$J = 4.54$, 1 H), 7.10–7.34 (m, 5 H); IR (KBr) 3028, 2950, 2227, 1735, 1680, 1396, 1305, 1198, 1086, 704 cm^{-1}; MS *m/e* 284 (M$^+$), 242, 183, 182, 181, 155, 128, 115, 105, 91.

Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.86. Found: C, 67.67; H, 5.69; N, 9.95.

Isomer of 11d (colorless oil): ^{1}H NMR ($CDCl_3$) δ 2.35 (b, 3 H), 2.84–2.90 (m, 1 H), 3.70 (s, 3 H), 3.85–3.88 (m, 2 H), 4.11 (b, 1 H), 6.18–6.19 (d, $J = 3.48$, 1 H), 7.16–7.37 (m, 5 H); IR (CH_2Cl_2) 3028, 2952, 2226, 1734, 1683, 1435, 1395, 1331, 1031, 702 cm^{-1}; MS *m/e* 285 (M$^+$ + 1), 284 (M$^+$), 242, 241, 232, 183, 182, 181, 155, 129, 128, 127, 115, 105, 91; HRMS calcd for $C_{16}H_{16}N_2O_3$ 284.1162, found 284.1160.

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Supplementary Material Available: NMR spectra of **2c,d 4d**, **5c**, **6**, isomers of **8**, **10a,b**, isomers of **10a**, **11d**, and **13–15** (13 pages). Ordering information is given on any current masthead page.

Notes

Kinetic Isotope Effects and Possible Brønsted Curvature in a Simple Enolization Reaction

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Among the methods used to probe transition-state structure and to assess the changes in such structures that are brought about by substitution, two of the most important are (i) the Brønsted relationship and the matter of curvature of therein[1-9] and (ii) kinetic isotope effects and the question of changes in their magnitude.[8-12]

We have previously conducted an exhaustive examination of the enolization of acetone catalyzed by general acids and bases,[13-15] using both carboxylic and phosphonic species, and in those systems that could be examined, we have observed neither curvature of the Bønsted line for any individual system nor variations in the magnitude of the deuterium kinetic isotope effect. It should be noted, however, that in most instances where Brønsted curvature has been reported, it was necessary to embrace a wider range of catalyst acid or base strengths than we had been able to use. With regard to kinetic isotope effects, one expects to find pronounced changes therein only when base strengths of the species removing the proton from the substrate are considerably different from the base strengths of the species formed in the reaction, that is, when the proton in question could not be described as being half-transferred in the transition state. In the carboxylic acid catalyzed enolization of acetone (where we observed no significant change in the isotope effect), the species formed in the reaction (acetone enol) and the base that removed the proton in the rate-controlling step (a carboxylate ion) have comparable base strengths.[13]

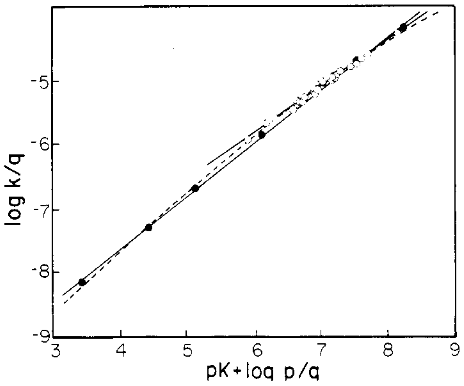

Figure 1. Brønsted plots for the reaction given in eq 1. The dotted line represents a quadratic equation and includes all points; the solid lines for alkylphosphonates (closed circles) and arylphosphonates (open circles) are the least-squares straight lines.

