H, t), 1.33 (8 H, bs), 2.20 (2 H, bs), 5.2–5.8 (1 H, m), 6.2–6.6 (1 H, m).

Anal. Calcd for $C_{16}H_{15}F_{17}$: C, 36.24; H, 2.85; F, 60.91. Found: C, 36.14; H, 2.94; F, 60.95.

Synthesis of Olefin 16. This compound, prepared as described above from 10.9 g (0.02 mol) of **1a**, 4.1 g (0.021 mol) of methyl undec-10-enoate, and 0.9 g (0.005 mol) of sodium *p*-toluenesulfinate, had the following properties: proton NMR (δ, $CDCl_3/Me_4Si$) 1.1–1.9 (12 H, m), 1.9–2.5 (4 H, m), 3.68 (3 H, s), 5.2–6.0 (1 H, M), 6.0–6.7 (1 H, M); fluorine NMR (δ, $CDCl_3/CFCl_3$) –81.52 (3 F), –126.67 (2 F), –124.04 (2 F), –123.21 (2 F), –122.35 (6 F), –111.79 and –107.14 (2 F).

Anal. Calcd for $C_{20}H_{21}O_2F_{17}$: C, 38.97; H, 3.43; F, 52.40. Found: C, 39.15; H, 3.43; F, 52.40.

Synthesis of 1:2 Adduct 3. The above general procedure with 9.1 g (0.02 mol) of 1,4-diiodoperfluorobutane, 9.4 g (0.1 mol) of norbornene, and 1.8 g (0.01 mol) of sodium *p*-toluenesulfinate gave 12.21 g of crude product. The product was chromatographed over 300 g of silica gel packed in hexane. The column was eluted with 3 L of hexane, taking 100-mL fractions. Fractions 12–25 were combined and concentrated to 10.6 g (83%) of **3** as a white solid: mp 114–115 °C; proton NMR (δ, $CDCl_3/Me_4Si$) 1.1–2.7 (9 H, m), 4.33 (1 H, m); fluorine NMR (δ, $CDCl_3/CFCl_3$) –121.28 (4 F), –117.8 (4 F, AB quartet, J = 282 Hz).

Anal. Calcd for $C_{18}H_{20}F_8I_2$: C, 33.66; H, 3.14; F, 23.67. Found: C, 33.58; H, 2.97; F, 23.52.

Reaction of Perfluorooctyl Iodide, Ethene, and Sodium *p*-Toluenesulfinate in DMF. A nitrogen-swept 200-mL pressure vessel was charged with 3.6 g (0.02 mol) of sodium *p*-toluenesulfinate, 90 mL of DMF, and 10.9 g (0.02 mol) of perfluorooctyl iodide. The vessel was closed, cooled in dry ice and acetone, and evacuated. Ethene (10 g, 0.42 mol) was condensed in the vessel. The mixture was agitated overnight at room temperature. The vessel was vented to 1 atmosphere pressure, and the contents were poured into 300 mL of ether and 300 mL of water. The ether solution was washed with 3 × 100 mL of water and dried over anhydrous magnesium sulfate. GLPC analysis of the ether solution showed three major peaks after the solvent:

peak	R_t, min	area, %
1	1.87	31.2
2	5.18	20.0
3	11.77	34.0

The first peak is unreacted perfluorooctyl iodide. The ether solution was concentrated on the rotary evaporator to 10.03 g of oily orange solid. The crude product adsorbed on 30 g of silica gel was added to a column of 300 g of silica gel packed in hexane. The column was eluted with 1 L of hexane, 1 L of 5% ether in hexane, 0.5 L of 10% ether in hexane, 1 L of 25% ether in hexane, and 3 L of 35% ether in hexane, taking 100-mL fractions. From fractions 6–9 was isolated 1.92 g (17%) of 1,1,2,2-H_4-perfluorodecyl iodide (**17**): mp 56–57 °C; proton NMR (δ, $CDCl_3/Me_4Si$) 2.3–3.1 (2 H, m), 3.1–3.5 (2 H, m); fluorine NMR (δ, $CDCl_3/CFCl_3$) –81.38 (3 F), –126.63 (2 F), –122.26 (6 F), –123.15 (2 F), –123.85 (2 F), –115.45 (2 F). From fractions 32–58 was isolated 3.94 g (33%) of $C_8F_{17}CH_2CH_2SO_2C_6H_4CH_3$ (**18**) as a white solid: mp 109–111 °C; proton NMR (δ, $CDCl_3/Me_4Si$) 2.47 (3 H, s) overlapping 2.2–2.9 (2 H, m), 3.1–3.4 (2 H, m), 7.6 (4 H, q); fluorine NMR (δ, $CDCl_3/CFCl_3$) –81.40 (3 F), –126.64 (2 F), –121.8 to –123.9 (12 F).

Anal. Calcd for $C_{17}H_{11}F_{17}SO_2$: C, 33.90; H, 1.84; F, 53.63; S, 5.32. Found: C, 33.83; H, 1.92; F, 53.57; S, 5.49.

Reaction of Perfluorooctyl Iodide with the Sodium Salt of Diethyl Methylmalonate. Perfluorooctyl iodide (10.9 g, 0.02 mol) was added in one portion to a degassed solution of 3.9 g (0.02 mol) of sodium diethyl methylmalonate in 75 mL of Me_2SO. The cloudy yellow solution was stirred overnight. A short-path distillation head and receiver cooled in dry ice and acetone were attached to the flask. The system was gradually evacuated to 0.5 mm. After $^1/_2$ h, the receivor contained 2.3 g (27%) of 1-H-perfluorooctane, identified by GLPC and NMR comparisons with an authentic sample. The liquid remaining in the reaction flask was poured into 200 mL of ice water containing 5 mL of concentrated HCl. The aqueous solution was extracted with 3 × 100 mL of ether. The combined extracts were washed with 3 × 100 mL of water and dried over anhydrous magnesium sulfate. GLPC analysis, as above, showed only two peaks after solvent which were assigned to unreacted **1a** and the malonate dimer **21**. The ether solution was concentrated on a rotary evaporator to an oil. Bulb-to-bulb distillation of the oil at 0.5 mm and a bath temperature of 160 °C gave 2.7 g (39%) of **21** as a colorless liquid: proton NMR (δ, $CDCl_3/Me_4Si$) 1.08–1.48 (15 H, two triplets + singlet), 3.51 (1 H, t), 4.14 and 4.16 (8 H, two quartets).

Registry No. **1a**, 507-63-1; **2a**, 89883-21-6; **2b**, 34542-08-0; **2c** (isomer 1), 96791-92-3; **2c** (isomer 2), 96893-59-3; **3**, 96791-83-2; **4**, 96791-88-7; **5** (Rt = $F(CF_2)_8$), 96791-86-5; **6**, 96791-81-0; **7**, 38550-35-5; **8**, 96791-89-8; **9**, 96825-33-1; **11** (R = $F(CF_2)_8$), 96791-87-6; **12**, 96107-50-5; **13**, 67103-04-2; **14**, 96791-90-1; **15**, 96791-91-2; **16**, 96791-82-1; **17**, 2043-53-0; **18**, 96791-84-3; **19**, 335-65-9; **20**, 96791-80-9; **21**, 17696-77-4; $PhsC_8F_{17}$, 89883-19-2; $NaC(CH_3)(CO_2C_2H_5)_2$, 18424-77-6; $(CF_3)_2CFI$, 677-69-0; $C_7F_{15}C$-$FICF_3$, 96791-85-4; *p*-$CH_3CONHC_6H_4SO_2Na$, 15898-43-8; sodium diethyl phenylmalonate, 28744-77-6; sodium benzenesulfinate, 873-55-2; sodium *p*-toluenesulfonate, 824-79-3; sodium diethyl methylmalonate, 18424-77-6; sodium diethyl malonate, 996-82-7; norbornene, 498-66-8; 1-octene, 111-66-0; methyl 10-undecenoate, 111-81-9; 1,4-diiodoperfluorobutane, 375-50-8; ethene, 74-85-1; propene, 115-07-1; allylbenzene, 300-57-2; allyl acetate, 591-87-7; norbornadiene, 121-46-0; cyclopentene, 142-29-0; sodium methylsulfinate, 20277-69-4.

Single Electron Transfer in the Reaction of Enolates with Alkyl Halides

E. C. Ashby* and J. N. Argyropoulos

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

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Single electron transfer (SET) in the reaction of a model system consisting of lithiopropiophenone with primary neopentyl type alkyl halides and tosylate was investigated by (1) the use of an appropriate cyclizable alkyl radical probe, (2) observing the effect of varying the leaving group on reaction rate and product distribution, (3) studying the effect of light, di-*tert*-butyl nitroxyl radical, and *p*-dinitrobenzene on the rate of reaction, (4) observing the consequence of varying solvent composition on both the reaction rate and product distribution, and (5) studying the effects of the radical traps, dicyclohexylphosphine and 1,4-cyclohexadiene, on product composition. The results of these studies indicate that single electron transfer is the major reaction pathway involved in the reaction of the enolate with the alkyl iodide in HMPA and that the corresponding bromide and tosylate react by an S_N2 process.

