206–208°, **16** and **17**; (2) 2.95 g, mp 135–138°, **16**; (3) 1.17 g. The infrared spectra ($CHCl_3$) of all fractions were very similar and identical with that obtained in run F. They exhibited peaks at 2.95 (w), 3.4 (s), 3.6 (w), 4.1 (w), 5.85 (s), 6.15 (m), 6.28 (w), 6.72 (m), 6.92 (s), 7.25 (w), 7.95 (w), 8.05 (w), 8.15 (w), 8.8 (w), 9.0 (s), and 10.0 (m) μ. The peaks at 6.15 and 6.28 μ (1628 and 1590 cm^{-1}) varied in intensity in the different fractions. Fraction 1 (0.449 g) was dissolved in warm water and treated with 1 *N* sodium hydroxide to give an immediate precipitation of 0.305 g of a mixture of triphenylphosphine and the keto ylid **18**, mp 74–82° (identified by infrared and tlc). The mixture was shown to be *ca.* 1:9 keto ylid–triphenylphosphine as follows. An aliquot (0.125 g) was treated with mercuric chloride in acetone to give 0.185 g of $HgCl_2 \cdot (C_6H_5)_3P$, mp 301–305° dec. Therefore fraction 1 contained 89% 3-keto- and 11% of 2-ketocyclohexyltriphenylphosphonium bromide **17** and **16**. Fraction 2 (2.95 g, 0.0033 mole) was similarly treated with sodium hydroxide to give the keto ylid **18** only, 0.814 g (0.0023 mole, 70%), mp 237–239°, and no triphenylphosphine (tlc). Fraction 3 gave no precipitate with sodium hydroxide. These results correspond to minimum yields of 3.15 g of the 2-keto salt **16** (0.0072 mole, 18%) and 1.95 g of the 3-keto salt **17** (0.0044 mole, 11%). The keto ylid **18** was recrystallized twice from ethyl acetate to give mp 245–247°, mmp 228–238° with an impure genuine sample of **18** (mp 228–232°).[18] The conversion of **16** to keto ylid with sodium methoxide in methanol[26] gave much poorer yields. The keto ylid **18** exhibited diagnostic infrared peaks at 6.65 (s) and 9.15 (s) μ.

The Reaction of 2-Mesyloxycyclohexanone with Triphenylphosphine.[19]—A mixture of 2-mesyloxycyclohexanone 19 (11.30 g, 0.0059 mole) and triphenylphosphine (15.49 g, 0.0059 mole) in dry 1,2-dimethoxyethane (25 ml) was refluxed for 5 hr to give 2-ketocyclohexyltriphenylphosphonium mesylate **20** (12.80 g, 48.5%), mp 212.5–214°. The infrared spectrum of **20** (CH_2Cl_2) was similar to that of **16** or **17** and exhibited peaks at 5.83 (m), 6.15 (s), 6.28 (w), 6.68 (m), 6.90 (s), 7.16 (m), 7.32 (w), 7.42 (w), 7.50 (w), 8.05 (m), 8.2–8.35 (s), 8.95 (s), 9.55 (s) and 9.95 (s) μ. Treatment of **20** with 1 *N* aqueous sodium hydroxide gave the keto ylid **18** (76%), mp 215–217°; the infrared spectrum was identical with genuine **18**.

The Reaction of Triphenylphosphine with Mercuric Chloride.[31]—Typically triphenylphosphine to be determined was titrated with mercuric chloride in dry acetone until no further precipitation occurred. This led to quantitative yields of the complex and no triphenylphosphine was left (tlc). If excess mercuric chloride was used the complex occasionally was contaminated by mercuric chloride. Atypically the following experiment established the 1:1 nature of the complex. Triphenylphosphine (0.7928 g, 0.0030 mole) was dissolved in 100 ml of benzene. To this solution was added 3.124 g (0.0115 mole) of mercuric chloride in 25 ml of ethanol to give the complex (2.5855 g, 0.00296 mole if 1:1 $HgCl_2$–PPh_3) and recovered mercuric chloride (2.417 g, 0.0089 mole recovered or 0.0026 mole used). The complex had mp 322–326° and was insoluble in benzene, acetone, petroleum ether, ethyl acetate, and chloroform. *Anal.* Calcd for $C_{18}H_{15}$-$PHgCl_2$: P, 5.80. Found. P, 5.84.

