate (0.03 mmol., *ca.* 1 ml of 0.03 *M* solution in THF). The mixture was brought to the appropriate temperature and trimethylaluminum (1.0 mmol, *ca.* 1 ml of 1 *M* solution in ether) added over a 2-min period causing a yellow to brown color to develop immediately. After the desired period of time, the reaction was quenched with water (*ca.* 0.3 ml) and dried over MgSO$_4$; 1.0 mmol of internal standard was added, and the product was analyzed by gas chromatography. Ethyl benzoate was employed as the standard for reactions involving isophorone, and the glc column temperature was 140°. Under these conditions, retention times of 11.7, 13.5, and 26.1 min were observed for 1,3,5,5-tetramethyl-2-cyclohexenol, 3,3,5,5-tetramethylcyclohexanone, and isophorone, respectively. When 2-cyclohexenone was the substrate, *n*-octyl alcohol was employed as the internal standard and the glc column temperature was 125°. Under these conditions, retention times of 11.2, 13.0, and 20.5 min were noted for 1-methyl-2-cyclohexenol, 3-methylcyclohexanone, and 2-cyclohexenone, respectively. In all cases the identity of products (including adduct 1) was confirmed by comparison with authentic samples.

Conjugate Methylation with Lithium Tetramethylaluminate. To a 50-ml reaction vessel was added sufficient solvent to bring the final volume to 10 ml, trimethylaluminum (1.0 mmol, *ca.* 1 ml of 1 *M* solution in ether), and methyllithium (1.0 mmol, *ca.* 1 ml of 1 *M* solution in ether). Without delay the substrate ketone (1.0 mmol) and the appropriate metal acetylacetonate (0.03 *M*, *ca.* 1 ml of 0.03 *M* solution in THF) were added, the latter causing formation of a yellow to brown color. After reaction, water (0.3 ml) was added and the mixture dried (MgSO$_4$); internal standard was added, and the product analyzed as described above.

Acknowledgment. We are happy to acknowledge support of this work by the National Science Foundation.

Registry No.—(CH$_3$)$_3$Al, 75-24-1; isophorone, 78-59-1; Ni(acac)$_2$, 3264-82-2; 3,3,5,5-tetramethylcyclohexanone, 14376-79-5; 2-cyclohexenone, 930-68-7; Cu(acac)$_2$, 13395-16-9; lithium tetramethylaluminate, 14281-94-8; 4-methyl-2-cyclohexenone, 5515-

76-4; *trans*-3,4-dimethylcyclohexanone, 28023-45-2; *cis*-3,4-dimethylcyclohexanone, 27922-05-0.

References and Notes

(1) G. H. Posner, *Org. React.*, **19,** 1 (1972).
(2) H. C. Brown and G. W. Kabalka, *J. Amer. Chem. Soc.*, **92,** 712 (1970).
(3) H. C. Brown and G. W. Kabalka, *J. Amer. Chem. Soc.*, **92,** 714 (1970).
(4) G. W. Kabalka and R. F. Daley, *J. Amer. Chem. Soc.*, **95,** 4428 (1973).
(5) T. Mole, CSIRO, P. O. Box 4331, Melbourne, Australia, private communication. A. E. Jeffery, A. Meisters, and T. Mole, *J. Organometal. Chem.*, in press.
(6) Y. Baba, *Bull. Chem. Soc. Jap.*, **41,** 928 (1968).
(7) N. T. Luang-Thi and H. Riviere, *C. R. Acad. Sci.*, **267,** 776 (1968).
(8) H. Riviere and J. Tastain, *Bull. Soc. Chem. Fr.*, 568 (1969).

Effects of Base Association upon Geometrical Orientation in Elimination from 1-Phenyl-2-propyl Chloride in Potassium *tert*-Butoxide–*tert*-Butyl Alcohol

Sergio Alunni, Enrico Baciocchi,* Renzo Ruzziconi, and Marco Tingoli

Dipartimento di Chimica, Università di Perugia, 06100 Perugia, Italy

Received April 22, 1974

Base association was clearly shown to exert a strong influence upon positional and geometrical orientation in base-promoted anti β-eliminations from 2-alkyl halides and arenesulfonates in t-BuOH.[1] Regarding geometrical orientation it was observed that base association is responsible for the generally low trans:cis 2-alkene ratios found for the reaction of these substrates with t-BuOK. Accordingly, the trans:cis 2-alkene ratios were found to significantly increase when the reaction is carried out in the presence of crown ethers which are able to convert contact ion pairs or ion pair aggregates into separated ions. This trend was suggested to be originated by the larger steric requirements of the associated base.

Interestingly, low trans:cis olefin ratios in t-BuOK–t-BuOH (especially with respect to those in EtO$^-$–EtOH and MeO$^-$–MeOH) are considered as the "normal pattern" of β-elimination reactions which proceed *via* an anti mechanism, since, by this mechanism, contact ions are expected to lead to preferential formation of cis olefin.[2] Deviations from this pattern are considered highly indicative of the intervention of a syn mode of β-elimination, since it is well known[2c] that syn elimination leads nearly exclusively to the trans olefin and is favored by base association.