The reaction of an enolate anion with an alkyl substrate (halide or tosylate) is well-recognized as an important synthetic reaction in organic chemistry.[1] Although the mechanism of this reaction is generally believed to proceed

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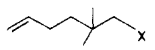
Table I. Effect of Leaving Group on the Reaction of Lithiopropiophenone with 1-Halo-2,2-dimethyl-5-hexenes 12–14 in HMPA[a]

expt		time, h	unreacted starting material	% yield 1	2	3	4	5	6	7
1	X = I	10	48	0[c]	tr[b,d]	tr	42	8.2	0.74	0
2	X = I	60	8.0	0	1.0	0.88	66	11	1.0	0
3	X = Br	60	76	0	0	0	20	0.70	0	0
4	X = Br	170	57	0	0	0	30	0.73	0	0
5	X = OTs	60	98	0	0	0	4.4	0	0	0

[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl substrate:lithiopropiophenone) and 0.10 M in alkyl substrate at room temperature. [b] 0.10 < % yield < 0.50. [c] % yield < 0.10. [d] tr = trace.

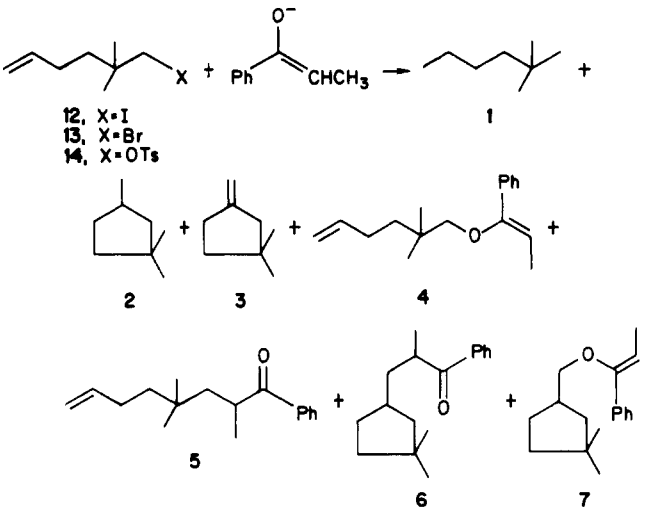
by an S_N2 process, Kornblum has demonstrated that for reactions involving *p*-nitrobenzyl chloride a $S_{RN}1$ type radical–radical anion chain mechanism is involved.[2] Russell has also shown that the $S_{RN}1$ mechanism is involved in the reaction of $XCMe_2NO_2$ (X = Cl, NO_2, or *p*-$MeC_6H_4SO_2$) with lithium enolates.[3] Bunnett later proposed this mechanistic pathway for aromatic substitution reactions.[4] Furthermore, Zook suggested that typical aliphatic halides could be reacting with enolate anions by an electron-transfer process when he observed small quantities of alkanes in his reaction mixtures.[5]

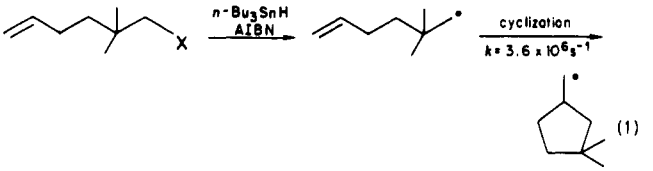
The ability of an enolate anion to serve as a one electron donor toward a variety of other organic substrates is well documented. Examples of such substrates include *p*-dinitrobenzene,[6] *p*-nitrobenzoyl esters,[7] and diaryl ketones.[6,8] With this background and our results with reactions of metal hydrides,[9] alkoxides,[10] amides,[11] and cuprates[12] with cyclizable alkyl halide probes, we chose to embark on a detailed mechanistic study involving lithiopropiophenone with cyclizable alkyl halide and tosylate probes.[13]

The radical probe chosen for the present study was 2,2-dimethyl-1-iodo-5-hexene and its bromo and tosylate derivatives. We have successfully used this probe in a number of investigations[9–12] including the mechanistic study of Grignard reagent addition to aromatic ketones.[14] More recently, Beckwith[15] reported that the 2,2-dimethyl-5-hexen-1-yl radical undergoes cyclization at a rate about 15 times faster than that of the parent 5-hexen-1-yl radical[16] (eq 1). Furthermore, the 1-halo-2,2-dimethyl-5-hexenes and the corresponding tosylate cannot undergo elimination when allowed to react with bases such as enolates.[5] If single electron transfer (SET) is taking place in the reaction of lithiopropiophenone with the neopentyl type probes, the radical recombination step of the resulting bulky neopentyl type radical should be slower than that of the 5-hexen-1-yl radical and hence there should be a better opportunity for observing cyclization of the probe. In addition, the steric hindrance of the alkyl substrate should raise the activation energy for the S_N2 process more than that for an SET process. Thus for a sterically hindered system, it is possible that an SET pathway is preferred because the S_N2 pathway is discouraged.[17] For the above reasons, 2,2-dimethyl-1-iodo-5-hexene and its derivatives seemed to be ideal candidates to study the degree that an SET process is possible in the reaction of a lithium enolate with a primary alkyl halide or tosylate.

In the present study, we report the results of reacting a simple enolate, lithiopropiophenone, with primary neopentyl type alkyl halide and tosylate probes in various solvents including HMPA. No systematic studies of simple

Scheme I





(1)

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Table II. Effect of Light, Absence of Light, and Radical Scavenger on the Reaction of Lithiopropiophenone with 2,2-Dimethyl-1-iodo-5-hexene (12) in HMPA[a]

			% yield						
expt	conditions	time, h	12	1	2	3	4	5	6
1	light	10	48	0	tr[b]	tr	42	8.2	0.74
6	no light	10	47	0	tr	tr	44	7.4	0.55
7	0.10 equiv of $(t\text{-Bu})_2NO$	10	48	0	tr	tr	44	7.3	tr

[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl iodide:lithiopropiophenone) and 0.10 M in alkyl iodide at room temperature. [b] tr = trace.

enolates in HMPA are known to our knowledge.[1c] Furthermore, previous attempts to utilize neopentyl type alkyl halides as alkylating agents toward enolates have led to poor yields of alkylation product.[18] In order to determine the degree to which an SET pathway participates in this reaction, we examined the effects of radical scavengers, radical traps, solvent, and leaving group on both reaction rate and product distribution.

Results and Discussion

The reactivity and product orientation of enolate anions in their reactions with alkyl halides and tosylates have been the subject of considerable interest.[1c,19] In this connection we have studied the reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene (12) and its bromo (13) and tosylate (14) derivatives. Scheme I shows the products 1–7 which can be formed in this reaction. The straight-chain O-alkylation product, compound 4, and C-alkylation product, compound 5, can arise from either an S_N2 or SET pathway. The cyclic alkylation products, compounds 6 and 7, as well as the hydrocarbon products, compounds 1–3, can only arise via a radical pathway. The effects of a variety of factors on this product distribution will now be examined in detail.

Effect of Leaving Group. The results of the reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene and its bromo and tosylate derivatives are reported in Table I. The nature of the leaving group has a pronounced effect on both product distribution and rate of reaction.

In all of the reactions (experiments 1–5), the major product is the straight-chain O-alkylation compound. This is not surprising since the O-terminus of the enolate anion lacks the encumbrance due to the lithium cation in a solvent such as hexamethylphosphoramide (HMPA).[1c] Furthermore, O-alkylation is favored in the order RI < RBr < ROTs as is predicted by Pearson's theory of hard and soft acids and bases (HSAB theory).[20] Since the O-terminus is "harder" than the C-terminus, O-alkylation is most favored by the "hardest" leaving group, OTs > Br > I. The O/C ratio at the half-life of the alkyl iodide reaction, experiment 1, is 4.7. On the other hand, the O/C ratio at the half-life of the alkyl bromide reaction, experiment 4, is 41. The reason for the large difference in the O/C ratio of the alkyl iodide and bromide cannot be completely rationalized by HSAB theory; indeed, the two alkyl halides may be reacting by different pathways. It is known that radical reactions give lower O/C ratios than that observed for an S_N2 process.[2]

Further evidence that 2,2-dimethyl-1-iodo-5-hexene may be reacting by a different pathway from its bromo and tosylate derivatives is indicated by the formation of small amounts of hydrocarbons 2 and 3 as well as cyclized C-alkylation product, compound 6. The hydrocarbons can arise from disproportionation of the cyclized radical (radical 2-a in Scheme III). The cyclized C-alkylation product (6), which represents 8.3% of the total C-alkylation products (5, 6), can also arise from radical 2-a in Scheme III by the coupling reaction of the cyclized radical with the enolate radical. Interestingly, no cyclized O-alkylation product, compound 7, was observed. None of the radical byproducts present in the alkyl iodide reaction, experiments 1 and 2, could be detected in the alkyl bromide and tosylate reactions, experiments 3–5, suggesting that the alkyl iodide may be reacting by a different pathway from the alkyl bromide and tosylate. In fact the only product formed in significant amount in the reaction of lithiopropiophenone with the alkyl bromide and tosylate is the O-alkylation product, compound 4.

