Acknowledgment. This work was supported by the National Science Foundation (CHE 83-10109 and CHE 87-96257). Acknowledgment is also made to the American Chemical Society's Petroleum Research Fund (PRF 13172-AC4,6) and to the National Institutes of Health (GMO8521-26) for partial support of this research. We are grateful to Drs. W. Kutzelnigg and M. Schindler for a copy of the IGLO program and to Dr. J. W. Downing for adapting the program to our computer.

Methylaluminum Bis(2,6-di-*tert*-butyl-4-methylphenoxide) as a Protecting Group for Multifunctional Molecules: Synthetic Utility in Selective Carbonyl Reductions

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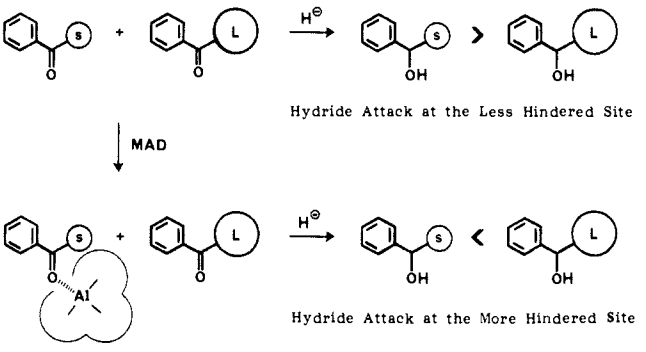
Selective reduction of one out of two different carbonyl moieties is an important synthetic operation.[1] The selectivity is commonly achievable by using modified hydride reagents formed by the replacement of hydride with sterically bulky substituents or electron-withdrawing groups in order to discriminate the structural or electronical environment of the carbonyl group, in which the sterically less hindered or electronically more labile carbonyl substrate is more easily reduced.[1,2] However, the opposite selectivity, i.e., selective reduction of the sterically more hindered or electronically less labile carbonyl substrate has never been attained.[3,4] Here we wish to disclose a conceptionally new approach to this problem. Our study began with experiments to test discrimination between two different carbonyl compounds by first complexing the less hindered carbonyl selectively with methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)[5] and subsequent reduction of the more hindered carbonyl with nucleophilic hydride reagent as illustrated in Scheme I.

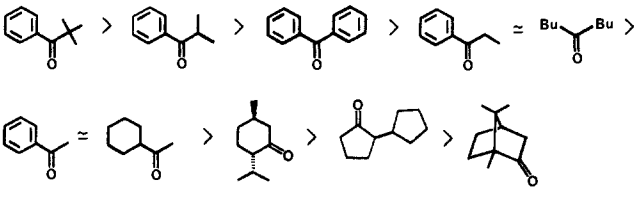
Treatment of a mixture of 1 equiv each of acetophenone and pivalophenone in CH_2Cl_2 with diisobutylaluminum hydride (DIBAH) (1 equiv) at −78 °C for 1 h gave 1-phenylethanol and 2,2-dimethyl-1-phenyl-1-propanol in 99% combined yield (ratio, 2.6:1). However, initial treatment of the two carbonyl substrates with MAD (1 equiv)[6] followed by reduction with DIBAH (1 equiv) at −78 °C resulted in the reversal of selectivity, producing

Scheme I



the corresponding alcohols (66% combined yield) in a ratio of 1:10. Although selective complexation between two different carbonyl groups with MAD is consistent with the above experiments, more direct evidence was obtained by low-temperature ^{13}C NMR spectroscopy. The 67.8 MHz ^{13}C NMR measurement of a mixture of 1 equiv each of MAD, acetophenone, and pivalophenone in CD_2Cl_2 at −70 °C showed that the original signal of acetophenone carbonyl at δ 198.3 shifted downfield to δ 213.6, whereas the signal of pivalophenone carbonyl remained unchanged.[7] Treatment of these ketones with excess MAD (2 equiv) and subsequent addition of DIBAH (1 equiv) resulted in greater selectivity (ratio = 1:16; 51% yield). Furthermore, use of 2 equiv each of MAD/DIBAH gave a satisfactory result in both selectivity and chemical yield (ratio = 1:16; 85% yield), suggesting that decomplexation of the more hindered pivalophenone and MAD is more readily facilitated by the action of DIBAH.[8] The effect of various aluminum hydride reagents was then examined by using a mixture of acetophenone and isobutyrophenone; Br_2AlH[9] was found to be more satisfactory in the case of aromatic ketones as illustrated in Table I. Other selected examples included in Table I clearly indicate the effectiveness of our approach in selective carbonyl reduction. The good selectivity is observed by pairing acetophenone with propiophenone, isobutyrophenone, and pivalophenone (entries 1–10). An electronic effect of substituents on the aromatic ring of acetophenone is also seen (entries 14 and 15). The strong resistance in camphor reduction should be interpreted in terms of the higher Lewis basicity of camphor combined with the sterically hindered camphor–MAD complex (entries 22 and 23). Discrimination between an aldehyde and a ketone with MAD was unsuccessful in view of the high reactivity of an aldehyde–MAD complex-to-hydride attack.