We here report the results of our final study of the enolization of acetone, in which we have used a series of phosphonate dianions of widely varying base strength, and for which we could obtain kinetic isotope effects in regions far removed from those in which the proton is expected to be half-transferred in the transition state. The rate-

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Table I. Data for the Enolization of Acetone and Acetone-d_6[a] Catalyzed by the Dianions of Phosphonic Acids in Water at 25 °C, Ionic Strength 0.1

acid	pK_2[b]	10^6k_H	10^7k_D	k_H/k_D
$(CH_3)_3CPO_3H_2$	8.71	206 ± 3	298 ± 5	6.91 ± 0.15
$2,6-(CH_3)_2C_6H_3PO_3H_2$	8.62	159 ± 3	303 ± 5	5.29 ± 0.13
$2,4-(CH_3)_2C_6H_3PO_3H_2$	8.07	65.1 ± 2.0	141 ± 2	4.62 ± 0.08
$CH_3PO_3H_2$	8.00	60.8 ± 1.0	133 ± 2	4.57 ± 0.10
$3,4-(CH_3)_2C_6H_3PO_3H_2$	7.76	42.1 ± 0.8	92.8 ± 0.9	4.54 ± 0.10
$3-ClC_6H_4PO_3H_2$	7.10	14.8 ± 0.1	42.7 ± 0.7	3.47 ± 0.06
$4-CNC_6H_4PO_3H_2$	6.79	7.88 ± 0.24	24.9 ± 0.4	3.16 ± 0.11
$ClCH_2PO_3H_2$	6.59	4.42 ± 0.27	15.0 ± 0.6	2.90 ± 0.21
$2,4-(NO_2)_2C_6H_3PO_3H_2$	6.38	3.80 ± 0.02	13.6 ± 0.5	2.79 ± 0.10
$Cl_2CHPO_3H_2$	5.61	0.658 ± 0.030	2.66 ± 0.01	2.47 ± 0.02
$Cl_3CPO_3H_2$	4.93	0.161 ± 0.010	0.695 ± 0.020	2.32 ± 0.16
$F_3CPO_3H_2$	3.93	0.023 ± 0.002	0.114 ± 0.001	2.02 ± 0.18

[a] Deuterium, 99.9 atom %, Merck Frosst Canada. [b] Either reported in ref 21 or determined as described therein.

Table II. Brønsted Slopes and Correlation Coefficients for the Reaction of Eq 1

series	β	corr coeff
combined set (38 points)		
(a) linear treatment	0.816	0.9960
(b) quadratic treatment	–	0.9985
alkylphosphonates (6 points)	0.830	0.9997
arylphosphonates (32 points)	0.703	0.9944

controlling step of the reaction in question is given by eq 1.

$$CH_3COCH_3 + ZPO_3^{2-} \rightarrow CH_3COCH_2^- + ZPO_3H^- \quad (1)$$

Results and Discussion

Kinetic data for the reaction of acetone and acetone-d_6 with a series of alkyl- and arylphosphonate dianions are listed in Table I. The Brønsted plot for the protio compound is shown in Figure 1, which also includes points for 26 phosphonate dianions previously reported.[15] Although a straight line accommodates all points fairly well, the best fit is a quadratic equation (eq 2) representing a gentle curve (the dashed line in the figure). If one splits the catalysts into alkyl- and arylphosphonates, however, the result is two lines of somewhat different slope that are much closer to being linear (the two solid lines in the figure). The slopes and correlation coefficients for the quadratic and the pertinent straight lines are given in Table II.

$$y = -12.046\ (\pm0.1872) + 1.2470x\ (\pm0.0625) - 0.035764x^2\ (\pm0.005151) \quad (2)$$

These results show how difficult it is to determine whether or not a Brønsted line departs from linearity. Since an extended series of catalysts is usually required for the purpose, one is likely to encounter structural changes in the catalyst that raise questions about whether all of them belong to a single series. In the present case there is a confluence of the points for the aryl- and alkylphosphonates but their individual Brønsted slopes are somewhat different, suggesting that even the change from alkyl to aryl is sufficient to produce two different series. And might not further subdivisions appear if there were a sufficiently large number of catalysts available for study within each of these series? (The ortho, meta, and para compounds appear to form a single set although there is slightly more scatter for the ortho compounds.[15]) This having been said, it should be pointed out that in the present work (including the results for acetone-d_6) the Brønsted lines for the individual alkyl and aryl species all appear to curve in the expected direction (concave downward), if only to a slight degree in most cases. These small effects may not be obvious from the plots in Figure 1, and furthermore, it is not clear what significance, if any, should be attached to them, particularly since the correlation coefficients for the linear relationships shown in Table II are all satisfactory.