The reactivity of the cyclizable alkyl halide and tosylate probes was found to strongly rely on the nature of the leaving group. As seen from Table I, the alkyl iodide reaction has an approximate half-life of 10 h. The alkyl bromide reaction is not 50% complete even after 170 h, whereas the tosylate is virtually unreactive. The lack of reactivity for the tosylate appears surprising when one notes that alkyl tosylates normally exhibit reactivity that is similar to that of the corresponding alkyl iodides in their reactions with enolate anions.[21] In fact, Mosher reports that neopentyl tosylate undergoes normal nucleophilic displacements in HMPA solvent with a variety of nucleophiles, except enolates.[22] Hence, the ordering of leaving group ability in the S_N2 process I ~ OTs > Br apparently is not obeyed in the reaction of lithiopropiophenone with the neopentyl type probes in HMPA.

An alternate explanation based on the reduction potentials of alkyl substrates can be given. Electrochemical data concerning the reduction potentials of alkyl halides and tosylates demonstrate that alkyl iodides have lower reduction potentials than alkyl bromides, whereas in tosylates the C–O bond is not electrochemically cleaved.[23] Lipshutz et al. have recently reported electrochemical data that are "in line with the anticipated propensity of an iodide to undergo a one-electron reduction to afford an intermediate radical" but for tosylates "the S–O bond is ultimately broken, suggesting that in their substitution reactions, tosylates participate in a direct two-electron process." Hence, for an SET process, the order of reactivity based on leaving group is R–I > R–Br ≫ R–OTs which is consistent with our observations (Table I).

Effect of Light and Radical Scavenger. The possibility that the O- and C-alkylation products are arising from an $S_{RN}1$ pathway, as illustrated in Scheme II, is

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Scheme II

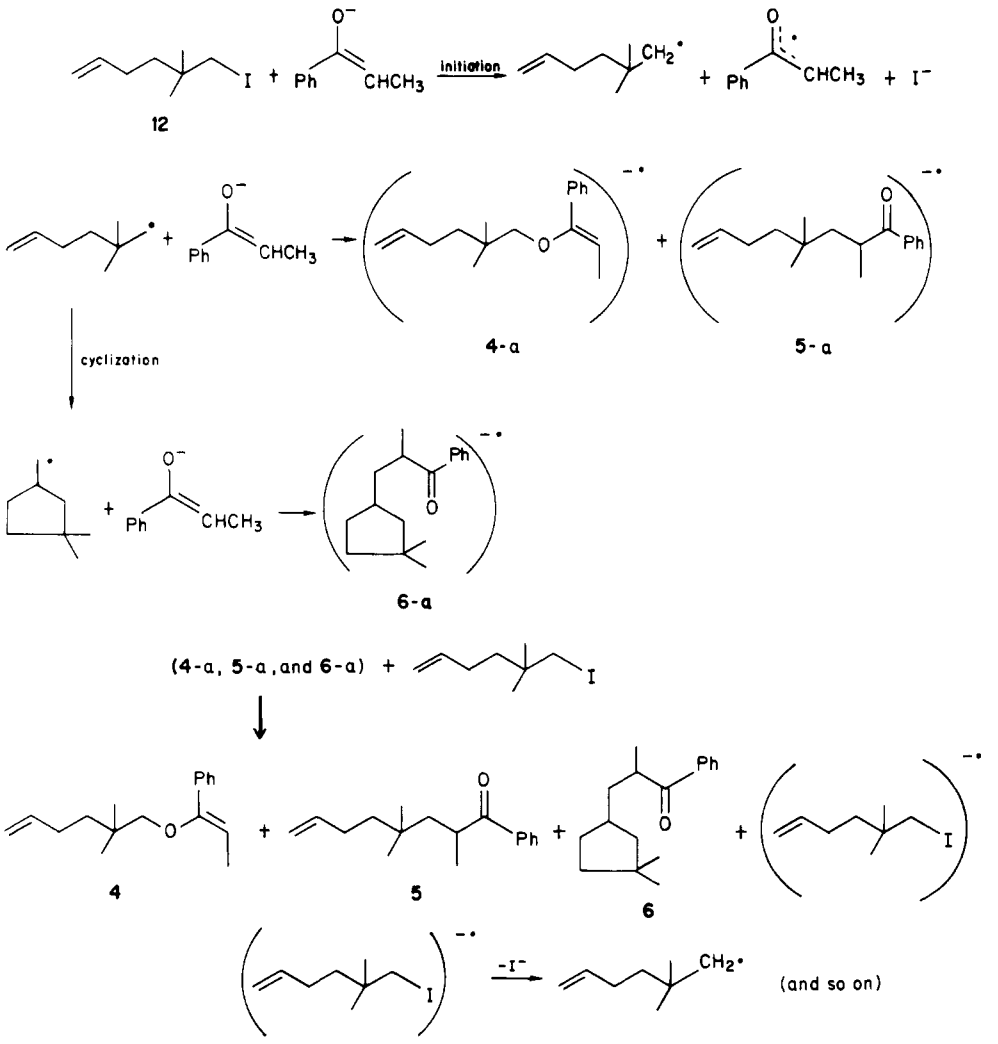

Table III. Effect of Solvent on the Reaction of Lithiopropiophenone with 2,2-Dimethyl-1-iodo-5-hexene (12)[a]

			% yield							4 + 5
expt	solvent	time, h	12	1	2	3	4	5	6	1 + 2 + 3 + 6
2	HMPA	60	8.0	0	1.0	0.88	66	11	1.0	26.7[c]
8	20% THF in HMPA[b]	60	25	0	2.2	2.0	60	12	1.2	13.3
9	20% PhH in HMPA[b]	60	22	0	3.0	2.9	49	10	2.1	7.4
10	15% HMPA in THF[b]	60	98	0	0	0	0	0	0	
11	THF	60	99	0	0	0	0	0	0	

[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl iodide:lithiopropiophenone) and 0.10 M in alkyl iodide at room temperature. [b] Percentage based on volume. [c] ±10%.

reasonable for the formation of the substitution products, compounds **4–6**.[2-4]

Reactions were carried out under ambient fluorescent light, absence of light, and with an efficient free radical scavenger, di-*tert*-butyl nitroxyl radical, in order to determine what effect these factors have on both the reaction rate and product distribution. The results of these experiments are shown in Table II. The reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene was found to be insensitive to the factors that normally influence the $S_{RN}1$ pathway. Furthermore, the product distributions in going from experiment 1 to experiments 6 and 7 in Table II remain fairly constant and, hence, further suggest that the $S_{RN}1$ pathway is not operating in this reaction.

Effect of Solvent. The reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene showed a strong dependence on the nature of the solvent. In HMPA the reaction is essentially complete in 60 h; conversely, the reaction does not proceed at all in THF (experiment 11, Table III). These results are not surprising when one considers that lithium enolates are more reactive in a class C solvent such as HMPA than in a class B solvent like THF.[1] House[24] and then Jackman[19] showed that the addition of 4 equiv of HMPA to a solution of a lithium enolate in a class B solvent causes a significant upfield shift in the ^{13}C spectrum of the carbon bearing the oxygen. This observation is indicative of selective solvation of the lithium cation. The further addition of 1 equiv of HMPA causes no additional upfield shift of the carbon. Hence, the addition of 4 equiv of HMPA "converts lithium enolates into highly reactive solvent-separated ion pairs", and if additional quantities of HMPA are employed, "enolate

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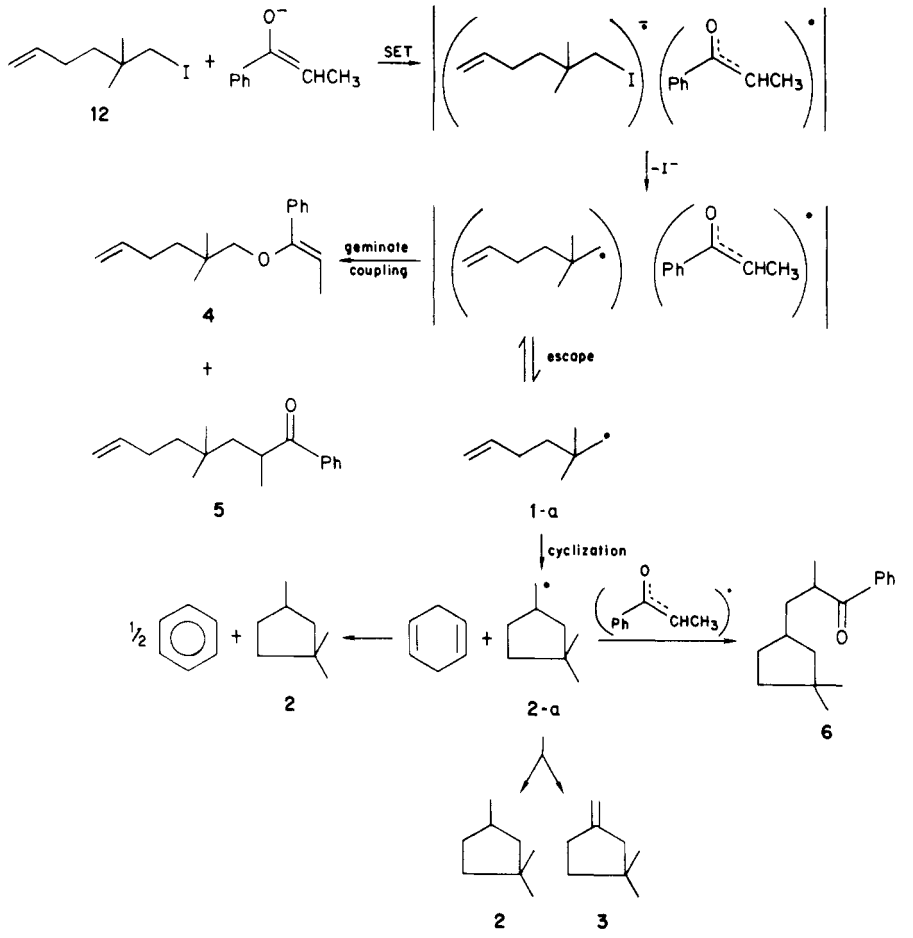
Scheme III



