

# Steric effects on the mechanism of reaction of nucleophilic substitution of $\beta$ -substituted alkoxyvinyl trifluoromethyl ketones with four secondary amines<sup>†</sup>

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**ABSTRACT:** The kinetics of the reaction of  $\beta$ -substituted  $\beta$ -alkoxyvinyl trifluoromethyl ketones  $R^1O-CR^2=CH-COCF_3$  (**1a–e**) [(**1a**),  $R^1=C_2H_5$ ,  $R^2=H$ ; (**1b**),  $R^1=R^2=CH_3$ ; (**1c**),  $R^1=C_2H_5$ ,  $R^2=C_6H_5$ ; (**1d**),  $R^1=C_2H_5$ ,  $R^2=V^-pNO_2C_6H_4$ ; (**1e**),  $R^1=C_2H_5$ ,  $R^2=C(CH_3)_3$ ] with four aliphatic amines (**2a–d**) [(**2a**),  $(C_2H_5)_2NH$ ; (**2b**),  $(i-C_3H_7)_2NH$ ; (**2c**),  $(CH_2)_5NH$ ; (**2d**),  $O(CH_2CH_2)_2NH$ ] was studied in two aprotic solvents, hexane and acetonitrile. The least reactive stereoisomeric form of (**1a–d**) was the most populated (**E-s-Z-o-Z**) form, whereas in (**1e**), the more reactive form (**Z-s-Z-o-Z**) dominated. The reactions studied proceeded via common transition state formation whose decomposition occurred by ‘uncatalyzed’ and/or ‘catalyzed’ route. Shielding of the reaction centre by bulky  $\beta$ -substituents lowered abruptly both  $k'$  (‘uncatalyzed’ rate constant) and  $k''$  (‘catalyzed’ rate constant) of this reaction. Bulky amines reduced  $k''$  to a greater extent than  $k'$  as a result of an additional steric retardation to the approach of the bulky amine to its ammonium ion in the transition state. An increase in the electron-withdrawing ability of the  $\beta$ -substituent increased ‘uncatalyzed’  $k'$  due to the acceleration of the initial nucleophile attack ( $k_1$ ) and ‘uncatalyzed’ decomposition of transition state ( $k_2$ ) via promoting electrophilic assistance (through transition state **8**). The amine basicity determined the route of the reaction: the higher amine basicity, the higher  $k_3/k_2$  ratio (a measure of the ‘catalyzed’ route contribution as compared to the ‘uncatalyzed’ process) was. ‘Uncatalyzed’ route predominated for all reactions; however in polar acetonitrile the contribution of the ‘catalyzed’ route was significant for amines with high  $pK_a$  and small bulk. Copyright © 2007 John Wiley & Sons, Ltd.

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**KEYWORDS:** nucleophilic substitution; alkoxyvinyl trifluoromethyl ketones; amine basicity

## INTRODUCTION

The replacement of a hydrogen atom by a fluorine atom or by a fluoroalkyl group in organic molecules may exert extreme influence on their physical and biological properties.<sup>1,2</sup> In particular today, fluorine-containing heterocycles are widely recognized as important organic materials exhibiting interesting biological activities due to their potential use in medicine and agriculture.<sup>3</sup> From this point of view,  $\alpha,\beta$ -unsaturated trifluoromethyl ketones (trifluoromethyl- $\alpha,\beta$ -enones) are very convenient ‘building blocks’ for the synthesis of various fluorine-containing heterocycles, enamines (which may be used as versatile intermediates for the synthesis of fluorine-

containing analogues of natural products<sup>4</sup>), dyes, drugs, and protective reagents for amino group in peptide synthesis.<sup>5–7</sup>

Recent achievements in the chemistry of  $\beta$ -alkoxyvinyl trifluoromethyl ketones<sup>6,8,9</sup> have resulted in increasing interest in the mechanistic peculiarities of reactions of titled vinyl ketones with nucleophiles.<sup>10,11</sup> Substitution of  $CH_3$  by  $CF_3$  enhances electron-withdrawing ability of COR-group,<sup>8</sup> and hence rises the electrophilicity of  $\beta$ -position of the  $C=C$  double bond in alkene: observed second-order rate constant of the ethoxyvinyl trifluoromethyl ketone reaction with diethyl amine is about  $10^4$ -fold larger than  $k_{obsd}$  of the methoxyvinyl methyl ketone reaction with appropriate amine ( $4.44$  and  $2.61 \times 10^{-4} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ , respectively<sup>10</sup>). According to the variable-transition-state model developed for nucleophilic vinylic substitution by Rappoport<sup>12–16</sup> the reaction proceeds via a single step (concerted) route when the leaving group is a very good nucleofuge and the alkene is a weak electrophile, whereas highly electrophilic alkenes, especially those carrying a poor or moderate nucleofuge,

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<sup>†</sup>Electronic supplementary information (ESI) is available: Table 4 summarizing all the kinetic data for reaction of compounds (**1a–d**) with amines (**2a–d**). The synthesis of 4-ethoxy-1,1,1-trifluoro-5,5-dimethylhex-3-en-2-one (**1e**) is described.

react via the multi-step route. When the nucleophile is neutral, mostly an amine, the first-formed intermediate is the zwitterion. In moderately electrophilic alkenes, that is, when only one of  $\alpha$ -substituents is a strongly electron-withdrawing group (EWG), the kinetics is overall second order, that is, first order in amine.<sup>12</sup> However, for  $\beta$ -alkoxyvinyl trifluoromethyl ketones, systems with one strong EWG-group and poor leaving OAlk, appearance of a third-order rate coefficient was observed in equation at high amine concentrations.<sup>10</sup>

In the present work, we extended these studies to five additional enones (**1a–e**) with  $\beta$ -substituents, *viz.* H, CH<sub>3</sub>, C<sub>6</sub>H<sub>5</sub>, *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, and C(CH<sub>3</sub>)<sub>3</sub>, expecting to observe amine catalysis at least for some secondary amines. We reasoned that a  $\beta$ -substituent changes not only the charge on the reaction centre, thus modifying the enone electrophilicity, but also makes intermediate zwitterion more 'crowdy', and thereby destabilizes it. At the same time we have studied the influence of basicity and bulk of secondary amines on kinetic routes. The presence of rotational isomerism in  $\beta$ -substituted alkoxyvinyl methyl ketones<sup>17–19</sup> prompted us to investigate the effect of the structure of enones (**1a–e**) on their reactivity.