Acknowledgment.—The authors wish to thank Professor C. Griffin, University of Pittsburgh, for early nmr spectra and Mr. R. Lazarus, Lehigh University, for nmr aid. We are indebted to Dr. Grace Borowitz for stimulating discussions. This investigation was supported in part by National Science Foundation Grant No. GP-1354. Their generous funding of a Varian A-60A nmr spectrometer is also gratefully acknowledged.

[31] Unpublished results of H. Parnes and M. Thames, Lehigh University.

Solvent Effects. III. The Influence of Aqueous Dimethyl Sulfoxide on Alkyl Benzoate Ester Saponification Reactions

DONALD D. ROBERTS

Department of Chemistry, Louisiana Polytechnic Institute, Ruston, Louisiana 71270

Received May 31, 1966

The rates of alkaline hydrolysis of seven alkyl benzoate esters have been determined in aqueous dimethyl sulfoxide (DMSO) solvent mixtures of 0.25 to 0.65 mole fraction of DMSO. The rate constant in all cases increases with increasing DMSO content and is well correlated with solvent dielectric constant. The rate constant increase is nearly independent of the alkyl group steric substituent constant but the linear correlation with mole fraction of DMSO readily distinguishes between the branched and nonbranched alkyl benzoate esters. The DMSO catalyst effect is discussed in terms of a solvent cavity model.

The effect of variation of the acyl group in a series of ethyl esters on the saponification rate constant as the dimethyl sulfoxide content of the aqueous DMSO solvent changes was reported in the previous two papers of this series.[1,2] Generally, it was noted that an increase in the steric substituent constant for R was reflected by an enhanced sensitivity to dimethyl sulfoxide catalysis (RCO_2R').

More specifically, it was observed that the dimethyl sulfoxide profile (rate constant *vs.* mole fraction DMSO) for branched R groups is a single linear correlation in contrast to a set of two intersecting linear correlations for the straight-chain esters.

These observations were interpreted largely in terms of solvent assistance to the development of the transition state. For branched esters, electrostatic forces between bulk dielectric[3] and transition state were proposed while a combination of electrostatic and specific solvation forces were associated with the nonbranched esters.[2] The effect of the frequently mentioned[4,5] anion desolvation as the major contributing cause for the rate constant increases was considered to be inconsistent with the data.

The present paper reports the influence of changing R′ upon the dimethyl sulfoxide catalysis effect as a logical continuation of the study. By this means the previous mechanistic speculations can be both confirmed and extended. The choice of alkyl benzoates as the substrate was dictated by several reasons: (a) the convenient rates of reactions over the range

---

[1] D. D. Roberts, *J. Org. Chem.*, **29**, 2039 (1964).

[2] D. D. Roberts, *ibid.*, **30**, 3516 (1965).

[3] (a) K. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, p 388 ff; (b) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 266–267; (c) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 519, 535.

[4] A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

[5] E. Tommila and M. L. Murto, *Acta Chem. Scand.*, **17**, 1947 (1963).