reactivity is not influenced significantly".[1b] Our attempt to react lithiopropiophenone with the alkyl iodide probe in THF utilizing 4 equiv of HMPA led to no reaction (experiment 10). Even when 8 equiv of HMPA were used, no reaction occurred. Furthermore, the addition of even a small amount of THF or benzene to the HMPA solution of lithiopropiophenone, experiments 8 and 9, had a retarding effect on the rate of reaction of the lithium enolate with the alkyl iodide. Clearly, in this reaction, HMPA must play a greater role than just complexing the lithium cation.

Recently, Lipshutz[23] showed that solvent plays a pivotal role in determining the reduction potentials of alkyl halides, with a significant increase in the reduction potential of the alkyl halide in going from THF to CH_3CN to DMF. The rate of reaction of lithiopropiophenone with the alkyl iodide probe as shown in Scheme III depends on the extent of single electron transfer which in turn is governed by the reduction potential of the alkyl iodide. Hence, as more and more THF is added to the solution of the lithium enolate and alkyl iodide in HMPA, the reduction potential of the iodide becomes a more negative value until at some point the reduction potential is too unfavorable for electron transfer to occur and no reaction is observed.

As shown in Scheme III, the amount of cyclized products, compounds **2**, **3**, and **6**, depends on the rate of cyclization of radical 1-a vs. geminate coupling. Since $k_{(\text{cyclization})} = 3.6 \times 10^6\ s^{-1}$ for radical 1-a,[15] whereas rate constants for geminate coupling range from 10^8–$10^{10}\ M^{-1}\ s^{-1}$,[25] it is not surprising that the straight-chain alkylation products predominate. Furthermore, if Scheme III describes the mechanism of reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene, then solvent viscosity should have an effect on the ratio of straight-chain alkylation products to cyclic products since the relative rates of coupling within the solvent cage and diffusion from the cage are viscosity dependent.[25,26] Koenig[27] has used a simple diffusion model to develop a relationship between viscosity and the yield of geminate coupled product (eq 2). Hence, as the viscosity of the solvent (η) decreases,

$$1/\phi - 1 = a + b/\eta^{1/2} \qquad (2)$$

the yield of product formed in the cage (ϕ) should also decrease. As shown in Table III, the ratio of compounds **4** and **5** (the cage combination products) to compounds **2**, **3**, and **6** (the cyclic products formed outside the cage) is dependent on the solvent viscosity. As the solvent viscosity decreases in going from HMPA to 20% THF or benzene in HMPA ($\eta^{20\,°C}_{\text{THF}} = 0.55$, $\eta^{20\,°C}_{\phi\text{H}} = 0.6487$, $\eta^{20\,°C}_{\text{HMPA}} = 3.47$),[28] the ratio of (**4** + **5**)/(**2** + **3** + **6**) decreases. The viscosity dependence lends strong support to the cage process in Scheme III.

Effect of Hydrogen Atom Donors. The trapping of free radicals by hydrogen atom donors is an important method for establishing the intermediacy of free radicals.[25] In particular two hydrogen atom donors that have found

(25) Kochi, J. K., Ed. "Free Radicals"; Wiley and Sons: New York, 1973; Vol. 1, Chapters 2, 4, and 7.

(26) Wursthorn, K. R.; Kuivila, H. G.; Smith, G. F. *J. Am. Chem. Soc.* **1978**, *100*, 2779.

(27) Koenig, T. *J. Am. Chem. Soc.* **1969**, *91*, 2558.

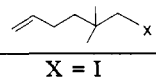
(28) Riddick, J. A.; Bunger, W. B. "Organic Solvents", 3rd ed.; Wiley and Sons: New York, 1970; Chapter 3.

Table IV. Effect of 1,4-Cyclohexadiene on the Reaction of Lithiopropiophenone with 2,2-Dimethyl-1-iodo-5-hexene (12) in HMPA[a]

			% yield							
expt	 [b]	time, h	12	1	2	3	4	5	6	
2	0	60	8.0	0	1.0	0.88	66	11	1.0	
12	5	60	12	0	11	0	54	9.1	0.50	5.8[b]
13	15	60	18	1.0	28	0	36	6.1	tr[d]	16
14[c]	15	70	99	0	0	0				

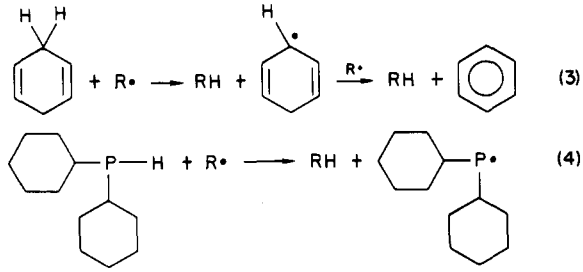
[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl iodide:lithiopropiophenone) and 0.10 M in alkyl iodide at room temperature unless otherwise stated. [b] Equivalents based on alkyl iodide. [c] No lithiopropiophenone (control experiment). [d] tr = trace.

Table V. Effect of Dicyclohexylphosphine on the Reaction of Lithiopropiophenone with 1-Halo-2,2-dimethyl-5-hexenes 12 and 13 in HMPA[a]

				% yield					
expt 	additives	time, h	unreacted starting material	1	2	3	4	5	6
1 X = I	none	10	48	0	tr[c]	tr	42	8.2	0.74
15 X = I	1.0 equiv of DCPH[b]	1	49	0.84	44	1.2	2.2	tr	2.1
16 X = I	1.0 equiv of DCPH	4	19	0.85	58	1.2	4.2	0.70	2.3
17 X = I	10 equiv of DCPH	4	0	13	93	0	0	0	0
18 X = I	1.0 equiv of DCPD (99% d_1)	4	26	0	47 (99% d_1)	2.6	10	1.8	6.2
19 X = I	1.0 equiv of DCPH; 0.15 equiv of PDNB	4	58	tr	21	tr	12	2.4	tr
20 X = I	1.0 equiv of DCPH; 0.20 equiv of lithiopropiophenone	45	76	0	20	0	0	0	0
21 X = I	10 equiv of DCPH; no lithiopropiophenone	24	99	0	0	0			
3 X = Br	none	60	76	0	0	0	20	0.70	0
22 X = Br	1.0 equiv of DCPH	60	79	0	0	0	12	0.70	0

[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl substrate:lithiopropiophenone) and 0.10 M in alkyl substrate at room temperature unless otherwise. [b] Amount relative to alkyl iodide. [c] tr = trace.

wide use as radical traps are 1,4-cyclohexadiene[13,29] (eq 3) and dicyclohexylphosphine[9c,13,29a,30] (eq 4).



The effect of 1,4-cyclohexadiene on the reaction of lithiopropiophenone with 2,2-dimethyl-1-iodo-5-hexene is shown in Table IV. The use of 5 equiv of 1,4-cyclohexadiene (experiment 12) resulted in an increased amount of cyclic hydrocarbon (compound **2**) at the expense of the alkylation products (compounds **4**, **5**, and **6**). When 15 equiv of the diene trap were utilized, the yield of cyclic hydrocarbon increased to 28% (experiment 13). Hence, 1,4-cyclohexadiene is trapping the cyclic radical (**2**-a) at a faster rate than it can disproportionate or be captured by enolate radical (see Scheme III). Furthermore, the ratio of cyclic to straight-chain hydrocarbon (2/1 = 28) indicates that cyclization is faster than trapping by the diene. The fate of 1,4-cyclohexadiene upon trapping radical **2**-a is also shown in Scheme III. For every mole of cyclic hydrocarbon formed, approximately one-half mole of benzene was formed (see Table IV). The decrease in the amount of straight-chain alkylation products in going from experiment 2 to experiments 12 and 13 in part can be explained if more diffusion occurs from the solvent cage as the viscosity of the solvent system decreases with increasing amounts of diene added. The escaped radical can then cyclize and be trapped by the diene. Interestingly, the ratio of straight-chain alkylation products **4**/**5** remains constant in experiments 2, 12, and 13 (Table IV), suggesting that products **4** and **5** arise from a common intermediate. Hence the results using 1,4-cyclohexadiene as a radical trap further support the pathway depicted in Scheme III for the reaction of lithiopropiophenone with the alkyl iodide probe.