## EXPERIMENTAL

### Materials

*n*-Hexane (obtained from Aldrich) was purified using standard techniques and was dried over the appropriate drying agent before use. Acetonitrile (Merk, Uvasol) was purified additionally by a four-step method as previously described,<sup>10</sup> stored under N<sub>2</sub> and distilled prior to use. All amines were purified as described,<sup>20</sup> stored under dry N<sub>2</sub> in darkness and were distilled just before use. All enones (**1a–e**) were stored under dry N<sub>2</sub> at +4°C and were purified by distillation before use.

Compounds (**1a**),<sup>8</sup> (**1b**),<sup>21</sup> (**1c**),<sup>21</sup> and (**1d**)<sup>22</sup> were prepared as described. 4-Ethoxy-1,1,1-trifluoro-5,5-dimethylhex-3-en-2-one (**1e**) was obtained by applying the procedure described for (**1a**)<sup>8</sup> and using 2-ethoxy-3,3-dimethylbut-1-ene and trifluoroacetic acid anhydride. (87%, bp 69°C (13 mmHg) (see Supplementary part). (Found: C, 53.72; H, 6.61. C<sub>10</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub> requires C, 53.57; H 6.74%); *Z*-isomer:  $\delta_{\text{H}}$ (CDCl<sub>3</sub>; 300 MHz; Me<sub>4</sub>Si) 1.20 (9 H, s, *CMe*<sub>3</sub>), 1.36 (3 H, t, *J* 7.0, CH<sub>3</sub>), 4.23 (2 H, q, *J* 7.0, OCH<sub>2</sub>) and 5.76 (1 H, s, CH=);  $\delta_{\text{F}}$ (CDCl<sub>3</sub>; 282.3 MHz; CCl<sub>3</sub>F) –78.18 (s, CF<sub>3</sub>); *E*-isomer:  $\delta_{\text{H}}$ (CDCl<sub>3</sub>; 300 MHz; Me<sub>4</sub>Si) 1.30 (9 H, s, *CMe*<sub>3</sub>), 1.43 (3 H, t, *J* 7.0, CH<sub>3</sub>), 3.97 (2 H, q, *J* 7.0, OCH<sub>2</sub>) and 5.50 (1 H, s, CH=);  $\delta_{\text{F}}$ (CDCl<sub>3</sub>; 282.3 MHz; CCl<sub>3</sub>F) –78.29 (s, CF<sub>3</sub>).

### Kinetic measurements

Kinetic measurements were carried out under pseudo-first-order conditions by adding 10  $\mu\text{l}$  of a 10<sup>–2</sup> M (if not

stated otherwise, see subscripts for Table 1) solution of the substrate (**1a–e**) to 2 ml of the amine solution in thermostated (with accuracy  $\pm 0.2^\circ\text{C}$ ) quartz 1.0 cm cells (Hellma) at temperatures 20 and 40°C. The kinetic measurements were followed by UV-visible spectrophotometry at fixed wavelengths (303–332 nm, depending on the product absorption). The product accumulation was recorded by registration of the optical density changes at the analytical wavelength. All kinetic runs were followed on at least 3–4 half-lives. The reaction rate constants were calculated by Guggenheim method using Eqn (1)

$$\ln(D_{t+\Delta t} - D_t) = -kt + \ln(D_\infty - D_0)(1 - e^{-k\Delta t}) \quad (1)$$

where  $D_0$  is initial optical density of the substrate,  $D_t$  and  $D_{t+\Delta t}$  are the optical densities of product at time  $t$  and  $(t + \Delta t)$ , respectively,  $\Delta t$  being constant time increment,  $D_\infty$  is the final optical density of product, and  $k$  is the rate constant. Eqn (1) is the equation of a straight line whose slope yields the rate constant  $k$ . Guggenheim's method is more reliable<sup>23</sup> than the traditional 'infinity' method as it does not require the determination of final  $D_\infty$ , since at high amine concentrations precise measurement of  $D_\infty$  often is impossible in view of amine oxidation. The observed second-order coefficients ( $k_{\text{obsd}}$ ) were obtained dividing the pseudo-first-order coefficients by the amine concentration. In many systems the observed second-order constant  $k_{\text{obsd}}$  increased linearly with increase in the amine concentration according to Eqn (2):

$$k_{\text{obsd}} = k' + k''[\text{Amine}] \quad (2)$$

In the systems where  $k_{\text{obsd}}$  was independent of amine concentration, the second-order rate constants were determined as the average of at least 10 experiments.