TABLE I

RATES OF ALKALINE HYDROLYSIS OF SEVEN BENZOATE ESTERS, $C_6H_5CO_2R$, IN AQUEOUS DIMETHYL SULFOXIDE

Mole fraction of DMSO	Temp, °C	$k_2 \times 10^4$ CH_3	i-C_3H_7	i-C_4H_9	t-C_4H_9
0.25	15	348			
	25	680			
	30		79		
	35		108		
	40		189		
	45		193		
0.30	10	330			
	15	455			
	20	660		37	
	25	950	63	65	
	30		84	87	1.85
	35		112	150	3.2
	40		147		5.2
	45				9.0
0.35	15	645			
	20		56	103	
	25	1280	80	158	
	30		110		4.8
	35		150	390	7.4
	40				10.7
	45				16.6
0.40	10	560			
	15	875		165	
	20	1140	79	214	
	25	1700	110	276	
	30		140	362	7.4
	35		192	477	11.3
	40				17.1
	45				26.0
0.45	10	780			
	15	1140		255	
	20	1620	125	390	
	25	2430	165	556	
	30		225	842	11.7
	35		292		18.0
	40				26.0
	45				38.8
0.51	10	1250			
	15	1600		300	
	20	2250	164	460	
	25	2960	225	700	
	30		300	1020	18
	35		414		27
	40				40
	45				59
0.55	10	1400			
	15	2020		550	
	20	2870	225	740	
	25	4150	325	1030	
	30		464	1400	26.2
	35				40
	40				60
	45				94
0.60	10	1900			
	15	2800	205	860	
	20	4000	296	1200	
	25	5800	440	1570	28
	30		630	2200	41
	35				60
	40				89
0.65	15	4330	370	1420	
	20		534		
	25		730	2520	48
	30		1090		74
	35				103
	40				145
0.70	15		720		
	20		1040		
	25		1480		117
	30		2050		144
	35				177
	40				220

Mole fraction of DMSO	Temp, °C	$k_2 \times 10^4$ n-C_3H_7	$(CH_3)_3$-CCH_2	$(C_2H_5)_2$-$CHCH_2$
0.30	25	200		
		204		
0.35	25	290	170	
			170	
0.40	25	412	216	192
		408	214	192
0.45	25	566	346	250
		574	350	250
0.51	25	760	502	470
		740	508	470
0.55	25	1080	760	670
			760	670
0.60	25	1720	1115	960
			1105	960
0.65	25	2710	1780	1600
		2740	1780	1600

15 to 40°, (b) the well-studied reaction mechanism,[6] and (c) the ready availability of benzoate esters.

Results and Discussion

The kinetic findings of this work are presented in Table I. All of the reactions followed second-order kinetics from low to 75% conversion; unless otherwise stated, an uncertainty of ±2.0% is assumed. The data in Table II reveal that ethyl benzoate is 2.9 times more sensitive to dimethyl sulfoxide catalysis than ethyl acetate. The reduced reactivity of benzoate esters in aqueous ethanol is associated with resonance stabilization of the ground state.[7] In contrast, the increased sensitivity of ethyl benzoate to DMSO catalysis suggests a benzene ring enhancement of the carbonyl carbon polarizability in a manner somewhat similar to the benzyl system in S_N2-type reactions.

TABLE II

SENSITIVITY OF ETHYL BENZOATE TO DMSO CATALYSIS RELATIVE TO ETHYL ACETATE

Ester	10^4k_2 at 25° 0.69 N_{DMSO}[a]	0.69 N_{EtOH}[b]	k_s[c]	k_{rel}[d]
CH_3CO_2Et	20,000	62.10	310	1.0
$C_6H_5CO_2Et$	5,750	6.31	910	2.9

[a] 90% (by volume) aqueous DMSO. [b] 85% (by weight) aqueous ethanol. [c] The ratio of k_2 for a given ester in aqueous DMSO relative to k_2 in aqueous ethanol. [d] The ratio of k_s for a given ester relative to k_s for ethyl acetate.

The sensitivity, m, of the substrates to the dimethyl sulfoxide content in the varying solvent compositions (obtained from eq 1 by linear regression analysis)

$$\log k_2 = mN_{DMSO} + a \tag{1}$$

---

[6] (a) M. L. Bender, *J. Am. Chem. Soc.*, **73**, 1626 (1951); (b) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 12.

[7] (a) F. H. Westheimer and R. P. Metcalf, *J. Am. Chem. Soc.*, **63**, 1339 (1941); (b) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 604.