We wish now to report that similar conclusions do not apply to the elimination reactions of β-phenyl activated systems. We have studied the β-elimination reactions of 1-phenyl-2-propyl chloride in t-BuOK–t-BuOH and found (see Table I) that the *trans*- to *cis*-1-phenylpropene ratio is significantly larger than those in EtONa–EtOH and MeONa–MeOH; a significant decrease of this ratio is obtained using t-BuON-n-Bu$_4$ or crown ether complexed t-BuOK. Clearly, base association plays an important role in determining the trans:cis olefin ratios also in the elimination reactions of 1-phenyl-2-propyl halides; however, the pattern is exactly the opposite of that found for the elimination reactions of nonactivated alkyl halides. This striking difference cannot be attributed to the intervention of a syn mechanism of elimination in the phenyl activated series, since we have evidence that this reaction path is of very little importance in the case of 1-phenyl-2-propyl chloride;[3] it results therefore that the geometrical orientation in the anti eliminations from β-phenyl activated substrates is influenced by steric effects and/or basicity in a different way from the anti eliminations of nonactivated substrates.

Table I
Trans:Cis Olefin Ratios in the E2 Eliminations from 1-Phenyl-2-propyl Chloride in Various Solvent–Base Systems at 60° [a]

Solvent–Base	*trans*- to *cis*-1-Phenylpropene
MeOH–MeONa[b]	23.5 ± 0.1
EtOH–EtONa[c]	25.0 ± 0.1
t-BuOH–t-BuOK[d]	72 ± 5
t-BuOH–t-BuOK[e]	45 ± 1
t-BuOH–t-BuON-n-Bu$_4$[f]	37.7 ± 0.1

[a] Determined by glpc. Each value is the average of at least three determinations. The initial concentration of 1-phenyl-2-propyl chloride was ~0.02 M. According to blank experiments the trans:cis ratios are not significantly affected by the isomerization reactions of allylbenzene (formed in a very little amount) and of *cis*- and *trans*-1-phenylpropene. [b] [MeONa] = 2.3 M. Reaction time 15 hr. In the absence of MeONa no production of chloride ions was observed after 70 hr. [c] S. Alunni and E. Baciocchi, *Tetrahedron Lett.*, 205 (1973). With EtOK the trans:cis ratio is 28. [d] [t-BuOK] = 0.2–0.8 M. Reaction time 50–210 min. No appreciable variation of the trans:cis ratio with t-BuOK concentration was observed. [e] In the presence of dicyclohexyl-18-crown-6. [t-BuOK] = 0.17 M. Reaction time 5–15 min. [f] Prepared by mixing 0.3–0.5 M t-BuOK-t-BuOH with appropriate amounts of n-Bu$_4$NBr. Reaction time 30–75 min.

At present, we have no explanation of this phenomenon, even though it may be recalled that in the eliminations from β-phenyl activated substrates the trans/cis ratios derive from differences in the conjugation extent of the phenyl group with the developing negative charge at the β carbon in addition to differences in the nonbonded interactions at C_α and C_β, as it occurs in the resulting olefins. However, it seems important to point out, in the light of this result and the recent data on the leaving group effects,[5] that considerable caution must be exerted in applying conclusions reached from studies of elimination reactions of β-phenyl activated substrates to the elimination reactions of nonactivated substrates and vice versa.

Experimental Section

Materials. 1-Phenyl-2-chloropropane. A solution of 29 g of thionyl chloride in 125 ml of anhydrous benzene was added at 0° and under stirring to a solution of 25 g of 1-phenyl-2-propanol (Fluka) and 4 g of pyridine in 420 ml of anhydrous benzene. After standing overnight the mixture was refluxed for 3 hr. The mixture was then cooled and washed with cold water, diluted sulfuric acid, 10% solution of sodium bicarbonate, and a solution of sodium thiosulfate. After the mixture was dried on sodium sulfate and the solvent was removed, distillation at reduced pressure gave 16.4 g (55% yield) of 1-phenyl-2-chloropropane, bp 100° (30 mm). *Anal.* Calcd for $C_9H_{11}Cl$: Cl, 22,9. Found: Cl, 22,6.

***cis*-1-Phenylpropene** was prepared by decarboxylation of α-metylcinnamic acid, according to a procedure described in the litterature,[6] and purified by fractional distillation on a Todd column, bp 65° (12 mm), $n^{22.5}\text{D}$ 1.5415 (lit.[6] $n^{20}\text{D}$ 1.5430). Its purity (>99.5%) was checked by glpc.

***trans*-1-Phenylpropene** and **allylbenzene** were commercial products (Fluka) purified by distillation. Their purity (glpc) was 99%.

Dicyclohexyl-18-crown-6 ether was prepared according to the procedure described by Pedersen.[7]

Base–Solvent Solution. Methanol was refluxed with magnesium and resublimed iodine and fractionally distilled. Absolute ethanol was refluxed with sodium and diethyl phthlate and fractionally distilled. t-Butylalcohol was distilled after treatment with potassium metal. Solutions of alkoxide were obtained by reactions,