(4) M. Rosenblum, *Acc. Chem. Res.*, **7**, 122 (1974).
(5) T. Kauffmann, *Angew. Chem., Int. Ed. Engl.*, **13**, 627 (1974).
(6) R. Eidenschink and T. Kauffmann, *Angew. Chem., Int. Ed. Engl.*, **11**, 292 (1972).
(7) J. Shabtai and H. Pines, *J. Org. Chem.*, **26**, 4225 (1961); M. Kolobielski and H. Pines, *J. Am. Chem. Soc.*, **79**, 5820 (1957).
(8) G. F. Luteri and W. T. Ford, *J. Organomet. Chem.*, **105**, 139 (1976).
(9) G. Boche and D. Martens, *Angew. Chem., Int. Ed. Engl.*, **11**, 724 (1972).
(10) J. P. Marino and W. B. Mesbergen, *J. Am. Chem. Soc.*, **96**, 4050 (1974).
(11) T. Kauffmann and E. Köppelmann, *Angew. Chem., Int. Ed. Engl.*, **11**, 290 (1972); T. Kauffmann, K. Habersaat, and E. Köppelmann, *ibid.*, **11**, 291 (1972).
(12) A. Maercker, *J. Organomet. Chem.*, **18**, 249 (1969).
(13) J. A. Howard and K. U. Ingold, *Can. J. Chem.*, **45**, 793 (1967).
(14) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley-Interscience, New York, N.Y., 1965, pp 242–243.
(15) R. Huisgen, *J. Org. Chem.*, **41**, 403 (1976), and references cited therein.
(16) K. N. Houk, *Acc. Chem. Res.*, **8**, 361 (1975), and references cited therein.
(17) S. Nakahama, A. Hirao, Y. Ohira, and N. Yamazaki, *J. Macromol. Sci., Chem.*, **9**, 563 (1975).
(18) E. J. Panek, *J. Am. Chem. Soc.*, **95**, 8460 (1973).
(19) M. A. Doran and R. Waack, *J. Organomet. Chem.*, **3**, 94 (1965); G. Levin, T. A. Ward, and M. Szwarc, *J. Am. Chem. Soc.*, **96**, 270 (1974); T. A. Ward, G. Levin, and M. Szwarc, *ibid.*, **97**, 258 (1975); S. Sorensen, G. Levin, and M. Szwarc, *ibid.*, **97**, 2341 (1975).
(20) M. Newcomb and W. T. Ford, *J. Am. Chem. Soc.*, **96**, 2968 (1974).
(21) For a review see E. A. Hill, *J. Organomet. Chem.*, **91**, 123 (1975).
(22) H. Lehmkuhl, W. Bergstein, D. Henneberg, E. Janssen, O. Olbrysh, D. Reinehr, and G. Schomburg, *Justus Liebigs Ann. Chem.*, 1176 (1975), and references cited therein.
(23) M. Ogawa, M. Takagi, and T. Matsuda, *Tetrahedron*, **29**, 3813 (1973); M. Tomoi and H. Kakiuchi, *Polym. J.*, **5**, 195 (1973).
(24) Further details are available in the Ph.D. Thesis of G.F.L., University of Illinois at Urbana-Champaign, 1976.
(25) J. A. Zapp, Jr., *Chem. Eng. News*, 3 (Feb 2, 1976).
(26) H. Gilman and F. K. Cartledge, *J. Organomet. Chem.*, **2**, 447 (1964).
(27) R. E. Buckles and K. Bremer, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 777; R. E. Buckles and N. G. Wheeler, *ibid.*, 857.
(28) R. Y. Mixer, R. F. Heck, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **75**, 4094 (1953).
(29) S. F. Reed, Jr., *J. Org. Chem.*, **30**, 3258 (1965).
(30) D. S. Tarbell, *Chem. Rev.*, **27**, 495 (1940); V. L. Tweedie and M. Curcurida, *J. Am. Chem. Soc.*, **79**, 5463 (1957).
(31) O. Achmatowicz, M. Leplawy, and A. Zamojski, *Rocz. Chem.*, **30**, 215 (1956); *Chem. Abstr.*, **51**, 1087*d* (1957).
(32) G. Levin, J. Jagur-Grodzinski, and M. Szwarc, *J. Org. Chem.*, **35**, 1702 (1970).
(33) S. Dixon, *J. Org. Chem.*, **21**, 400 (1956).
(34) M. Schlosser and V. Ladenberger, *J. Organomet. Chem.*, **8**, 193 (1967).
(35) W. J. Middleton, German Patent 1 950 933 (1970); *Chem. Abstr.*, **73**, 14425 (1970); U.S. Patent 3 683 009 (1972).
(36) A. I. Meyers, D. L. Temple, D. Haidukewych, and E. D. Mihelich, *J. Org. Chem.*, **39**, 2787 (1974).
(37) H. L. Wehrmeister, *J. Org. Chem.*, **27**, 4418 (1962).
(38) H. C. Brown, P. M. Weissmann, and N. M. Yoon, *J. Am. Chem. Soc.*, **88**, 1458 (1966).