Table III

Effect of Mole Fraction DMSO on Saponification Rate

Ester	m_I[a]	m_{II}[b]
α Series		
$C_6H_5CO_2CH_3$	3.2 ± 0.1	3.4
$C_6H_5CO_2CH_2CH_3$	3.2 ± 0.1	3.4
$C_6H_5CO_2CH(CH_3)_2$	3.2 ± 0.1[c]	
$C_6H_5CO_2C(CH_3)_3$	3.8 ± 0.3[c]	
β Series		
$C_6H_5CO_2CH_2CH_3$	3.2 ± 0.1	3.4
$C_6H_5CO_2CH_2CH_2CH_3$	3.2 ± 0.1	3.4
$C_6H_5CO_2CH_2CH(CH_3)_2$	6.0 ± 0.2	3.4
$C_6H_5CO_2CH_2C(CH_3)_3$	3.3 ± 0.2[c]	
$C_6H_5CO_2CH_2CH(CH_2CH_3)_2$	3.4 ± 0.3[c]	

[a] Value of m calculated for the <.050 mole fraction DMSO solvent composition region. [b] Value of m estimated for the >0.45 mole fraction DMSO solvent composition region. [c] Includes data from entire solvent composition range.

is recorded in Table III. In agreement with previous findings,[2] the rate constant in all cases increases with increasing DMSO content and in the critical solvent composition region[8] of N_{DMSO} = about 0.50 (*cf.* Figure 1 and 2) the branched alkyl benzoates fail to exhibit the deviations from linearity (with the single exception of the isobutyl ester) associated with the nonbranched alkyl benzoates. All of the investigated benzoates have a similar m_{II} value. Accordingly, $m_{II} \simeq 3.4$ is taken to be a measure of the normal DMSO catalytic constant for this ester series.

It is instructive to divide the data in Table III into an α- and β-substituted series. The α series (increasing substitution of α hydrogens by methyl) yields m_I values differing little from the normal DMSO catalytic constant. In the β series (increasing substitution of β hydrogens by methyl), m_I is invariant to both mono- and trimethyl substitution but varies significantly from the normal DMSO catalytic constant with dimethyl substitution. These results suggest that above a minimal steric bulk the DMSO catalyst effect is constant in the alkyl benzoate series.

Table IV lists the activation parameters for reaction at the various DMSO levels. Both the reduced enthalpy[9] and entropy as predicted by the Hughes-Ingold theory[10] suggests the involvement of a more highly solvated transition state of the investigated alkyl benzoates in dimethyl sulfoxide. The previously reported[1,2] activation enthalpy minimum observed for the saponification reaction of ethyl acetate and ethyl benzoate at 0.51 N_{DMSO} is again observed for methyl benzoate. The branched alkyl benzoate data are too irregular to analyze.