On the basis of data in Table I in combination with additional ketone discrimination experiments, the order of reducing susceptibility for various ketones is as follows[10]



It is often required to reduce specific carbonyl groups in a regioselective manner in complex multifunctional molecules. A

(1) Reviews of selective reduction: (a) House, H. O. *Modern Synthetic Reaction*, 2nd ed.; W. A. Benjamin: New York, NY, 1972. (b) Brown, H. C. *Boranes in Organic Chemistry*; Cornell University Press: Ithaca, NY, 1972. (c) Walker, E. R. H. *Chem. Soc. Rev.* **1976**, *5*, 23. (d) Hajős, C. Sc. A. *Complex Hydrides and Related Reducing Agents in Organic Synthesis*; Elsevier: New York, 1979. (e) Brown, H. C.; Krishnamurthy, S. *Tetrahedron Lett.* **1979**, *35*, 567. (f) Brown, H. C.; Krishnamurthy, S. *Aldrich. Acta* **1979**, *12*, 3. (g) Hudlický, M. *Reductions in Organic Chemistry*; Ellis Hoewood Limited: Chichester, England, 1984.

(2) Highly selective reduction of sterically less hindered keto group with lithium dibutyl-9-borabicyclo[3.3.1]nonane: Yamamoto, Y.; Toi, H.; Sonoda, A.; Murahashi, S. *J. Am. Chem. Soc.* **1976**, *98*, 1965.

(3) Selective carbonyl alkylation of a sterically more hindered keto group has been accomplished via chemoselective in situ protection of a less hindered keto group with titanium tetrakis(dialkylamide): Reetz, M. T.; Wenderroth, B.; Pelter, R. *J. Chem. Soc., Chem. Commun.* **1983**, 406. See, also: Reetz, M. T. *Top. Curr. Chem.* **1982**, *106*, 1.

(4) Selective oxidation or esterification of the more hindered hydroxy group in diol systems has been accomplished by selective adsorption of the less hindered hydroxy group on alumina (private communication by Professor Gary H. Posner).

(5) (a) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573. (b) Maruoka, K.; Sakurai, M.; Yamamoto, H. *Tetrahedron Lett.* **1985**, *26*, 3853.

(6) MAD was prepared from 2,6-di-*tert*-butyl-4-methylphenol (2 equiv) and Me_3Al in hexane at room temperature and purified before use by crystallization from hexane followed by filtration in an argon box. Attempted use of unpurified MAD significantly lowered the selectivity.

(7) The signal of pivalophenone carbonyl appears at δ 209.2 compared to the original peak at δ 208.9. In contrast, the signal of pivalophenone–MAD complex appears at δ 232.6. For details, see Supplementary Material.

(8) Initial decomplexation of the more hindered ketone and MAD by the action of DIBAH followed by reduction of the resulting free ketone with DIBAH seems to be plausible, since the cis/trans ratio in the reduction of menthone or camphor are similar in the presence or absence of MAD.

(9) Prepared from $LiAlH_4$ and anhydrous $AlBr_3$ (3 equiv) in ether at 0 °C for 20 min.

(10) The order of reducing susceptibility in aliphatic ketone systems might be interpreted by the electronic effect of carbonyl groups which is correlated to the strength of the carbonyl absorption frequencies: cyclohexyl methyl ketone, 1709 cm^{-1} (C=O); menthone, 1710 cm^{-1}; 2-cyclopentylcyclopentanone, 1740 cm^{-1}; camphor, 1746 cm^{-1}.

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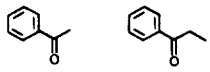
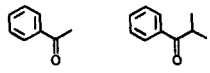
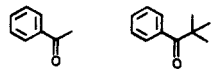
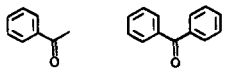
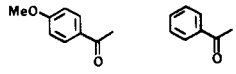
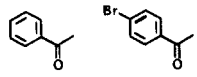
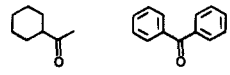
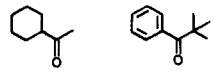
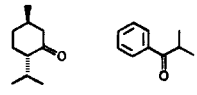
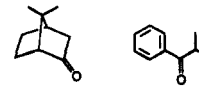
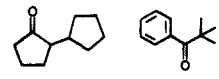
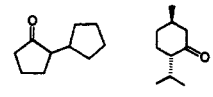
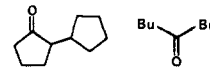
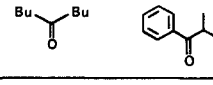
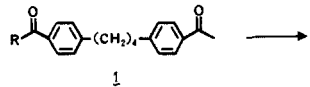
Table I. Selective Reduction of Ketones[a]