## RESULTS AND DISCUSSION

Results of the kinetic investigations of reactions of (**1a–e**) with diethylamine (**2a**), diisopropylamine (**2b**), piperidine (**2c**), and morpholine (**2d**) are shown in Table 1. These amines were selected on  $\text{p}K_{\text{a}}$  and bulk criteria: the amine (**2a–c**)  $\text{p}K_{\text{a}}$ 's were similar [*viz.* 11.09 (**2a**); 11.07 (**2b**); 11.1 (**2c**)], but their sizes different, whereas amines (**2c**) and (**2d**) were of similar bulk but differed markedly in  $\text{p}K_{\text{a}}$  [8.3 (**2d**)]. For most systems, the kinetic curves were straight lines (as in Fig. 1) but in some cases, the kinetic curve can be seen as a sequence of straight-line portions with different slopes (*cf.* Fig. 2). The plausible reason of this behaviour was accounted for by difference in rate coefficients of the spatial forms of enones (**1a–e**). Eight stereoisomeric forms are to be expected for the  $\beta$ -alkoxyvinyl trifluoromethyl ketones (**1a–e**) (see Fig. 3), but as we showed previously,<sup>19</sup> (**1a,b**) are in (*E*)-form only, whereas enones (**1c–d**) are mixtures of both (*E*) and (*Z*) isomers. Moreover, the number of stereoisomeric forms of the titled compounds was reduced by