Rate Enhancement of the Meerwein–Ponndorf–Verley–Oppenhauer Reaction in the Presence of Proton Acids[1]

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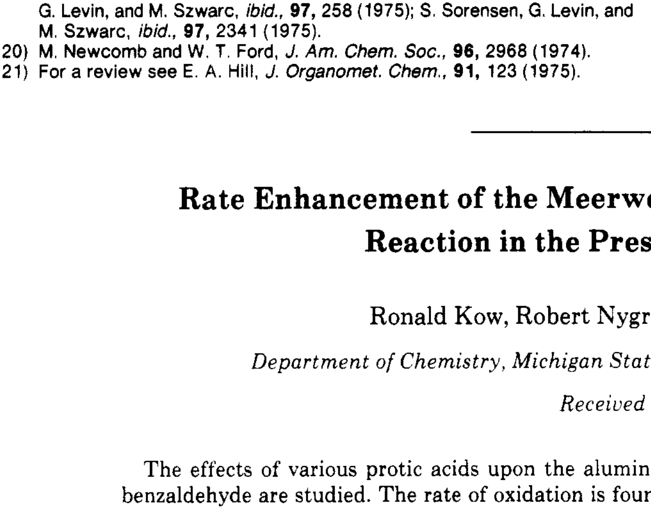
The effects of various protic acids upon the aluminum *tert*-butoxide catalyzed oxidation of cyclohexanol by benzaldehyde are studied. The rate of oxidation is found to be markedly enhanced by an acid to aluminum ratio of 0.5 for HCl, FSO_3H, $CH_3CH_2CO_2H$, and CF_3CO_2H, with CF_3CO_2H giving the greatest rate enhancement. Synthetic applications of this method, however, are limited by the observation that trifluoroacetic acid–aluminum alkoxide mixtures are potent aldol catalysts.

The Meerwein–Ponndorf–Verley–Oppenhauer (MPVO) reaction is the aluminum alkoxide catalyzed equilibration of alcohols with aldehydes or ketones[2], eq 1. A key step in the reaction is thought to be hydride transfer within the polymeric aluminum complexes I and II.[3]



$$R_2CHOH + R_2'CO \xrightleftharpoons{[Al(OR)_3]_n} R_2CO + R_2'CHOH$$

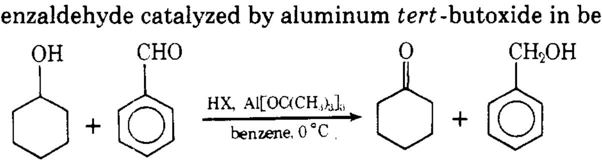
(1)

I II

Replacement of alkoxy groups on aluminum with more electronegative ligands should increase the rate of MPVO reactions by facilitating coordination of aluminum to the carbonyl compound.[4] This replacement should be achieved most simply by addition of a suitable proton acid (HX) to a solution of the aluminum alkoxide (eq 2).

$$[Al(OR)_3]_n + HX \rightarrow HOR + [XAl(OR)_2]_n \qquad (2)$$

For study, we chose the reaction between cyclohexanol and benzaldehyde catalyzed by aluminum *tert*-butoxide in benzene solution at 0 °C (eq 3). The rate of reaction was followed by removing aliquots at various times and analyzing by GLC for cyclohexanone. With a twofold excess of benzaldehyde, equilibrium is established when 88% of the starting cyclohexanol is converted to cyclohexanone. Results obtained in the presence of a variety of proton acids are shown in Table I.



(3)

The most effective catalyst is trifluoroacetic acid, present at an acid to aluminum ratio of 0.5. Data obtained with this acid are presented graphically in Figure 1.

With all acids studied, the reaction fails when a critical ratio of acid to aluminum is exceeded. In some cases this is perhaps due to the precipitation of aluminum compounds which occurs with the higher ratios of acid. However, with trifluoroacetic acid no precipitate is formed at an acid to aluminum ratio of 2.0, yet at this point the MPVO reaction fails. It is conceivable that only nonbridging alkoxy groups in complexes I and II are able to transfer hydride[5] and that at a critical acid to aluminum ratio all such groups are replaced with trifluoroacetate ligands.