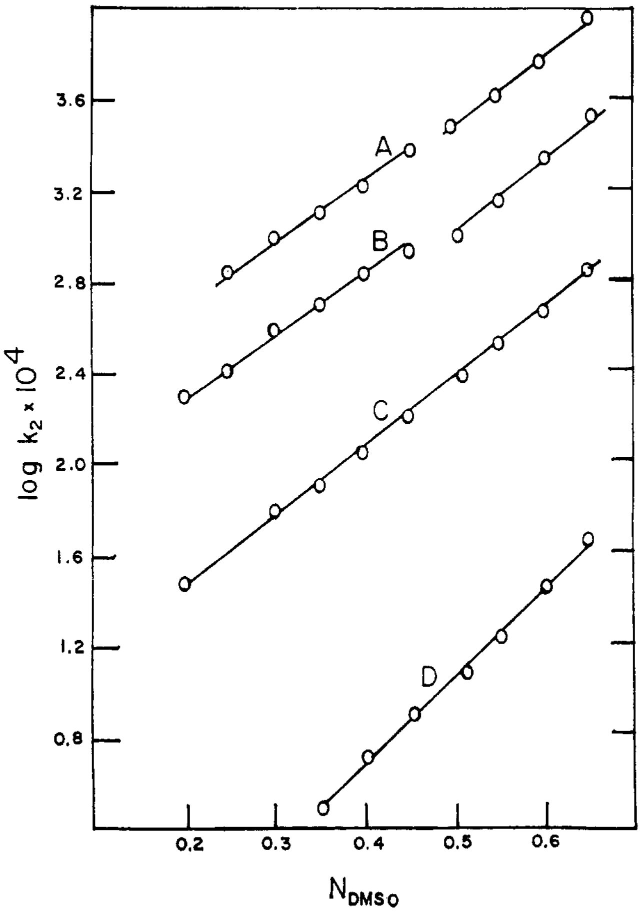

Figure 1.—Effect of mole fraction of DMSO on reaction rate: A, methyl benzoate; B, ethyl benzoate; C, isopropyl benzoate; and D, *t*-butyl benzoate.

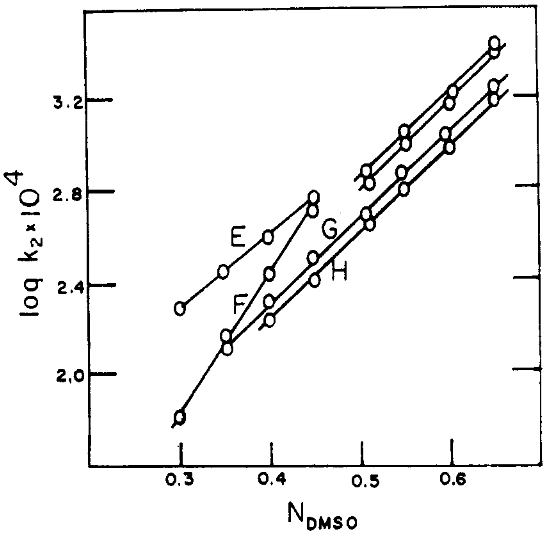

Figure 2.—Effect of mole fraction of DMSO on reaction rate: E, *n*-propyl benzoate; F, isobutyl benzoate; G, neopentyl benzoate; and H, 2-ethylbutyl benzoate.

The multiple regression analysis of the saponification rate constants of a series of ethyl esters,[1,2] RCO_2Et, in aqueous DMSO solvents gave an excellent correlation with eq 2 where k_0 is the regression value for the saponification constant of ethyl acetate, ρ^* is the polar reaction constant,[11a] σ^* is the polar substituent constant[11b] for the R group, δ is the steric reaction constant,[11c] and E_s is the steric substituent constant[11d] for the R group.

$$\log k = \log k_0 + \rho^*\sigma^* + \delta E_s \qquad (2)$$

---

(8) J. M. G. Cowie and P. M. Toporowski [*Can. J. Chem.*, **39**, 2240 (1961)] report a maximum degree of structuredness for the solvent system, water-DMSO, at 0.35 N_{DMSO}. Similar viscosity measurements in this laboratory for the same solvent system 0.03 M in sodium hydroxide replicated the above results.

(9) In 56% aqueous acetone, the activation enthalpies for the saponification of methyl, ethyl, isopropyl, and *t*-butyl benzoate are 14.4, 14.6, 14.9, and 17.2 kcal/mole, respectively: E. Tommila, *Ann. Acad. Sci. Fennicae Ser. A*, **57**, 3 (1941). In 48 to 94% aqueous ethanol, the activation enthalpy for the saponification of ethyl benzoate ranges from 15.7 to 19.0 kcal/mole.

(10) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 345–350.

(11) Reference 7b: (a) p 606; (b) p 587; (c) p 643; (d) p 643.