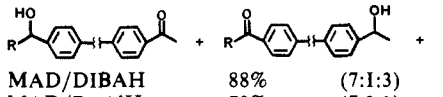
entry	ketones	MAD[b] (equiv)	hydride (equiv)	yield[c] (%)	ratio[d]
1		1	DIBAH (1)	79	1/2.6 (1.2/1)
2		2	Br_2AlH (2)	68	1/6
3		1	DIBAH (1)	82	1/6 (1.2/1)
4		2	DIBAH (1)	63	1/6
5		2	DIBAH (2)	101	1/6
6		2	Cl_2AlH (2)	119	1/5.3
7		2	Br_2AlH (2)	93	1/9.3 (1.3/1)
8		1	DIBAH (1)	66	1/10 (2.6/1)
9		2	DIBAH (1)	51	1/16
10		2	DIBAH (2)	85	1/16
11		1	DIBAH (1)	80	1/4 (1.2/1)
12		2	DIBAH (2)	84	1/5
13		2	Br_2AlH (2)	103	1/9.3 (2/1)
14		2	DIBAH (2)	89	1/3.5 (1.3/1)
15		2	DIBAH (2)	99	1/2 (1/1.2)
16		1	DIBAH (1)	71	1/11 (1/1.2)
17		2	DIBAH (2)	80	1/15
18		1	DIBAH (1)	57	1/7 (1.7/1)
19		2	DIBAH (2)	82	1/200
20		1	DIBAH (1)	65	1/9 (1/1)
21		2	DIBAH (1.2)[e]	98	1/13
22		1	DIBAH (1)	80	1/12 (1/1)
23		2	DIBAH (2)	101	1/100
24		1	DIBAH (1)	60	1/5
25		2	DIBAH (2)	83	1/82
26		2	DIBAH (2)	74	1/4 (1/1)
27		2	DIBAH (2)	71	1/3
28		1	DIBAH (1)	82	1/8
29		2	Br_2AlH (2)	110	1/3.6 (1.7/1)

[a] The reaction was carried out by treatment of a mixture of the two ketones (molar ratio, 1:1) with MAD and subsequent reduction with aluminum hydride reagent at −78 °C for several hours. [b] Purified MAD was utilized. See footnote 6. [c] Combined yields of the reduced alcohols. [d] Determined by ^1H NMR or GLC analysis. The ratios in the absence of MAD are designated in parentheses. [e] Use of 2 equiv of DIBAH accelerated the reduction of menthone.

simple example is the regioselective reduction of diketone **1** by using each 2 equiv of MAD/aluminum hydride reagent as illustrated below.

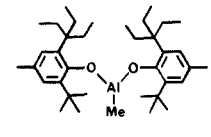


1



R = Ph : MAD/DIBAH	88%	(7:I:3)
R = Ph : MAD/Br_2AlH	72%	(7:0:1)
R = *i*-Pr : MAD/DIBAH	96%	(2:0:1)
R = *i*-Pr : MAD/Br_2AlH	87%	(28:0:1)

In conclusion, this process uses MAD as a protecting group for the normally more reactive functionality of a bifunctional molecule. Although the use of commercially available 2,6-di-*tert*-butyl-4-methylphenol as its aluminum salt is highly appealing from a practical point of view, selectivity in carbonyl reduction can be enhanced by using a more bulky aluminum ligand. Accordingly, when methylaluminum bis(2-*tert*-butyl-6-(1,1-diethylpropyl)-4-methylphenoxide) (MAB)[11] was utilized in place of MAD, the better selectivity was achievable in combination with acetophenone and isobutyrophenone: (MAB/DIBAH: 92% (ratio, 1:12); MAB/Br_2AlH: 100% (1:13)).



MAB

(11) 2-*tert*-Butyl-6-(1,1-diethylpropyl)-4-methylphenol was prepared from *p*-cresol by the following sequence: (i) 1,1-diethylpropylation with 3-ethyl-2-pentene and catalytic H_2SO_4 and (ii) tert-butylation with isobutene and catalytic H_2SO_4 in benzene. See: Stillson, G. H.; Sawyer, D. W.; Hunt, C. K. *J. Am. Chem. Soc.* **1945**, *67*, 303.

Acknowledgment. We are grateful to Dr. K. Kigoshi of Nagoya University for the low-temperature ^{13}C NMR measurement.