^1H NMR examination of the catalyst system is hampered by precipitation of aluminum compounds in the absence of added alcohol or aldehyde. Thus, when 0.3 equiv of trifluoroacetic acid was added to aluminum *tert*-butoxide in benzene, a precipitate was formed and ^1H NMR analysis of the supernatent revealed only the normal spectrum of the aluminum *tert*-butoxide dimer[6] together with 0.3 equiv of *tert*-butyl alcohol.

Table I. MPVO Reaction of Cyclohexanol with Benzaldehyde in the Presence of Proton Acids (HX)[a]

Registry no.	HX	HX/Al[b]	T_{50}[c]	T_{80}[d]
	[e]		8	80
76-05-1	CF_3CO_2H	0.5	<1	1
	CF_3CO_2H	1.0	<1	5
	CF_3CO_2H	2.0	[f]	
7647-01-0	HCl	0.5	<1	9
	HCl	1.0	[f]	
79-09-4	$CH_3CH_2CO_2H$	0.5	5	40
	$CH_3CH_2CO_2H$	1.0	[f]	
7789-21-1	FSO_3H	0.5	2	30
	FSO_3H	1.0	[f]	

[a] Reactions run at 0 °C in benzene solutions, 1 M in cyclohexanol, 2 M in benzaldehyde, and 0.05 M in $Al[OC(CH_3)_3]_3$. [b] Molar ratio of proton acid to Al. [c] Time in minutes for 50% of the starting cyclohexanol to be oxidized to cyclohexanone. [d] Time in minutes for 80% of the starting cyclohexanol to be oxidized to cyclohexanone. [e] No proton acid was added. [f] No oxidation of starting cyclohexanol occurred after at least 12 h.

We have observed rate enhancements for the trifluoroacetic acid promoted MPVO reaction of a number of alcohols with aldehydes or ketones. However, synthetic applications of the method are limited by the fact that trifluoroacetic acid–aluminum alkoxide mixtures are potent aldol catalysts, especially for simple aliphatic aldehydes. As an example, the rate of condensation of heptanal in benzene solutions containing aluminum *tert*-butoxide in the presence and absence of trifluoroacetic acid was observed (eq 4).

$$CH_3(CH_2)_5CHO \xrightarrow[\text{benzene, 0 °C}]{Al(OR)_3} CH_3(CH_2)_5CHOHCH(CHO)(CH_2)_4CH_3 \quad (4)$$

With no added trifluoroacetic acid, 50% of the heptanal was condensed in 3 h. In the presence of trifluoroacetic acid (acid to aluminum ratio of 0.5), over 90% of the aldehyde was condensed in 5 min. Trifluoroacetic acid alone, in the absence of aluminum alkoxide, did not cause condensation.

Experimental Section

Trifluoroacetic acid was obtained from Matheson Coleman and Bell. Fluorosulfonic acid was obtained from Aldrich Chemical Co. Hydrogen chloride gas was purchased in a lecture bottle from Matheson Gas Corp. Propanoic acid was obtained from Fisher Scientific Co. Aluminum *tert*-butoxide was obtained from Alfa Inorganics and stored in a vacuum desiccator. Benzene was dried by distillation from calcium hydride and stored under a nitrogen atmosphere. Other reagents were obtained commercially and distilled before use. GLC analyses were performed on a Varian 920 gas chromatograph equipped with a 4 ft × 0.25 in. stainless steel column of 10% Carbowax 20M on Chromosorb W 80/100 mesh. ^1H NMR spectra were determined on a Varian T-60.

MVPO Reactions. The following procedure for the oxidation of cyclohexanol with benzaldehyde using aluminum *tert*-butoxide and trifluoroacetic acid (acid/aluminum ratio of 0.5) is representative. A 100-ml round-bottomed flask equipped with a septum inlet, magnetic stirring, and mercury bubbler is flushed with nitrogen and charged with 0.246 g (1 mmol) of aluminum *tert*-butoxide dissolved in 20 ml of benzene. The flask is immersed in an ice–water bath and stirring is initiated. Cyclohexanol (2.08 ml, 20 mmol) is injected, followed by 37 μl (0.5 mmol) of trifluoroacetic acid. Tridecane (2.44 ml, 10 mmol) is added as GLC standard. After 5 min of stirring, benzaldehyde (4.08 ml, 40 mmol) is injected to start the reaction. One-milliliter aliquots are removed periodically and quenched by addition to 4 ml of a saturated solution of tartaric acid in H_2O (to dissolve aluminum salts), extracted with 8 ml of pentane, dried with $MgSO_4$, and analyzed by GLC for cyclohexanone.