**Table 1.** Kinetic data for the reaction of enones (**1–e**) with amines (**2a–d**)

Enone	Amine	Solvent	T, °C	Amine concentration, M <sup>a</sup>	Stereoisomer	Uncatalyzed process <sup>b</sup> k'	Catalyzed process k'' <sup>c</sup>	k''/k' <sup>d</sup>	
<b>1a</b>	<b>2a</b>	<i>n</i> -Hexane <sup>e</sup>	20	(2.5–2) × 10 <sup>-4</sup>	E-s-Z-o-Z	4.24	1.43 × 10 <sup>2</sup>	34	
			40	(2.5–12) × 10 <sup>-4</sup>		7.85	3.49 × 10 <sup>2</sup>	45	
	<b>2b</b>	<i>n</i> -Hexane	20	(5–50) × 10 <sup>-2</sup>	E-s-Z-o-Z	3.04 × 10 <sup>-3f</sup>	(1.55 × 10 <sup>-3</sup> ) <sup>f,j</sup>	(5.1 × 10 <sup>-1</sup> ) <sup>j</sup>	
			40	(5–50) × 10 <sup>-2</sup>		7.27 × 10 <sup>-3f</sup>	(2.87 × 10 <sup>-3</sup> ) <sup>f,j</sup>	(3.9 × 10 <sup>-1</sup> ) <sup>j</sup>	
		Acetonitrile	20	(1–50) × 10 <sup>-2</sup>	E-s-Z-o-Z	1.52 × 10 <sup>-1f</sup>	6.14 × 10 <sup>-1f</sup>	4.0	
			40	(1–5) × 10 <sup>-2</sup>		2.17 × 10 <sup>-1f</sup>	3.89 <sup>f</sup>	18	
	<b>2c</b>	<i>n</i> -Hexane <sup>e</sup>	12	(3–10) × 10 <sup>-4g</sup>	E-s-Z-o-Z	4.05 × 10 <sup>1</sup>	2.37 × 10 <sup>3</sup>	58	
			20 <sup>i</sup>	(3–9) × 10 <sup>-4g</sup>		4.94 × 10 <sup>1</sup>	3.40 × 10 <sup>3</sup>	69	
	<b>2d</b>	<i>n</i> -Hexane	40	–	E-s-Z-o-Z	7.77 × 10 <sup>1h</sup>	7.77 × 10 <sup>3h</sup>	1.0 × 10 <sup>2</sup>	
			20	(3–12) × 10 <sup>-4</sup>		8.76	0.00	0.00	
	<b>1b</b>	<b>2a</b>	<i>n</i> -Hexane	40	(3–11) × 10 <sup>-4</sup>		1.25 × 10 <sup>1</sup>	0.00	0.00
				20	(5–50) × 10 <sup>-2</sup>	E-s-Z-o-Z	2.04 × 10 <sup>-3</sup>	(2.01 × 10 <sup>-3</sup> ) <sup>j</sup>	(9.9 × 10 <sup>-1</sup> ) <sup>j</sup>
Acetonitrile <sup>e</sup>		40	(5–50) × 10 <sup>-2</sup>		5.27 × 10 <sup>-3</sup>	(2.89 × 10 <sup>-3</sup> ) <sup>j</sup>	(5.5 × 10 <sup>-1</sup> ) <sup>j</sup>		
		20	(1–10) × 10 <sup>-2</sup>	E-s-Z-o-Z	8.74 × 10 <sup>-2</sup>	3.67 × 10 <sup>-2</sup>	4.2 × 10 <sup>-1</sup>		
Acetonitrile		40	(1–5) × 10 <sup>-2</sup>		1.96 × 10 <sup>-1</sup>	2.20 × 10 <sup>-1</sup>	1.1		
		20	(1–10) × 10 <sup>-1</sup>	E-s-Z-o-Z	1.26 × 10 <sup>-3</sup>	0.00	0.00		
<b>2b</b>		<i>n</i> -Hexane <sup>e</sup>	40	(1–8) × 10 <sup>-1</sup>		2.66 × 10 <sup>-3</sup>	0.00	0.00	
			20	(3–10) × 10 <sup>-3</sup>	E-s-Z-o-Z	8.18 × 10 <sup>-2</sup>	1.20	14.7	
<b>2c</b>		Acetonitrile <sup>e</sup>	40	(1–10) × 10 <sup>-3</sup>		1.83 × 10 <sup>-1</sup>	1.64	9.0	
			20	(3–11) × 10 <sup>-4</sup>	E-s-Z-o-Z	3.67	4.52 × 10 <sup>2</sup>	1.2 × 10 <sup>2</sup>	
<b>2d</b>		<i>n</i> -Hexane	40	(3–11) × 10 <sup>-4</sup>		6.41	8.88 × 10 <sup>2</sup>	1.4 × 10 <sup>2</sup>	
			20	(1–12) × 10 <sup>-2</sup>	E-s-Z-o-Z	1.87 × 10 <sup>-2</sup>	1.16 × 10 <sup>-1</sup>	6.2	
Acetonitrile	40	(0.5–8.5) × 10 <sup>-2</sup>		3.88 × 10 <sup>-2</sup>	1.41 × 10 <sup>-1</sup>	3.6			
	20	(1–10) × 10 <sup>-3</sup>	E-s-Z-o-Z	4.85 × 10 <sup>-1</sup>	4.70	9.7			
<b>2c</b>	<i>n</i> -Hexane	40	(0.5–5) × 10 <sup>-3</sup>		9.28 × 10 <sup>-1</sup>	17.40	18.8		
		20	(5–60) × 10 <sup>-2</sup>	E-s-Z-o-Z	5.49 × 10 <sup>-3</sup>	(3.04 × 10 <sup>-4</sup> ) <sup>j</sup>	(5.5 × 10 <sup>-2</sup> ) <sup>j</sup>		
<b>1c</b>	Acetonitrile	40	(5–50) × 10 <sup>-2</sup>		1.36 × 10 <sup>-2</sup>	(7.55 × 10 <sup>-4</sup> ) <sup>j</sup>	(5.6 × 10 <sup>-2</sup> ) <sup>j</sup>		
		20	(1–5) × 10 <sup>-2</sup>	E-s-Z-o-Z	1.77 × 10 <sup>-2</sup>	2.67 × 10 <sup>-2</sup>	1.5		
<b>1c</b>	<b>2a</b>	Acetonitrile	40	(1–5) × 10 <sup>-2</sup>	E-s-Z-o-Z	4.70 × 10 <sup>-2</sup>	1.05 × 10 <sup>-2</sup>	2 × 10 <sup>-1</sup>	
			20	(3–9) × 10 <sup>-2</sup>	Z-s-Z-o-Z	2.66 × 10 <sup>-3</sup>	8.19 × 10 <sup>-3</sup>	3.1	
<b>1c</b>	<b>2b</b> <sup>1</sup>	Acetonitrile <sup>k</sup>	20	(1–3) × 10 <sup>-1</sup>	E-s-Z-o-E	1.75 × 10 <sup>-3</sup>	1.26 × 10 <sup>-2</sup>	7.2	
			40	(1–10) × 10 <sup>-1</sup>	E-s-Z-o-Z	2.39 × 10 <sup>-4</sup>	(–8.12 × 10 <sup>-5</sup> ) <sup>j</sup>	(–0.3) <sup>j</sup>	
	<b>2c</b>	<i>n</i> -Hexane	40	(1–5) × 10 <sup>-2</sup>	Z-s-Z-o-Z	2.08 × 10 <sup>-2</sup>	4.26 × 10 <sup>-1</sup>	20.5	
			40	(1–5) × 10 <sup>-2</sup>	E-s-Z-o-E	7.78 × 10 <sup>-3</sup>	6.05 × 10 <sup>-2</sup>	7.8	
			40	(1–10) × 10 <sup>-1</sup>	E-s-Z-o-Z	3.84 × 10 <sup>-4</sup>	(–3.92 × 10 <sup>-3</sup> ) <sup>j</sup>	(–10) <sup>j</sup>	
			20	(0.1–1) × 10 <sup>-2</sup>	E-s-Z-o-Z	2.14 × 10 <sup>-1</sup>	(6.60 × 10 <sup>-1</sup> ) <sup>j</sup>	(3.09) <sup>j</sup>	
	Acetonitrile	40	(0.1–1) × 10 <sup>-2</sup>		4.45 × 10 <sup>-1</sup>	(6.27 × 10 <sup>-1</sup> ) <sup>j</sup>	(1.41) <sup>j</sup>		
		20	(0.5–1.2) × 10 <sup>-3</sup>	E-s-Z-o-Z	5.69 × 10 <sup>-1</sup>	1.03 × 10 <sup>2</sup>	1.81 × 10 <sup>2</sup>		
	<b>2d</b>	<i>n</i> -Hexane	40	(0.5–1.2) × 10 <sup>-3</sup>		1.05	3.92 × 10 <sup>2</sup>	3.73 × 10 <sup>2</sup>	
			20	(1–10) × 10 <sup>-2</sup>	E-s-Z-o-Z	9.20 × 10 <sup>-2</sup>	(6.57 × 10 <sup>-2</sup> ) <sup>j</sup>	(7.1 × 10 <sup>-1</sup> ) <sup>j</sup>	
	Acetonitrile	40	(1–10) × 10 <sup>-2</sup>		1.44 × 10 <sup>-1</sup>	(1.45 × 10 <sup>-1</sup> ) <sup>j</sup>	(1.01) <sup>j</sup>		
		20	(1–10) × 10 <sup>-3</sup>	E-s-Z-o-Z	1.06 × 10 <sup>-1</sup>	3.64 × 10 <sup>-1</sup>	3.44		
Acetonitrile	40	(1–10) × 10 <sup>-3</sup>		2.34 × 10 <sup>-1</sup>	3.49	14.94			
	20	0.04–0.4	E-s-Z-o-Z	9.87 × 10 <sup>-3</sup>	0.00	0.00			
<b>1d</b>	<b>2a</b>	<i>n</i> -Hexane	40	0.05–0.4		2.26 × 10 <sup>-2</sup>	0.00	0.00	
			20	(0.5–4.0) × 10 <sup>-2</sup>	E-s-Z-o-Z	3.44 × 10 <sup>-2</sup>	1.33 × 10 <sup>-2</sup>	3.86	
	Acetonitrile	40	(0.5–4.0) × 10 <sup>-2</sup>		8.65 × 10 <sup>-2</sup>	8.98 × 10 <sup>-2</sup>	1.04		
		20	0.5–1.40	E-s-Z-o-Z	1.89 × 10 <sup>-4</sup>	0.00	0.00		
	<b>2b</b>	Acetonitrile	40	0.5–1.30		3.36 × 10 <sup>-4</sup>	0.00	0.00	
			20	(0.1–1.0) × 10 <sup>-2</sup>	E-s-Z-o-Z	4.37 × 10 <sup>-1</sup>	(1.05) <sup>j</sup>	(2.41) <sup>j</sup>	
	<b>2c</b>	<i>n</i> -Hexane	40	(0.1–1.0) × 10 <sup>-2</sup>		8.49 × 10 <sup>-1</sup>	(8.76 × 10 <sup>-1</sup> ) <sup>j</sup>	(1.03) <sup>j</sup>	
			20	(0.1–1.0) × 10 <sup>-2</sup>	E-s-Z-o-Z	1.47	1.84 × 10 <sup>1</sup>	12.55	
	Acetonitrile	40	(0.5–5.0) × 10 <sup>-3</sup>		2.55	1.34 × 10 <sup>2</sup>	52.55		
		20	(0.5–5.0) × 10 <sup>-2</sup>	E-s-Z-o-Z	8.28 × 10 <sup>-2</sup>	(–1.24 × 10 <sup>-1</sup> ) <sup>j</sup>	(–1.5)		
	<b>2d</b>	<i>n</i> -Hexane	40	(0.5–5.0) × 10 <sup>-2</sup>		1.63 × 10 <sup>-1</sup>	0.00	0.00	
			20	(0.5–5.5) × 10 <sup>-2</sup>	E-s-Z-o-Z	1.81 × 10 <sup>-1</sup>	1.24 × 10 <sup>-1</sup>	7.0 × 10 <sup>-1</sup>	
<b>1d</b>	<b>2d</b>	Acetonitrile	40	(0.25–2.5) × 10 <sup>-2</sup>	E-s-Z-o-Z	3.95 × 10 <sup>-1</sup>	5.42 × 10 <sup>-1</sup>	1.37	