TABLE IV

THERMODYNAMIC ACTIVATION PARAMETERS FOR ALKALINE HYDROLYSIS OF VARIOUS BENZOATE ESTERS IN AQUEOUS DMSO

Mole fraction of DMSO	ΔH^*, cal/mole	ΔS^*, eu
	Methyl Benzoate	
0.10	12,100 ± 180[a]	−22 ± 2
0.30	11,100 ± 100	−26 ± 1
0.40	11,200 ± 250	−24 ± 2
0.45	11,800 ± 340	−22 ± 3
0.51	8,000 ± 500	−31 ± 4
0.55	10,800 ± 700	−22 ± 5
	Isopropyl Benzoate	
0.25	10,500 ± 240	−33 ± 2
0.30	9,900 ± 125	−34 ± 1
0.35	11,300 ± 170	−30 ± 1
0.40	10,000 ± 221	−34 ± 2
0.45	9,000 ± 140	−34 ± 1
0.51	10,500 ± 140	−31 ± 1
0.55	12,800 ± 140	−22 ± 1
0.60	12,500 ± 180	−23 ± 2
0.65	12,400 ± 120	−22 ± 1
0.70	11,700 ± 170	−23 ± 2
	Isobutyl Benzoate	
0.30	15,200 ± 140	−18 ± 1
0.35	15,800 ± 150	−14 ± 1
0.40	8,700 ± 140	−36 ± 1
0.45	13,100 ± 140	−20 ± 1
0.51	13,700 ± 190	−18 ± 2
0.55	10,400 ± 240	−28 ± 2
0.60	10,900 ± 280	−25 ± 2
	t-Butyl Benzoate	
0.30	19,600 ± 360	−11 ± 3
0.35	15,100 ± 200	−24 ± 2
0.40	15,400 ± 180	−22 ± 2
0.45	14,600 ± 220	−24 ± 2
0.51	14,800 ± 240	−22 ± 2
0.60	13,700 ± 320	−24 ± 3
0.65	12,100 ± 140	−31 ± 1
0.70	7,200 ± 160	−43 ± 1

[a] Two standard units from the mean.

A similar analysis for the esters listed in Table I, a series in which the R group of the ester, RCO_2R', is fixed while the R′ is varied, gives only fair correlations (R = 0.850 to 0.970). Including Δ6 values[12] in the multiple regression analysis gives a poorer fit for the data. More significantly, standard deviations as large or larger than the corresponding regression coefficients (ρ^* or δ) are obtained. This result is somewhat surprising in view of Hancock's[12] successful statistical treatment of the saponification rate constants of a series of alkyl benzoates in 60% aqueous dioxane. It appears that the indirect transmission of the substituent effect of R′ through the interposed oxygen atom to the carbonyl carbon is effected in an irregular way by the changing solvent composition. Relevant to this speculation is the work of Ritchie and Lewis[13] who observed that a series of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids failed to correlate with Roberts[14] linear-free-energy relationship and concluded that factors other than direct interaction of substituent and reaction site are of importance.

While the data do not permit a rigorous delineation of the solvent interaction mechanism, nevertheless, additional insight is gained from this work and equally important, the previous speculation[2] is corroborated and extended. Thus, the good fit between electrostatic forces and rate constants (as developed in eq 3[15]) when R in RCO_2R' is varied is extended to include

$$\ln k = Z_A^2e^2/2kTD(1/r - 1/r^*) + \ln k_0 \qquad (3)$$

variation in R′ by the data reported in Table V.

TABLE V

EFFECT OF SOLVENT DIELECTRIC ON SAPONIFICATION RATE

Benzoate ester	$\left(\frac{d \log k_2}{d10^2/D}\right)_{found}$ [a]	$\left(\frac{d \log k_2}{d10^2/D}\right)_{calcd}$ [b]
CH_3	3.9 ± 0.2	3.8
C_2H_5	3.9 ± 0.2	3.8
i-C_3H_7	3.8 ± 0.2	3.8
t-C_4H_9	4.6 ± 0.2	4.6
n-C_3H_7	4.6 ± 0.2[c]	4.7
i-C_4H_9	9.0 ± 0.3[c]	7.2
$(CH_3)_3CCH_2$	4.1 ± 0.1	4.0
$(C_2H_5)_2CHCH_2$	4.2 ± 0.1	4.1

[a] Calculated by simple regression of log k_2 *vs.* $10^2/D$. [b] Calculated by use of eq 4 of ref 2. [c] Calculated for the 0.30 to 0.45 mole fraction DMSO solvent composition region.