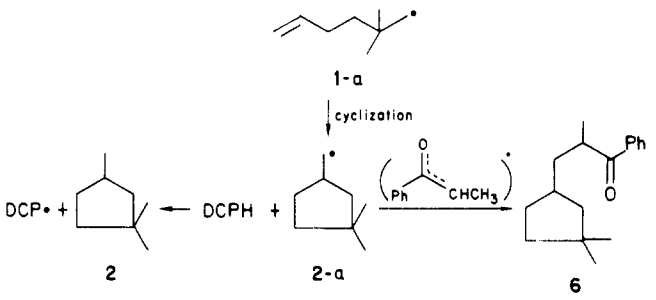
The effects of dicyclohexylphosphine (DCPH) on the reactions of 2,2-dimethyl-1-iodo-5-hexene and 1-bromo-2,2-dimethyl-5-hexene with lithiopropiophenone were also investigated. Experiments 15–17 in Table V indicate the effectiveness of DCPH as a radical trap in the reaction of the alkyl iodide with the lithium enolate. The use of even 1 equiv of DCPH lowers dramatically the yield of straight-chain alkylation products and gives instead a high yield of the cyclic hydrocarbon (experiment 16). When 10 equiv of DCPH are utilized (experiment 17), the only reaction products are hydrocarbons **1** and **2**. As in the case of 1,4-cyclohexadiene, the yield of cyclic hydrocarbon is much higher than the yield of straight-chain hydrocarbon and is due to the observation that radical **1**-a cyclizes at a faster rate than it accepts a hydrogen atom from DCP-H.[31] The source of the hydrogen atom was determined to be the P–H bond of DCPH by a deuterium labeling study. For example, when 1 equiv of DCPD (>99% d_1) was used as the hydrogen atom donor, the cyclic hydro-

(29) (a) Kuivila, H. G.; Alnajjar, M. S. *J. Org. Chem.* **1981**, *46*, 1053. (b) Halgren, T. A.; Howden, M. E. H.; Medof, M. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1967**, *89*, 3051. (c) Kira, M.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 3892.

(30) (a) Kuivila, H. G.; Smith, G. F. *J. Org. Chem.* **1980**, *45*, 2918. (b) Smith, G. F.; Kuivila, H. G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* **1981**, *103*, 833. (c) Ashby, E. C.; DePriest, R. N. *J. Am. Chem. Soc.* **1982**, *104*, 6144.

(31) The reaction of 1-iodo-2,2-dimethyl-5-hexene with 1.0 M DCPH in HMPA in the presence of a catalytic amount of AIBN at 60 °C gave 74% cyclic hydrocarbon to only 5.5% straight-chain hydrocarbon. These results are similar to Beckwith's data (ref 15) where n-Bu_3SnH is used as the hydrogen atom donor. Thus cyclization of radical **1**-a is faster than the rate of trapping by these hydrogen atom donors.

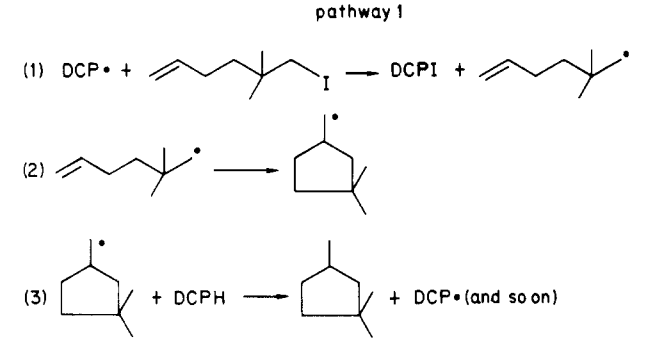
Scheme IV



carbon was found to have 99% deuterium incorporation (experiment 18). Interestingly the use of DCPD led to an increase in alkylation products as compared to DCPH. The increase may be attributed to the deuterium isotope effect where the P–D bond is stronger than the P–H bond and hence the former is a poorer hydrogen atom donor.

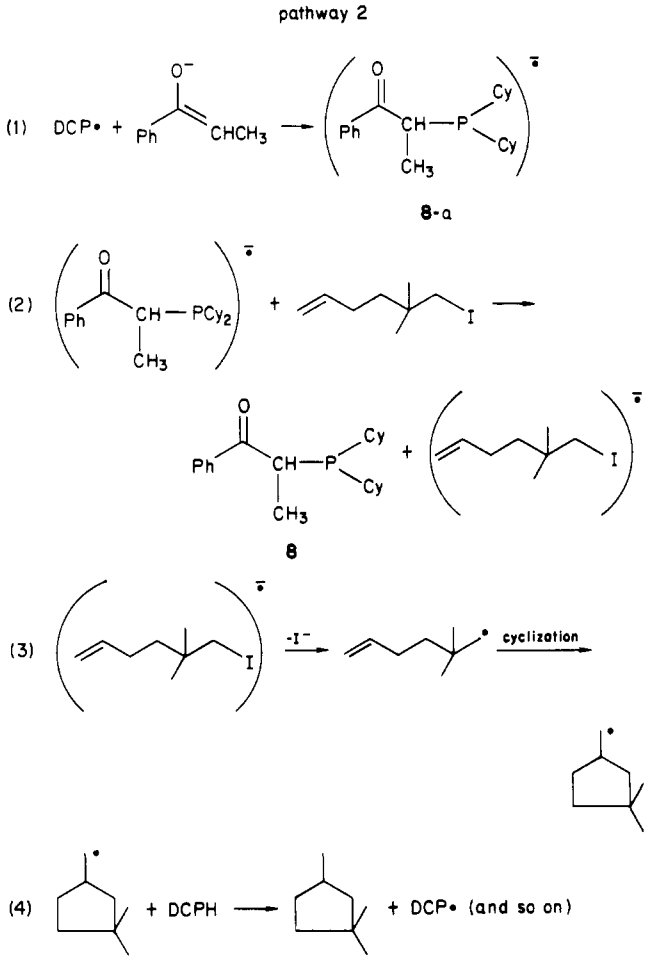
The question of whether DCPH is simply acting as a hydrogen atom donor or in some way playing an additional role in the reaction of lithiopropiophenone with the alkyl iodide was addressed. On the basis of Scheme III it is difficult to rationalize the dramatic effect that DCPH has on the product distribution. Furthermore as shown in experiment 15, the half-life for the reaction of alkyl iodide and enolate is 1 h when 1 equiv of DCPH is present. This represents a tenfold rate acceleration when compared to experiment 1 where no DCPH is present.

Our attempts to explain these results are shown in Scheme IV. Pathway 1 suggests that the DCP· radical



formed upon trapping of the cyclic radical 2-a by DCPH can induce a free-radical chain process. If indeed the free-radical chain reaction is occurring, then both the predominance of cyclic hydrocarbon and the rate acceleration as discussed previously can be rationalized. As a test for this reaction pathway, the reaction of DCPH and alkyl iodide was carried out in the presence of a catalytic amount of lithiopropiophenone (experiment 20). Even when the reaction was allowed to proceed for an extended period of time, the yield of 1,1,3-trimethylcyclopentane (the only product) never exceeded the amount of lithiopropiophenone used. Hence the notion that the lithium enolate is simply functioning as an initiator to a free-radical chain process was ruled out. Thus pathway 1 appears not to be operating since all it requires is a small amount of enolate as an initiator.

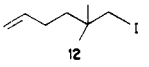
A second scheme can be envisioned to explain the ultimate fate of the DCP· radical formed upon hydrogen atom transfer from DCPH to the cyclic radical 2-a. This scheme is illustrated in pathway 2 and in essence involves the reaction of the DCP· radical with the enolate anion to produce a radical anion. The radical anion 8-a can now transfer an electron to the alkyl iodide to propagate an $S_{RN}1$ radical–radical anion chain process. If pathway 2 is operating, then the comparison of the half-lives of ex-

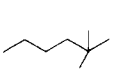
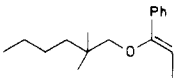
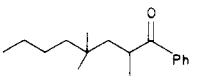
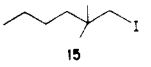


periments 1 and 15 suggests that the radical anion 8-a is about 10 times better an electron-transfer agent than lithiopropiophenone itself. Thus the pathway depicted in Scheme III for the reaction of lithiopropiophenone with alkyl iodide should compete poorly with pathway 2. As a result only a small amount of straight-chain alkylation products should be formed in the presence of 1 equiv of DCPH since the $S_{RN}1$ process should favor cyclization of radical 1-a over random coupling of radicals outside of the solvent cage. The verification of pathway 2 is shown by experiment 19 in Table V. The use of 0.15 equiv of *p*-dinitrobenzene (a good radical anion trap) had an inhibitory effect on the reaction of lithiopropiophenone with the alkyl iodide in the presence of 1 equiv of DCPH as would be expected if the $S_{RN}1$ process depicted in pathway 2 was operating.[2-4] Hence the rate of reaction and product distribution in experiment 19 lies somewhere between the results of experiments 1 and 15. The use of *p*-dinitrobenzene allows the pathway depicted in Scheme III to become more important in the reaction of the enolate with the alkyl iodide and DCPH by virtue of reducing the contribution of pathway 2. Further support for pathway 2 came with the isolation and identification of compound 8 (oxidized during workup) by column chromatography.