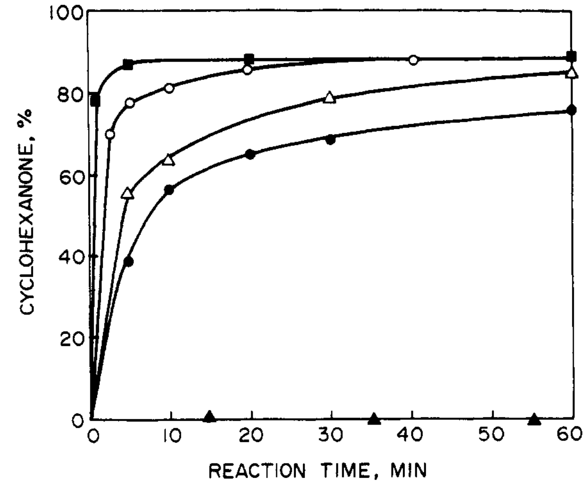


Figure 1. Formation of cyclohexanone in the trifluoroacetic acid promoted MPVO reaction of cyclohexanol with benzaldehyde: ●, no HX; △ HX/Al 0.1; ■, HX/Al 0.5; ○, HX/Al 1.0; ▲, HX/Al 2.0

Aldol Condensation of Heptanal. A solution of aluminum *tert*-butoxide (0.123 g, 0.5 mmol) in benzene (10 ml) containing 0.73 ml (2.5 mmol) of hexadecane as internal GLC standard is cooled in an ice–water bath. Heptanal (1.35 ml, 10 mmol) is injected and aliquots are removed periodically and analyzed for remaining heptanal. After 2 days of stirring the aldol product, 2-*n*-pentylnonanal was isolated by preparative GLC and identified by infrared spectroscopy. Experiments in the presence of trifluoroacetic acid were conducted in a similar fashion except that 18.5 μl (0.25 mmol) of CF_3CO_2H was added prior to addition of heptanal.

^1H NMR Examination of Catalyst System. ^1H NMR spectra were obtained on 0.1 M solutions of aluminum *tert*-butoxide in benzene containing internal tetramethylsilane standard. After addition of trifluoroacetic acid the precipitate was allowed to settle and spectra of the clear supernatant were obtained. The amount of *tert*-butyl alcohol formed on addition of acid was determined by integration of spectra for solutions containing known amounts of anisole as internal integration (methoxy signal) standard. The assignment of ^1H NMR signals was based on Shiner's report:[6] δ 1.5, singlet (bridging *tert*-butoxy); 1.4, singlet (nonbridging *tert*-butoxy); 1.1, singlet (*tert*-butyl alcohol).

Registry No.—$Al[OC(CH_3)_3]_3$, 3099-76-1; cyclohexanol, 108-93-0; benzaldehyde, 100-52-7.

References and Notes

(1) Grateful acknowledgment is made to the National Science Foundation for partial support of this work.

(2) The Meerwein–Ponndorf–Verley reduction of aldehydes and ketones has been reviewed by Wilds: A. L. Wilds, *Org. React.*, **2**, 178 (1944). Djerassi has reviewed the Oppenauer oxidation of primary and secondary alcohols: C. Djerassi, *ibid.*, **6**, 207 (1951).

(3) (a) H. Meerwein, B. Bock, B. Kirschnick, W. Lenz, and A. Migge, *J. Prakt. Chem.*, **147**, 211 (1936); R. B. Woodward, N. L. Wender, and F. J. Brutschy, *J. Am. Chem. Soc.*, **67**, 1425 (1945); L. M. Jackman and A. K. Macbeth, *J. Chem. Soc.*, 3252 (1952); W. von E. Doering and T. C. Aschner, *J. Am. Chem. Soc.*, **75**, 393 (1953). (b) The polymeric nature of complexes I and II was first clearly demonstrated by Shiner: V. J. Shiner, Jr., and D. Whittaker, *J. Am. Chem. Soc.*, **91**, 394 (1969).

(4) In agreement with this, replacement of 25–30% of the usual aluminum isopropoxide catalyst with chloroaluminum isopropoxide was reported to appreciably increase the rate of MPVO reactions: G. Gál and I. Kraznai, *Magy. Kem. Foly.*, **62**, 155 (1956); *Chem. Abstr.*, **52**, 10872*d* (1958).

(5) This assumption is implicit in prior formulations of the hydride transfer step.[3]

(6) V. J. Shiner, Jr., D. Whittaker, and V. P. Fernandez, *J. Am. Chem. Soc.*, **85**, 2318 (1963).