Supplementary Material Available: The low-temperature ^{13}C NMR spectra and data for acetophenone, pivalophenone, and a mixture of these ketones with MAD added in different molar ratios (8 pages). Ordering information is given on any current masthead page.

Determination of Long Distance Intramolecular Triplet Energy Transfer Rates. A Quantitative Comparison with Electron Transfer[1]

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Received December 24, 1987

Recent efforts in these laboratories have been directed toward understanding the factors governing long distance intramolecular electron transfer (ET).[2] In the models chosen for study the electronic coupling between donor and acceptor is sufficiently weak to assure nonadiabatic reactions. It occurred to us that long distance triplet energy transfer by the Dexter mechanism[3] (TT) of which there are several examples in the literature[4] should exhibit features similar to nonadiabatic electron transfer because both reactions are governed by the same theory of radiationless transitions. We therefore have started a program aimed at finding quantitative similarities and differences in these two processes when studied on directly comparable systems. Also, with one exception,[5] the absolute rates of intramolecular triplet energy transfer have never been measured directly in liquid solution. In this communication we report our first results and conclusions.

One of the series studied in ET, **1**, involves compounds in which a 4-biphenylyl group (D) is connected via a rigid spacer (Sp) with a 2-naphthyl group (A).[2a] The spacers used were cyclohexane

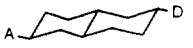
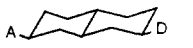
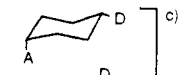
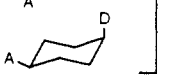
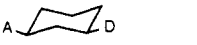
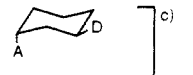
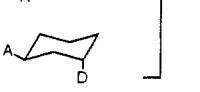
1: A = 2-naphthyl; D = 4-biphenylyl

2: A = 2-naphthyl; D = 4-benzophenoneyl

A-Sp-D

and decalin ring systems. Simply by replacing the 4-biphenylyl group with 4-benzophenonyl, the series can by converted to an almost ideal series **2** for triplet energy transfer. The spacers are listed in Table I. The triplet transfer rates were measured in benzene at room temperature by flash photolysis exciting the benzophenone chromophore and monitoring the decay of the $T_1 - T_n$ absorption of the benzophenone or the buildup of the naphthalene $T_1 - T_n$ absorption. The slower compounds were excited with a nitrogen laser, while the faster ones were measured on a picosecond spectrometer previously described.[6] Measurements at different concentrations allowed the separation of intermolecular from intramolecular processes.[7] The rate constants are listed in Table I. As expected the rate falls off with increasing number of bonds separating triplet donor and acceptor. In analogy to the findings of electron transfer in the equivalent systems, the

Table I.

compound		k_π[a] (s^{-1})	k_{ET}^{COR}[b] (s^{-1})
D-2,6ee		3.1×10^6	5.0×10^7
D-2,7ee		9.1×10^7	1.7×10^8
D-2,7ae		1.1×10^7	7.6×10^7
C-1,4ee		1.3×10^9	8.6×10^8
C-1,4ea	 [c]		7.2×10^8
C-1,4ae	 [c]	4.0×10^7	1.3×10^8
C-1,3ee		7.7×10^9	1.5×10^9
C-1,3ea	 [c]		
C-1,3ae	 [c]	3.3×10^9	
M		5.0×10^{10}	

[a] Measurement at room temperature, in benzene. The estimated errors are ±20%, with the exception of D-2,7ee, where the error is ±10%, and M, for which it is ±30%. [b] Rates from ref 2, but corrected for changes in solvent reorganization, normalized to D-2,6ee. [c] Assignment to either conformer is open at this time.

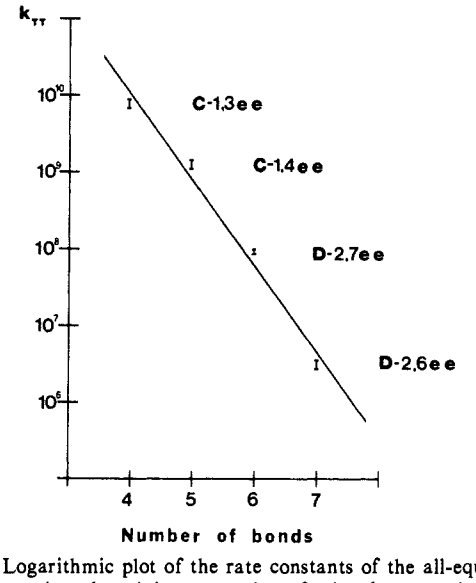


Figure 1. Logarithmic plot of the rate constants of the all-equatorial compounds against the minimum number of σ-bonds separating donor and acceptor. See Table I for key of compounds.

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