(Continues)

**Table 1.** (Continued)

Enone	Amine	Solvent	T, °C	Amine concentration, M <sup>a</sup>	Stereoisomer	Uncatalyzed process <sup>b</sup> k'	Catalyzed process k'' <sup>c</sup>	k''/k' <sup>d</sup>		
<b>1e</b>	<b>2a</b>	Hexane	25	(5–10) × 10 <sup>-1</sup>	Z-s-Z-o-Z	9.01 × 10 <sup>-4</sup>	(7.29 × 10 <sup>-4</sup> ) <sup>j</sup>	(0.81) <sup>j</sup>		
			40	(2–6.5) × 10 <sup>-1</sup>	Z-s-Z-o-Z	1.54 × 10 <sup>-3</sup>	(8.30 × 10 <sup>-4</sup> ) <sup>j</sup>	(0.54) <sup>j</sup>		
		Acetonitrile	25	25	(5–9) × 10 <sup>-1</sup>	E-s-Z-o-Z	4.15 × 10 <sup>-4</sup>	0.00	0.00	
				40	(5–9) × 10 <sup>-1</sup>	Z-s-Z-o-Z	1.13 × 10 <sup>-2</sup>	0.00	0.00	
			40	25	(2–6) × 10 <sup>-1</sup>	E-s-Z-o-Z	1.50 × 10 <sup>-3</sup>	0.00	0.00	
				40	(2–6) × 10 <sup>-1</sup>	Z-s-Z-o-Z	1.56 × 10 <sup>-2</sup>	0.00	0.00	
	<b>2c</b>	Hexane	25	25	(5–10) × 10 <sup>-1</sup>	Z-s-Z-o-Z	1.92 × 10 <sup>-3</sup>	(7.69 × 10 <sup>-4</sup> ) <sup>j</sup>	(4.0 × 10 <sup>-1</sup> ) <sup>j</sup>	
				40	(5–10) × 10 <sup>-1</sup>	E-s-Z-o-Z	3.08 × 10 <sup>-4</sup>	(1.40 × 10 <sup>-4</sup> ) <sup>j</sup>	(4.5 × 10 <sup>-1</sup> ) <sup>j</sup>	
			Acetonitrile	20	20	(2–7) × 10 <sup>-1</sup>	Z-s-Z-o-Z	4.30 × 10 <sup>-3</sup>	(3.87 × 10 <sup>-4</sup> ) <sup>j</sup>	(9.0 × 10 <sup>-2</sup> ) <sup>j</sup>
					40	(2–7) × 10 <sup>-1</sup>	E-s-Z-o-Z	7.43 × 10 <sup>-4</sup>	(7.32 × 10 <sup>-4</sup> ) <sup>j</sup>	(9.9 × 10 <sup>-1</sup> ) <sup>j</sup>
				40	20	(1–5) × 10 <sup>-1</sup>	Z-s-Z-o-Z	4.24 × 10 <sup>-2</sup>	(-2.13 × 10 <sup>-3</sup> ) <sup>j</sup>	0.00
					40	(1–5) × 10 <sup>-1</sup>	E-s-Z-o-Z	4.91 × 10 <sup>-3</sup>	(-1.30 × 10 <sup>-3</sup> ) <sup>j</sup>	0.00
		55	20	20	(5–24) × 10 <sup>-2</sup>	Z-s-Z-o-Z	1.02 × 10 <sup>-2</sup>	(-2.84 × 10 <sup>-2</sup> ) <sup>j</sup>	0.00	
				55	(5–28) × 10 <sup>-2</sup>	E-s-Z-o-Z	5.63 × 10 <sup>-3</sup>	1.01 × 10 <sup>-2</sup>	1.79	
			40	20	(1–8) × 10 <sup>-2</sup>	Z-s-Z-o-Z	3.97 × 10 <sup>-3</sup>	0.91	2.30 × 10 <sup>2</sup>	
				40	(1–10) × 10 <sup>-2</sup>	E-s-Z-o-Z	5.85 × 10 <sup>-2</sup>	(-2.70 × 10 <sup>-2</sup> ) <sup>j</sup>	0.00	
				55	20	(1–5) × 10 <sup>-1</sup>	Z-s-Z-o-Z	7.15 × 10 <sup>-4</sup>	(5.09 × 10 <sup>-4</sup> ) <sup>j</sup>	(7 × 10 <sup>-1</sup> ) <sup>j</sup>
					55	(1–5) × 10 <sup>-1</sup>	E-s-Z-o-Z	1.27 × 10 <sup>-4</sup>	6.54 × 10 <sup>-4</sup>	5.1
<b>2d</b>	Hexane	40	40	0.05–0.25	Z-s-Z-o-Z	1.60 × 10 <sup>-3</sup>	(1.19 × 10 <sup>-3</sup> ) <sup>j</sup>	(8 × 10 <sup>-1</sup> ) <sup>j</sup>		
			55	0.05–0.25	E-s-Z-o-Z	7.9 × 10 <sup>-5</sup>	1.00 × 10 <sup>-3</sup>	12.7		
		Acetonitrile	20	20	(5–1) × 10 <sup>-1</sup>	Z-s-Z-o-Z	6.96 × 10 <sup>-3</sup>	(-1.71 × 10 <sup>-4</sup> ) <sup>j</sup>	0.00	
	40			(5–1) × 10 <sup>-1</sup>	E-s-Z-o-Z	1.08 × 10 <sup>-3</sup>	(-1.23 × 10 <sup>-3</sup> ) <sup>j</sup>	0.00		
	40		20	(2–6) × 10 <sup>-1</sup>	Z-s-Z-o-Z	1.06 × 10 <sup>-2</sup>	2.15 × 10 <sup>-3</sup>	0.22		
		40	(2–6) × 10 <sup>-1</sup>	E-s-Z-o-Z	3.55 × 10 <sup>-3</sup>	0.00	0.00			
55	40	55	(5–35) × 10 <sup>-2</sup>	Z-s-Z-o-Z	3.85 × 10 <sup>-3</sup>	3.72 × 10 <sup>-2</sup>	9.7			
		55	(5–35) × 10 <sup>-1</sup>	E-s-Z-o-Z	1.18 × 10 <sup>-2</sup>	0.00	0.00			