The favorable comparison between the found and calculated slope values [for the series R′ = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7, t-C_4H_9, $(CH_3)_3CCH_2$, and $(C_2H_5)_2CHCH_2$] indicates[16] that the electrostatic interaction energies are of the correct order of magnitude to account for the observed rate changes over the entire solvent composition range while the unfavorable comparison (for R′ = i-C_4H_9 in the mole excess water region) reveals that solvent effects other than those based on the electrostatic model are involved.

Conclusion

From the results of this and the previous studies[1,2] it would appear that a major portion of the solvent effect can be associated with the dramatic influence of DMSO upon the solvation shell geometry. The larger solvation shell of DMSO[17] is better able to accommodate the loose,[1] polarizable transition state involved in the ester saponification reactions. Consistent with this hypothesis is the finding that sterically hindered substrates are insensitive to specific solvation; *i.e.*, the rate is linearly related to dielectric constant, and more significantly the m_I values are nearly constant for a large variation in the ester alkyl structure.

Furthermore, the fact that the solvent effect does not reflect the orderliness of solvent structure as measured by viscosity or heats of mixing[8] but is a function of solvent dielectric (or more significantly mole fraction of DMSO) suggests that the ability of

---

(12) C. K. Hancock, B. J. Yager, C. P. Falls, and J. O. Schreck, *J. Am. Chem. Soc.*, **85**, 1297 (1963).

(13) C. D. Ritchie and E. S. Lewis, *ibid.*, **84**, 591 (1962).

(14) J. D. Roberts and W. T. Moreland, *ibid.*, **75**, 637 (1953); **75**, 2167 (1953).

(15) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p 439.

(16) M. L. Bender and W. A. Glasson, *J. Am. Chem. Soc.*, **81**, 1590 (1959).

(17) (a) J. Miller and A. J. Parker, *ibid.*, **83**, 117 (1961); (b) D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *ibid.*, **83**, 3687 (1961); and (c) J. Miller, *ibid.*, **85**, 1628 (196

the solvation shell to stabilize the transition state is of primary importance.

Experimental Section

All boiling points are uncorrected for stem exposure. Purity of all distilled chemicals was established by gas chromatography.

Benzoate Esters.—Methyl benzoate, bp 48° (0.4 mm), *n*-propyl benzoate, bp 63–64° (0.4 mm), isopropyl benzoate, bp 48° (0.2 mm), and isobutyl benzoate, bp 69–70° (0.4 mm), were commercial samples fractionally distilled prior to use. *t*-Butyl benzoate, bp 61–62° (0.2 mm) [lit.[18] bp 67–68° (1 mm)], and neopentyl benzoate, bp 70° (0.4 mm) [lit.[19] bp 110–111° (10 mm)], were prepared from their respective alcohols and benzoyl chloride in the presence of pyridine. 2-Ethylbutyl benzoate, bp 34° (0.5 mm), was prepared in a similar manner.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.59; H, 8.90.

Purification of Solvent.—Dimethyl sulfoxide was purified by distillation from calcium hydride and was stored over 4A molecular sieves.

Rate Measurements.—The technique and method used were those reported in previous investigations.[1,2]

Treatment of Kinetic Data.—The simple and multiple regression analyses (IBM program 6.0.003) were executed by an IBM 1620 computer.

---

[18] M. L. Bender, *J. Am. Chem. Soc.*, **73**, 1626 (1951).

[19] A. Magnani and S. M. McElvain, *ibid.*, **60**, 813 (1938).

Amination of Aldehydes and Ketones by Tris(dimethylamino)arsine and Tetrakis(dimethylamino)titanium

Harold Weingarten and William A. White

Monsanto Company, Central Research Department, St. Louis, Missouri

Received June 20, 1966

Aldehydes and ketones are converted by $As[N(CH_3)_2]_3$ and $Ti[N(CH_3)_2]_4$ into *gem*-diamines and enamines. A number of highly hindered enamines were prepared by this method.

Recently the authors reported the novel amination of carboxylic acid derivatives using tetrakis(dimethylamino)titanium.[1,2] The subject of the present paper is the closely related amination of aldehydes and ketones using tris(dimethylamino)arsine as well as tetrakis(dimethylamino)titanium to yield *gem*-diamines and enamines.