The reaction of lithiopropiophenone with 1-bromo-2,2-dimethyl-5-hexene in the presence of 1 equiv of DCPH (experiment 22) gave the same results as experiment 3 where no DCPH was present. Since the reaction of the lithium enolate with the alkyl bromide gives no radical by product (experiment 3), then the formation of DCP· radical from DCPH can not occur to initiate the $S_{RN}1$ chain process depicted by pathway 2. Once again the data indicates that the alkyl bromide is not reacting via an SET pathway.

Table VI. Effect of Double Bond on the Reaction of Lithiopropiophenone with 2,2-Dimethyl-1-iodo-5-hexene (12) in HMPA[a]

expt	alkyl iodide	additives	time, h	% yield 12	1	2	3	4	5	6
2	 12	none	60	8.0	0	1.0	0.88	66	11	1.0

expt	alkyl iodide	additives	time, h	% yield 15	 9	 10	 11
23	 15	none	60	12	3.4	64	10
24	15	1.0 equiv of DCPH[b]	4	25	65	4.1	2.8

[a] All reactions were carried out at a reactant ratio of 1:2 (alkyl iodide:lithiopropiophenone) and 0.10 M in alkyl iodide at room temperature. [b] Amount relative to alkyl iodide.

Effect of the Double Bond in the Alkyl Iodide Probe. In order to ascertain whether the double bond present in the alkyl iodide probe was in some manner perturbing the reaction of the probe with lithiopropiophenone, perhaps by a neighboring group effect, the reaction of 2,2-dimethyl-1-iodohexane (**15**) with the lithium enolate was carried out. A comparison of experiments 2 and 23 in Table VI shows that the double bond of the probe iodide has little effect on either product distribution or reaction rate. Hence the reaction of lithiopropiophenone with the probe can be generalized to any neopentyl type alkyl iodide.

The reaction of lithiopropiophenone with 2,2-dimethyl-1-iodohexane in the presence of 1 equiv of DCPH gave as the major product 2,2-dimethylhexane (experiment 24). Once again the double bond of the alkyl iodide probe has no effect on product distribution or reaction rate as a comparison of experiments 16 and 24 shows. These observations are consistent with pathway 2 of Scheme IV and negate our earlier suggestion[13] that DCPH is trapping radical 1-a via a concerted process[32] to produce the cyclic hydrocarbon.

Conclusion

A variety of methods have been utilized in order to evaluate the occurrence of an electron-transfer pathway in the reaction of lithiopropiophenone with primary alkyl halides and tosylate. The effects of leaving group, solvent, and hydrogen atom donors on product distribution and reaction rate were thoroughly investigated and support SET as the major pathway for reaction of primary (neopentyl type) iodides with enolate anions. Conversely, the alkyl bromide and tosylate appear to be reacting via an S_N2 pathway. Hexamethylphosphoramide has also been shown to be an effective solvent for the alkylation of enolate anions with neopentyl type alkyl iodides at room temperature, whereas, previous attempts to perform these alkylation reactions have failed. Furthermore, the detailed investigation of the effects of dicyclohexylphosphine on the alkylation reactions should better clarify the role that this hydrogen atom donor can play in radical reactions.

Experimental Section

Materials. Solvent-grade pentane, hexane, and benzene were stirred over concentrated H_2SO_4, washed with water, dried over $MgSO_4$, and distilled from CaH_2. Reagent grade diethyl ether, tetrahydrofuran (THF), and benzene were purchased from Fisher and distilled under nitrogen from deep purple solutions of sodium benzophenone ketyl. Hexamethylphosphoramide (HMPA) from Aldrich was fractionally distilled from sodium at reduced pressure. Samples of *n*-decane, 1-heptene, *p*-dinitrobenzene, triphenylmethanol, and *p*-toluenesulfonic acid from Aldrich, hexaphenylditin and di-*tert*-butyl nitroxyl radical from Alfa, and 1,1,3-trimethylcyclopentane and 2,2-dimethylhexane from Wiley Organics were used as received. An authentic sample of 5,5-dimethyl-1-hexene was obtained as previously described.[9c] A sample of 3,3-dimethyl-1-methylenecyclopentane (from experiment 9, Table III) was obtained by preparative GLC (column C) and gave NMR and mass spectra identical with those previously reported for the hydrocarbon.[33]

Acetophenone, propiophenone, diisopropylamine, and 1,4-cyclohexadiene were purchased from Aldrich and distilled from CaH_2 under nitrogen. Reagent grade acetone from Fisher was distilled from P_2O_5 prior to use. Dicyclohexylphosphine (DCPH) from Aldrich was purified by distillation (bp 68–70 °C at 0.04 mmHg), and deuterated dicyclohexylphosphine (DCPD) was prepared as previously described.[34] Methyllithium and *n*-butyllithium were purchased from Aldrich and used after standardization by Eastham–Watson titration.

General Procedures. All glassware and syringes were oven-dried at 150 °C for at least 2 h and cooled under a flow of purified nitrogen just prior to use. Transfer of reagents was performed by using syringes equipped with stainless steel needles. Reactions were carried out in round-bottomed flasks equipped with T-bore stopcocks attached to male 24/40 standard taper joints (allows nitrogen flush while reagents are being added or removed through the stopcock by syringe) and a Teflon-coated magnetic stirring bar.

Proton NMR spectra were recorded on either a Varian T-60A or Bruker WM-300 instrument with chemical shifts reported relative to Me_4Si. Mass spectral analyses were performed on a Varian MAT-112S spectrometer. IR spectra were recorded on a Perkin-Elmer 299 infrared spectrophotometer. Elemental compositions were determined either by microanalysis (Atlantic Microlabs, Inc. of Atlanta, GA) or by high-resolution mass spectrometry.

Quantitative gas–liquid chromatographic (GLC) analyses were conducted on a Hewlett-Packard Model 700 instrument equipped with an automatic integrator and a flame ionization detector. GLC yields were determined by using internal standards and comparing peak areas which were corrected for response factors. Preparative GLC separations were performed on a F&M Model 720 instrument equipped with a thermal conductivity detector. For quantitative GLC analyses, the following columns and conditions were used (retention times are given relative to the internal standard): column A, 10% Apiezon L on Chromosorb P, 4 ft × $^1/_8$ in., 95 °C, *n*-decane (1.00), 1-bromo-2,2-dimethyl-5-hexene (1.43), 2,2-dimethyl-1-iodo-5-hexene (2.95), 2,2-dimethyl-1-iodohexane (3.04);

(32) Walling, C.; Cooley, J. H.; Ponares, A. A.; Racah, E. J. *J. Am. Chem. Soc.* **1966**, *88*, 5361.

(33) Adlercreutz, P.; Masnusson, G. *Acta Chem. Scand., Ser. B* **1980**, *B34*, 647.

(34) Ashby, E. C.; DePriest, R. N.; Su, W. Y. *Organometallics* **1984**, *3*, 1718.

column B, 10% SE-30 on Chromosorb W, 1.5 ft × 1/8 in., 115 °C, *p*-chlorobenzophenone (1.00), 2,2-dimethyl-1-tosyl-5-hexene (2.34); column C, 8% Apiezon L on Chromosorb P, 20 ft × 1/8 in., 60 °C, benzene (0.89), 1-heptene (1.00), 5,5-dimethyl-1-hexene (1.19), 2,2-dimethylhexane (1.29), 1,1,3-trimethylcyclopentane (1.43), 3,3-dimethyl-1-methylenecyclopentane (1.67); column D, 5% Carbowax 20M on Chromosorb G, 4 ft × 1/4 in., 135 °C, propiophenone (0.44), mesityl *tert*-butyl ketone (1.00), **10** (1.29), **4** (1.65), **11** (2.57), **5** (3.39), **6** (3.93).