<sup>a</sup> Concentration range of amine used for second-order kinetics.

<sup>b</sup> 1 mol<sup>-1</sup> s<sup>-1</sup>.

<sup>c</sup> 1<sup>2</sup> mol<sup>-2</sup> s<sup>-1</sup>.

<sup>d</sup> 1 mol<sup>-1</sup>.

<sup>e</sup> Enone concentration, 2.5 × 10<sup>-5</sup> M.

<sup>f</sup> From reference 10.

<sup>g</sup> At higher concentrations the reaction is too fast to be monitored.

<sup>h</sup> Calculated from linear dependence  $\ln k$  versus  $1/T$ .

<sup>i</sup> At higher temperatures the reaction is too fast to be monitored.

<sup>j</sup> Apparent value.

<sup>k</sup> Enone concentration 5 × 10<sup>-4</sup> M.

<sup>l</sup> In hexane, the reaction is too slow to be monitored.

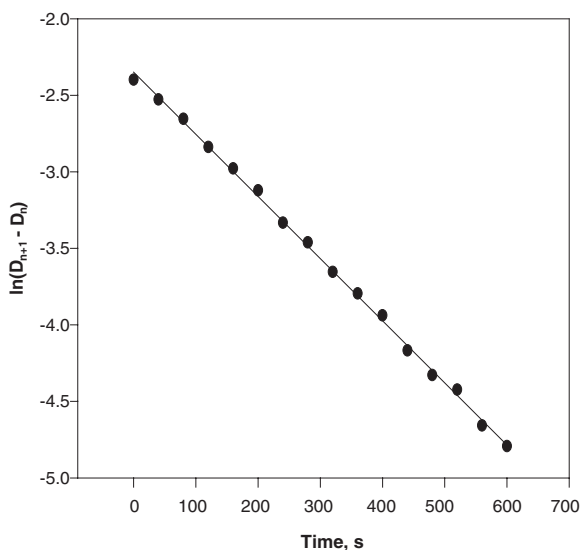
$\beta$ -substitution (*vide infra*). For systems [(**1e**) + (**2a,c,d**)], where only two forms of (**1e**) [namely (**Z-s-Z-o-Z**) and (**E-s-Z-o-Z**)] were present: the corresponding kinetic curve consisted of two straight-line sections: the slope of the first one was the sum of the rate coefficients for (**Z**) and (**E**) isomers whereas the slope of the second one was the rate coefficient for (**E**) isomer only (Fig. 2).