Our results indicate the reactions studied with the arsenic and titanium derivatives are of the same type reported by Nelson and Pelter[3] for the corresponding boron derivatives. In contrast to the arsenic, titanium, and boron derivatives which aminate carbonyl compounds the phosphorous analog has been reported by Mark[4] to give 1:1 adducts and epoxides on reaction with benzaldehydes.

Results and Discussion

Acetaldehyde and benzaldehyde were readily converted into *gem*-diamines by tris(dimethylamino)arsine. The metal is converted in near-quantitative yield to oxide (identified by XRD) in all cases described in this paper. While the benzylidinebisdimethylamine, $C_6H_5CH[N(CH_3)_2]_2$, has been previously reported[5] the ethylidinebisdimethylamine, $CH_3CH[N(CH_3)_2]_2$, appears to be a new compound and is unique among our products being the only *gem*-diamine isolated with a carbon–hydrogen bond in the β-position. All other systems containing a β-hydrogen yielded enamines.

Relatively unhindered ketones react readily with $As[N(CH_3)_2]_3$ to yield enamines. Cyclohexanone for example is converted rapidly to cyclohexenyl-1-dimethylamine. More sterically hindered ketones, however, react only sluggishly with $As[N(CH_3)_2]_3$ and it is necessary to use the much more reactive $Ti[N(CH_3)_2]_4$ to conveniently effect their conversion to enamines.

Thus 3-methyl-2-butanone is converted smoothly by $Ti[N(CH_3)_2]_4$ to N,N-dimethyl(2-methyl-2-methylenepropyl)amine, $CH_2{=}C[N(CH_3)_2]CH(CH_3)_2$, which on prolonged heating is converted to a 50:50 mixture of isomers including the above and the N,N-dimethyl-(1,2-dimethylpropenyl)amine, $(CH_3)_2C{=}C[N(CH_3)_2]CH_3$, as determined by nmr analysis. The latter isomer was not isolated. Isobutyrophenone is converted cleanly into N,N-dimethyl(2-methyl-1-phenylpropenyl)amine, $(CH_3)_2C{=}C[N(CH_3)_2]C_6H_5$. The highly hindered diisopropyl ketone is also converted by $Ti[N(CH_3)_2]_4$ into N,N-dimethyl(1-isopropyl)-2-methylpropenyl)amine, $(CH_3)_2C{=}C[N(CH_3)_2]CH(CH_3)_2$.

Nelson and Pelter[3] suggested that due to concomitant self-condensation pinacolone could not be converted to its enamines by $B[N(CH_3)_2]_3$. Self-condensation occurs in the reaction of pinacolone with $Ti[N(CH_3)_2]_4$ as well, but the high reactivity of the titanium derivative allowed us to choose reaction parameters minimizing the side reaction. Pinacolone is thus converted to N,N-dimethyl(2,2-dimethyl-1-methylenepropyl)amine, $CH_2{=}C[N(CH_3)_2]C(CH_3)_3$, in moderate yield.

The sterically hindered N,N-dimethylenamines described above are, to our knowledge, reported here for the first time.

The ability of titanium, arsenic, and boron amides to engage in this reaction arises from the combination of acid and base functionality in the same molecule as well as the great tendency of the reagents to form oxides. Their approximate order of reactivity appears to be Ti $\gg$ As $>$ B. A plausible mechanistic sequence is described in Scheme I. When R''' is anything but hydrogen the formation of *gem*-diamine is apparently unfavorable probably owing to steric crowd-

---

[1] H. Weingarten and W. A. White, *J. Am. Chem. Soc.*, **88**, 850 (1966).

[2] H. Weingarten and W. A. White, *J. Org. Chem.*, **31**, 2874 (1966).

[3] P. Nelson and A. Pelter, *J. Chem. Soc.*, 5142 (1965).

[4] V. Mark, *J. Am. Chem. Soc.*, **85**, 1884 (1963).

[5] S. V. Lieberman, *ibid.*, **77**, 1114 (1955).