The situation with respect to isotope effects is much clearer; a large and monotonic decrease in isotope effect accompanies a decrease in base strength of the catalyst (Table I). The largest isotope effect, 6.91, is quite substantial and is found for the dianion of *tert*-butylphosphonic acid, whose p*K* value is closest to that of acetone but is nonetheless separated from it by some 10 p*K* units. This suggests that a rather broad maximum would be found if the series could be extended to catalysts that are still more basic, assuming, of course, that the isotope effect does indeed reach a maximum when the two bases sharing the proton in the transition state are equal in strength. We resist the temptation to attempt a correlation between Brønsted curvature and isotope effect and conclude by pointing out that the latter gives straightforward results whereas the former tends to be ambiguous and, indeed, downright vexing. This situation arises partly because each compound in a series provides a value of the isotope effect whereas several (or many) compounds are needed to determine a single Brønsted value.[22]

Experimental Section

Reaction rates were determined iodometrically and the results analyzed as previously described.[15]

(2,4-Dinitrophenyl)phosphonic acid was prepared by the acid hydrolysis of the corresponding ethyl ester, prepared, in turn, from 1,2,4-trinitrobenzene by the method of Cadogan et al;[16] mp 200 °C dec. Anal. Calcd for $C_6H_5N_2O_7P$: C, 29.04; H, 2.03; N, 11.29. Found: C, 29.01; H, 2.01; N, 11.20. 1,2,4-Trinitrobenzene was obtained by oxidizing 2,4-dinitroaniline by the method of Emmons and Ferris.[17] The preparation of the other arylphosphonic acids has been described elsewhere.[15]

Methylphosphonic acid was prepared by the acid hydrolysis of the methyl ester. (Chloromethyl)- and (dichloromethyl)-phosphonic acids were prepared by the method of Kinnear and Perren.[18] (Trichloromethyl)phosphonic acid was prepared by the acid hydrolysis of the corresponding ethyl ester, and *tert*-butylphosphonic acid was prepared from *tert*-butyl chloride by the methods of Crofts and Kosolapoff.[19] (Trifluoromethyl)phosphonic acid was prepared by the method of Bennett et al.[20]

Registry No. $CH_3C(O)CH_3$, 67-64-1; $(CH_3)_3CPO_3H_2$, 4923-84-6; $2,6-(CH_3)_2C_6H_8PO_3H_2$, 85320-23-6; $2,4-(CH_3)_2C_6H_2PO_3H_2$, 111192-85-9; $CH_3PO_3H_2$, 993-13-5; $3,4-(CH_3)_2C_6H_3PO_3H_2$, 53104-47-5; $3-ClC_6H_4PO_3H_2$, 5431-34-5; $4-CNC_6H_4PO_3H_2$, 16672-78-9; $ClCH_2PO_3H_2$, 2565-58-4; $2,4-(NO_2)_2C_6H_3PO_3H_2$, 129239-67-4; $Cl_2CHPO_3H_2$, 13113-88-7; $Cl_3CPO_3H_2$, 5994-41-2; $F_3CPO_3H_2$, 374-09-4; D_2, 7782-39-0.

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(22) For a detailed discussion of the relationship between Brønsted curvature and substrate structure, see ref 9 and references therein. [Note added in proof. See also: Stefanidis, D.; Bunting, J. W. *J. Chem. Soc.* 1990, *112*, 3163.]