Earlier<sup>10</sup> we have shown that changes in configuration of products (**4**) are accompanied by changes in the band shape in their UV-spectrum. During all kinetic measurements we did not observe any change in the appropriate band shapes (obtaining only one isobestic point in the spectrum). Hence, similarly to<sup>12</sup> no (**E**) $\rightleftharpoons$ (**Z**) isomerization of enamines (**4**) was observed during the reaction. We assume that the (**E**)/(**Z**) ratio is established at the moment of the product formation. As can be seen from Table 1 for systems [(**1e**) + (**2c**)] and [(**1e**) + (**2d**)],  $k_{\text{obsd}}(\text{Z-s-Z-o-Z}) > k_{\text{obsd}}(\text{E-s-Z-o-Z})$ :  $k_{\text{obsd}}(\text{Z-s-Z-o-Z})/k_{\text{obsd}}(\text{E-s-Z-o-Z})$  ratio was 8.6 and 6.5 for these systems

in acetonitrile at 20°C, and 6.2 and 5.6 in hexane at 25 and 40°C, respectively;  $k_{\text{obsd}} = k'$  in the absence of  $k''$ , (see below). These ratios are in accord with data for methyl  $\beta$ -iodo- $\alpha$ -nitrocinnamates<sup>12</sup> where (**Z**) isomer was 2.4 and 2.0 fold more reactive than (**E**) isomer in their reaction with (**2c**) and (**2d**), respectively, in acetonitrile. Generally, the rate coefficient for each configuration ( $k_i$ ) can be evaluated from Eqn (3):

$$k_i = \sum_1^i k - \sum_1^{i-1} k \quad (3)$$

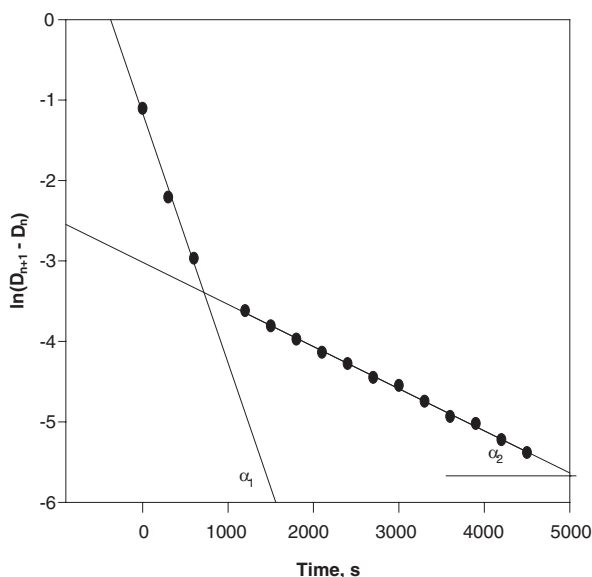
The reaction retardation in system [(**1c**) + (**2b**)] compared with system [(**1c**) + (**2a**)], as a result of strong steric hindrance, enabled us to estimate rate constants for the three rotamers of (**1c**) which existed in acetonitrile<sup>19</sup> using Eqn (3). By analogy with (**1e**) we attributed the smallest  $k_{\text{obsd}}$  to (**E**) isomer, namely (**E-s-Z-o-Z**), and the largest one to (**Z**) isomer [*viz.* (**Z-s-Z-o-Z**)], the



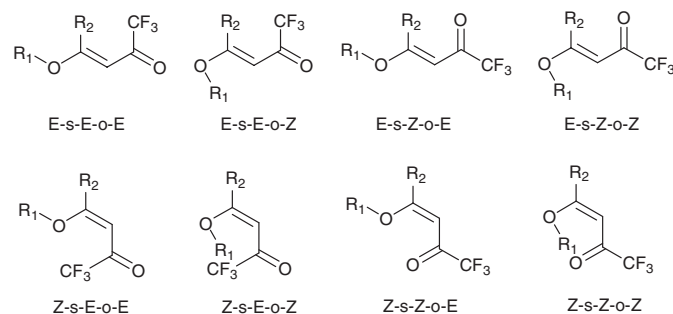
**Figure 1.** Kinetics of **(1a)** reaction with **(2d)** in hexane at 20°C.

intermediate value being  $k_{\text{obsd}}$  of the **(E-s-Z-o-E)** form. Reaction of **(1c)** with amine **(2b)** in hexane was too slow to be monitored. For the other systems the reaction rates of rotamers other than **(E-s-Z-o-Z)** were too high and/or the percentage of these spatial forms was too small<sup>19</sup> impeding the  $k_{\text{obsd}}$  determination. Therefore, in these cases only the rate constants of the most populated **(E-s-Z-o-Z)** form were evaluated and listed in Table 1.

The least-square intercepts, which were the ‘uncatalyzed’ second-order rate coefficients,  $k'$ , the slopes, which gave the ‘amine-catalyzed’ third-order rate coefficients  $k''$  and their ratios  $k''/k'$  are given in Table 1. We showed<sup>10</sup>



**Figure 2.** Kinetics of **(1e)** reaction with **(2d)** in acetonitrile at 20°C:  $\text{tg}\alpha_1 = k_{\text{obsd}}(\text{E-s-Z-o-Z}) + k_{\text{obsd}}(\text{Z-s-Z-o-Z})$ ;  $\text{tg}\alpha_2 = k_{\text{obsd}}(\text{E-s-Z-o-Z})$ .



**Figure 3.** Possible structures of enones **(1a-e)**.

previously that the reaction rate of enones **(1a,b)** with amines was strongly dependent on the relative permittivity of the reaction medium. Addition of polar substances [viz. amines **(2a-d)**] to an apolar solvent like *n*-hexane can affect the rate by changing the macro- and/or micro-relative permittivity of the medium. Thus, the ‘catalytic effects’ observed at high amine concentrations have to be considered with some caution. According to the classification proposed by Bunnett and Garst,<sup>24</sup> the conclusion that a genuine base catalysis was involved holds only for reactions where  $k''/k' > 50$ . When  $k''/k' < 5$ , it was suggested that the observed acceleration was not caused by catalysis. Moreover, addition of the less polar amines **(2a-d)** to highly polar acetonitrile decreased the relative permittivity of solution and reduced the rate constant,  $k_{\text{obsd}}$ . At high amine concentrations,  $k''$  can be even negative. In Table 1, all these dubious  $k''$  and  $k''/k'$  values were enclosed in brackets. As it can be seen from Table 1, the  $k''/k'$  ratios were quite small almost for all systems, excepting [**(1a-d)** + **(2c)**] and [**(1e)** + **(2c)**] at 55°C, **(Z-s-Z-o-Z)** where  $k''/k' > 50$ . Hence, the relative contribution of the ‘catalyzed’ process was so small that the reaction was nearly overall second order.