Preparations. 2,2-Dimethyl-5-hexen-1-ol, 1-Bromo-2,2-dimethyl-5-hexene, 2,2-Dimethyl-1-iodo-5-hexene, and 2,2-Dimethyl-1-tosyl-5-hexene. The alcohol was prepared by the method of Beckwith[35] and exhibited the following: ^{1}H NMR (CCl_4) δ 0.83 (s, 6 H), 0.85–2.40 (m, 5 H, contains OH), 3.25 (s, 2 H), 4.75–6.20 (m, 3 H). From the alcohol, the corresponding alkyl bromide, iodide, and tosylate were prepared by previously described methods.[9c]

2,2-Dimethyl-1-iodohexane. A 2-L flask was charged with 1.4 mol of *n*-BuLi in 1100 mL of hexane. After cooling the flask to −5 °C and with stirring, 95 g (1.6 mol) of acetone in 100 mL of dry hexane was added dropwise over a 1-h period. The reaction mixture was then stirred for an additional 0.5 h as it warmed to 25 °C, quenched with 1 M HCl (100 mL), and extracted twice with Et_2O. The combined ethereal layers were washed with saturated $NaHCO_3$ followed by brine, dried, and concentrated to give 140 g (86%) of crude 2-methyl-2-hexanol. From the alcohol, the title compound was prepared (14% overall) by an analogous route used for the preparation of 2,2-dimethyl-1-iodo-5-hexene and gave the following: bp 64–66 °C (3.0 mmHg); ^{1}H NMR (CCl_4) δ 0.90–1.4 (m, 9 H), 1.0 (s, 6 H), 3.1 (s, 2 H); IR (CCl_4) 2960, 1460, 1420, 1380, 1360, 1245, 1150, 860, 690 cm^{-1}; mass spectrum, *m/e* (relative intensity) 240 (M^+, 0.3), 183 (6) 113 (31), 71 (75), 57 (100), 55 (34). Anal. Calcd for $C_8H_{17}I$: C, 40.01; H, 7.15. Found: C, 40.19; H, 7.12.

2,2-Dimethyl-5-hexenal. In a 250-mL, round-bottomed flask fitted with a reflux condenser were suspended 16 g (73 mmol) of pyridinium chlorochromate and 1.1 g (14 mmol) of sodium acetate in 100 mL of anhydrous CH_2Cl_2. 2,2-Dimethyl-5-hexen-1-ol (6.2 g, 48 mmol) in 20 mL of CH_2Cl_2 was added in one portion to the magnetically stirred solution. After 2 h, the reaction mixture was worked up as previously described.[36] The residual oil was stirred over CaH_2 for 2 h, filtered, and then fractionally distilled to give 3.6 g (60%) of aldehyde (bp 63–64 °C at 17 mmHg) which gave NMR and IR spectra identical with those previously reported for the aldehyde.[37]

4,4-Dimethyl-1-phenyl-2,7-octadien-1-one. To a cold (−78 °C) solution of LDA, from 29 mmol of MeLi, 32 mmol of diisopropylamine, and 30 mL of Et_2O, was added dropwise and with stirring during 15 min, 3.5 g (29 mmol) of acetophenone in 10 mL of Et_2O. The resulting solution was stirred at −78 to −40 °C for 1 h and then 3.6 g (29 mmol) of 2,2-dimethyl-5-hexenal was added dropwise and with stirring during 5 min. The resulting pale yellow solution was stirred at −40 to 0 °C for 1 h and then 50 mL of ice-cold 1 M HCl was added. The mixture was extracted with Et_2O and the combined ethereal extracts were washed successively with 1 M HCl, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated to give 6.5 g of crude ketol. To the crude ketol in a 250-mL round-bottomed flask was added 200 mL of benzene and 0.260 g (1.36 mmol) of *p*-TsOH. The flask was fitted with a Dean–Stark trap and condenser and the benzene was refluxed for 30 min. The solution was then cooled, washed twice with saturated $NaHCO_3$ and then brine, dried over $MgSO_4$, and concentrated. The residual liquid was then fractionally distilled to give 4.7 g (72%) of enone (bp 114–116 °C at 0.10 mmHg): ^{1}H NMR (CCl_4) δ 1.0 (s, 6 H), 1.2–2.2 (m, 4 H), 4.8–6.2 (m, 3 H), 6.9 (d, 1 H), 7.2–8.0 (m, 6 H); IR (film) 3065, 2960, 1665, 1615, 1445, 1300, 1220, 1020, 910, 700 cm^{-1}; mass spectrum, *m/e* (relative intensity) 228 (M^+, 2), 157 (23), 105 (100), 91 (15), 77 (54), 51 (16), 43 (30), 41 (27). Anal. Calcd for $C_{16}H_{20}O$: C, 84.15, H, 8.84. Found: C, 83.99; H, 8.86.

1-Phenyl-2,4,4-trimethyl-7-octen-1-one (5). A solution of lithium in liquid ammonia was prepared by the addition of freshly cut lithium wire (0.0267 g, 3.85 mmol) to liquid ammonia (40 mL, distilled from sodium) and stirred 15 min. 4,4-Dimethyl-1-phenyl-2,7-octadien-1-one (0.400 g, 1.75 mmol) and Ph_3COH (0.455 g, 1.75 mmol) in 10 mL of anhydrous Et_2O were added dropwise. The reaction mixture was stirred 30 min and then diluted with 30 mL of Et_2O, and 1.49 g (10.5 mmol) of methyl iodide in 5.0 mL of Et_2O was then added dropwise. After 30 min the solution was worked up by a previously described method.[38] The residual liquid was chromatographed on silica gel with a hexane–ether eluent (96:4 v/v) to give 0.26 g (60%) of the ketone. Bulb-to-bulb distillation afforded the ketone as a colorless liquid: ^{1}H NMR (CCl_4) δ 0.85 (s, 6 H), 1.2 (d, 3 H, *J* = 7.0 Hz), 1.2–2.2 (m, 6 H), 3.6 (m, 1 H), 4.8–6.2 (m, 3 H), 7.4–8.0 (m, 5 H); IR (film) 3065, 2960, 1680, 1640, 1595, 1450, 1215, 970, 910, 710 cm^{-1}; mass spectrum, *m/e* (relative intensity) 244 (M^+, 0.5), 189 (4), 147 (31), 105 (100), 77 (23), 55 (22). Anal. Calcd for $C_{17}H_{24}O$: C, 83.54; H, 9.92. Found: C, 83.64; H, 9.94.

1-Phenyl-2,4,4-trimethyl-1-octanone (11). To the crude product (0.80 g) of the lithium ammonia reduction/methylation reaction was added 60 mL of absolute ethanol in a 100-mL, round-bottomed flask. This was followed by the addition of 80 mg of 5% Pd on C. The mixture was then hydrogenated at 1 atm and 25 °C for 3 h. After being filtered and concentrated, the residual liquid was chromatographed on silica gel with a hexane–ether eluent (99:1 v/v) to give 0.22 g (51%) of the ketone. Distillation (bulb to bulb) afforded the ketone as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 0.78, 0.81 (s, 6 H), 0.86 (t, 3 H, *J* = 6.6 Hz), 1.2 (d, 3 H, *J* = 7.0 Hz), 1.2–1.3 (m, 8 H), 3.6 (m, 1 H), 7.4–8.0 (m, 5 H); IR (film) 3060, 2960, 1680, 1595, 1455, 1215, 970, 795, 710 cm^{-1}; mass spectrum, *m/e* (relative intensity) 246 (M^+, 1), 189 (5), 147 (22), 105 (100), 77 (13), 57 (12). Anal. Calcd for $C_{17}H_{26}O$: C, 82.85; H, 10.66. Found: C, 82.87; H, 10.65.

3-(3,3-Dimethylcyclopentyl)-2-methyl-1-phenyl-1-propanone (6). To a cold (−78 °C) solution of LDA, from 63 mmol of MeLi, 66 mmol of diisopropylamine, and 40 mL of Et_2O, was added dropwise and with stirring during 15 min, 8.4 g (63 mmol) of propiophenone. The resulting solution was stirred at −78 °C for 1 h and then brought slowly to room temperature under vacuum to remove the solvent. The lithium enolate was then redissolved in 40 mL of THF containing 1.5 g (2.1 mmol) of hexaphenylditin, and 1.0 g (4.2 mmol) of 2,2-dimethyl-1-iodo-5-hexene was then added. The resulting solution was irradiated in a 200-mL Pyrex flask with a water-cooled 450-W high pressure Hanovia lamp for 20 h, and then 1.5 g of hexaphenylditin in 30 mL of THF was added to the flask and the irradiation was continued for an additional 20 h. The reaction mixture was then quenched with 1 M HCl (30 mL) and extracted twice with hexane. The combined hexane layers were washed successively with 1 M HCl and brine, dried, and concentrated. The residual liquid (10 g) was chromatographed on silica gel (950 g) with a hexane–ether eluent (99:1 v/v). Concentration of the fractions containing the cyclic alkylation product gave approximately 3 g of a crude liquid. The liquid was rechromatographed under the same conditions to give, after concentration of the appropriate fractions, 1.1 g of a liquid. GLC analysis (column D) of the liquid resulted in a GC trace containing two peaks: 80% propiophenone to 20% cyclic alkylation product. The mixture was then subjected to preparative GLC (5% Carbowax 20M on Chromosorb G, 1.5 ft, 155 °C) to give 0.20 g (20%) of alkylation product. Distillation (bulb to bulb) afforded the ketone as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 0.89, 0.91, 0.97, 0.98 (s, 6 H), 1.2 (d, 3 H, *J* = 6.9 Hz), 1.2–2.0 (m, 9 H) 3.5 (hextet, 1 H, *J* = 6.9 Hz), 7.3–8.0 (m, 5 H); IR (film) 3065, 2945, 2865, 1685, 1600, 1460, 1365, 1225, 975, 710 cm^{-1}; electron-impact mass spectrum *m/e* (relative intensity) 147 (5), 134 (82), 133 (17), 106 (9), 105 (100), 77 (40), 69 (7), 55 (22), 41 (17); chemical-ionization mass spectrum, *m/e* 245 ($M^+ + 1$). Anal. Calcd for $C_{17}H_{24}O$: C, 83.54; H, 9.92. Found: C, 83.36; H, 9.92.

1-((2,2-Dimethyl-5-hexenyl)oxy)-1-phenyl-1-propene (4). A solution of lithiopropiophenone (19 mmol) in Et_2O was prepared as described above. Upon evaporation of the solvent in vacuo, the lithium enolate was redissolved in 35 mL of HMPA, and 3.0

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g (13 mmol) of 2,2-dimethyl-1-iodo-5-hexene was added. The reaction mixture was stirred for 60 h at 25 °C, quenched with saturated NH_4Cl (20-mL), and extracted twice with hexane. The combined hexane layers were washed with saturated $NaHCO_3$ followed by five successive washings with water and then dried and concentrated. The residual liquid was chromatographed on silica gel with a hexane–ether eluent (99:1 v/v) to give 1.8 g (57%) of enol ether. Bulb-to-bulb distillation afforded the enol ether as a colorless liquid: ^1H NMR (CCl_4) δ 0.98 (s, 6 H), 1.2–2.2 (m, 4 H), 1.8 (d, 3 H, J = 6.8 Hz), 3.2 (s, 2 H), 4.8–6.2 (m, 4 H), 7.1–7.5 (m, 5 H); IR (film) 3070, 2960, 1655, 1635, 1320, 1065, 910, 760, 700 cm^{-1}; mass spectrum, m/e (relative intensity) 244 (M^+, 4), 202 (8), 135 (28), 134 (100), 133 (75), 117 (19), 105 (41), 91 (9), 77 (15), 69 (59), 55 (46), 41 (48); exact mass calcd for $C_{17}H_{24}O$ 244.1827, found 244.1836.

1-((2,2-Dimethylhexyl)oxy)-1-phenyl-1-propene (10). The enol ether was prepared in 56% yield from 2,2-dimethyl-1-iodohexane by the method described above and after purification gave the following: ^1H NMR (CCl_4) δ 0.97 (s, 6 H), 0.85–1.5 (m, 9 H), 1.8 (d, 3 H, J = 6.8 Hz), 3.2 (s, 2 H), 5.2 (q, 1 H, J = 6.8 Hz), 7.1–7.5 (m, 5 H); IR (film) 3045, 2960, 1650, 1315, 1060, 760, 700 cm^{-1}; mass spectrum, m/e (relative intensity) 246 (M^+, 3), 217 (11), 135 (12), 134 (100), 133 (50), 117 (12), 105 (21), 77 (9), 71 (23), 57 (39), 43 (37); exact mass calcd for $C_{17}H_{26}O$ 246.1984, found 246.1988.

2-(Dicyclohexylphosphino)-1-phenyl-1-propanone. A solution of lithiopropiophenone (9.4 mmol) in HMPA (20 mL) was prepared as described above and 1.2 g (6.3 mmol) of DCPH followed by 1.5 g (6.3 mmol) of 2,2-dimethyl-1-iodo-5-hexene were added. The reaction mixture was stirred for 24 h at 25 °C, quenched with saturated NH_4Cl (10 mL), and extracted twice with hexane. The combined hexane layers were washed 5 times with water, dried, and then concentrated. The residue was chromatographed on silica gel with an ethyl acetate–acetone eluent (1:1 v/v) to give 0.74 g (34%) of the ketone as a viscous oil which was dried in a vacuum dessicator and gave the following: ^1H NMR ($CDCl_3$) δ 1.0–2.1 (br m, 22 H), 1.5 (dd, 3 H), 4.2 (dq, 1 H), 7.3–8.0 (m, 5 H); IR (CCl_4) 3060, 2940, 2860, 1675, 1445, 1170 cm^{-1}; mass spectrum, m/e (relative intensity) 346 (M^+, 8), 264 (28), 263 (30), 182 (27), 133 (14), 117 (100), 105 (30), 83 (24), 77 (25), 55 (57), 43 (27), 41 (50); exact mass calcd for $C_{21}H_{31}O_2P$ 346.2062, found 346.2079.

General Procedure for Alkylation Reactions. Lithiopropiophenone (1.0 mmol) in 5.0 mL of HMPA was prepared as described above and 0.50 mmol of alkyl halide or tosylate was added to the stirring enolate solution at 25 °C. Whenever an additive was employed, the appropriate amount was added to the enolate solution just prior to the addition of the alkyl halide. The alkylation reactions were followed by taking 0.50-mL aliquots from the reaction mixtures at various time intervals and quenching them with saturated NH_4Cl in glass vials containing the necessary internal standards. The organic layer was then extracted (2 × 2.0 mL) with pentane and the combined pentane layers were washed 5 times with H_2O. GLC analyses were then conducted on columns A–D and all products were identified from their GLC retention times and mass spectra by comparison with authentic samples.

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Registry No. 2, 4516-69-2; **4**, 97467-22-6; **5**, 89746-00-9; **6**, 89746-01-0; **9**, 590-73-8; **10**, 97467-24-8; **11**, 97467-25-9; **15**, 97467-23-7; DCPD, 91523-73-8; DCPH, 829-84-5; PDNB, 100-25-4; CH_2=$CH(CH_2)_2C(CH_3)_2CH_2I$, 77400-57-8; CH_2=$CH(CH_2)_2C(CH_3)_2CH_2Br$, 56068-49-6; CH_2=$CH(CH_2)_2C(CH_3)_2CH_2OTs$, 89745-98-2; $(t\text{-Bu})_2NO$, 2406-25-9; CH_2=$CH(CH_2)_2C(CH_3)_2CH_2OH$, 56068-50-9; BuLi, 109-72-8; $CH_3C(O)CH_3$, 67-64-1; $CH_3(CH_2)_3C(OH)(CH_3)_2$, 625-23-0; CH_2=$CH(CH_2)_2C(CH_3)_2CHO$, 52278-99-6; CH_2=$CH(CH_2)_2C(CH_3)_2CH$=$CHC(O)Ph$, 97467-26-0; $PhC(O)CH_3$, 98-86-2; CH_2=$CH(CH_2)_2C(CH_3)_2CH(OH)CH_2C(O)Ph$, 97467-27-1; $PhC(O)CH_2CH_3$, 93-55-0; lithiopropiophenone, 70887-62-6; 1,4-cyclohexadiene, 628-41-1; 2-(dicyclohexylphosphino)-1-phenyl-1-propanone, 97467-28-2.

NAD(P)$^+$–NAD(P)H Models. 55. Transition Metal Catalyzed Reduction of Organic Halides: High Selectivity for Reductive Dehalogenation

Shinro Yasui,*[1a] Kaoru Nakamura,[1b] Masayuki Fujii,[1b] and Atsuyoshi Ohno[1b]

Tezukayama College, Gakuen-Minami, Nara, 631 Japan, and Institute for Chemical Research, Kyoto University, Uji, Kyoto, 611 Japan

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Various types of aryl, benzyl, vinyl, phenacyl, and allyl halides were subjected to reaction with *N*-benzyl-1,4-dihydronicotinamide (BNAH), in the presence of a catalytic amount of chlorotris(triphenylphosphine)rhodium(I) or palladium(II)acetate. The carbon–halogen bonds in these compounds were selectively reduced to the carbon–hydrogen bonds in moderate to excellent yield. This new kind of reduction system has synthetic advantages over many other procedures for reductive dehalogenation: the conditions are mild, nitro, carbonyl, hydroxyl, amino, alkenyl, and ester groups are inert under these conditions, and the halides that can be used are varied. The order of reactivity in a series of organic halides was Cl < Br < I. Substituent effects in the aryl iodides showed that the stronger the electron-withdrawing ability of the substituent, the more reactive the substrate. These results and other evidence suggest that the reaction involves oxidative addition of halides to the transition metal. The reduction of vinyl bromide gave predominantly the thermodynamically more stable isomer, after cis–trans interconversion. In addition, this reduction was accompanied by contamination by deuterium from the deuterated solvent. These facts reveal the intermediacy of vinyl free radicals in the course of the reaction. The free-radical species is probably generated through an electron transfer from BNAH.

Chemoselectivity is of special importance in organic synthesis. It is prerequisite to artificial production of some useful drugs such as antibiotics. Although up to now many types of "selective reactions" have been tried, and some are widely accepted to be useful in synthesis, most organic reactions reported so far are still open to improvement in terms of chemoselectivity.

The selective reduction of a carbon–halogen bond to a carbon–hydrogen one would be of interest to organic

(1) (a) Tezukayama College. (b) Kyoto University.

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