The reactivity ratios of pairs of nucleophiles, that is,  $k(\mathbf{2c})/k(\mathbf{2d})$ ,  $k(\mathbf{2c})/k(\mathbf{2b})$  and  $k(\mathbf{2c})/k(\mathbf{2a})$  for ‘uncatalyzed’ and ‘catalyzed’ routes are given in Table 2. Piperidine was always the most reactive nucleophile: in its reaction with **(1a)** in hexane at 20°C the relative reactivities were  $1(\mathbf{2b}) < 1.39 \times 10^3(\mathbf{2a}) < 2.88 \times 10^3(\mathbf{2d}) < 1.33 \times 10^4(\mathbf{2c})$  for the ‘uncatalyzed’ route, and  $1(\mathbf{2b}) < 9.23 \times 10^4(\mathbf{2a}) < 1.52 \times 10^6(\mathbf{2c})$  for ‘catalyzed’ process [concerning **(E-s-Z-o-Z)** form]. The same trend was observed for the **(Z-s-Z-o-Z)** form too [relative reactivities for ‘uncatalyzed’ route were  $1(\mathbf{2d}) < 1.62(\mathbf{2a}) < 6.09(\mathbf{2c})$ ]. An increase in bulk of  $\beta$ -substituent lowered both  $k'$  and  $k''$  but the latter to a greater extent. As a result,  $k''(\mathbf{2c})/k''(\mathbf{2a})$  reactivity ratios were 2–55 times higher than  $k'(\mathbf{2c})/k'(\mathbf{2a})$ . A similar effect was observed for solvent polarity changes:  $k'(\mathbf{2c})/k'(\mathbf{2d})$  were almost the same in hexane and acetonitrile whereas  $k''(\mathbf{2c})/k''(\mathbf{2d})$  were  $10^2$  times higher in acetonitrile than in hexane.

**Table 2.** Relative rates of (**1a–e**) in the reaction with amines (**2a–d**)

Enone	Solvent	T, °C	Uncatalyzed process <sup>a</sup>			Catalyzed process <sup>a</sup>		
			k'(2c)/k'(2a)	k'(2c)/k'(2b)	k'(2c)/k'(2d)	k''(2c)/k''(2a)	k''(2c)/k''(2b)	k''(2c)/k''(2d)
<b>1a</b>	<i>n</i> -Hexane	20	11.7	1.63 × 10 <sup>4</sup>	5.64	23.8	21.9 × 10 <sup>5</sup>	—
		40	9.9	1.07 × 10 <sup>4</sup>	6.23	22.3	27.1 × 10 <sup>5</sup>	—
<b>1b</b>	<i>n</i> -Hexane	20	40.9	<sup>b</sup>	4.37	5.97 × 10 <sup>2</sup>	—	10.34
		40	34.7	<sup>b</sup>	4.72	5.67 × 10 <sup>2</sup>	—	11.63
	Acetonitrile	20	42.0	2.91 × 10 <sup>3</sup>	7.57	1.23 × 10 <sup>4</sup>	—	96.15
		40	32.7	2.41 × 10 <sup>3</sup>	6.91	4.04 × 10 <sup>4</sup>	—	51.01
<b>1c</b>	<i>n</i> -Hexane	20	39.0	<sup>b</sup>	2.33	2.17 × 10 <sup>4</sup>	—	10.04
		40	32.8	<sup>b</sup>	3.10	0.0	—	0.0
	Acetonitrile	20	32.1	3.01 × 10 <sup>3</sup>	5.37	3.85 × 10 <sup>3</sup>	—	2.83 × 10 <sup>2</sup>
		40	22.2	3.49 × 10 <sup>3</sup>	4.49	—	—	1.12 × 10 <sup>2</sup>
<b>1d</b>	<i>n</i> -Hexane	20	44.3	<sup>b</sup>	5.52	—	—	—
		40	37.6	<sup>b</sup>	5.21	—	—	—
	Acetonitrile	20	42.7	7.78 × 10 <sup>4</sup>	8.12	1.38 × 10 <sup>3</sup>	—	1.49 × 10 <sup>2</sup>
		40	29.5	7.59 × 10 <sup>4</sup>	6.46	1.49 × 10 <sup>3</sup>	—	2.47 × 10 <sup>2</sup>
<b>1e</b>	<i>n</i> -Hexane	40	—	—	5.85	—	—	—
		25 <sup>c</sup>	2.13	—	—	—	—	—
		40 <sup>c</sup>	2.79	—	6.01	—	—	—
	Acetonitrile	20	—	—	4.55	—	—	—
		40	—	—	1.59	—	—	—
		20 <sup>c</sup>	3.75	—	6.09	—	—	—
		40 <sup>c</sup>	6.62	—	14.26	—	—	

<sup>a</sup> For (**E-s-Z-o-Z**), if not stated otherwise.

<sup>b</sup> Reaction with (**2b**) was too slow to be monitored.

<sup>c</sup> For (**Z-s-Z-o-Z**).

The activation parameters for the ‘uncatalyzed’ and the ‘catalyzed’ process are given in Table 3. Considering reactions of (**E-s-Z-o-Z**) form, we observed that the activation enthalpies  $\Delta H^{\ddagger}$  for the ‘uncatalyzed’ process were small and positive for all systems, being higher in hexane than in acetonitrile for systems [(**1a,b**) + (**2a–d**)] and *vice versa* for systems [(**1c–e**) + (**2a–d**)], whereas the entropies  $\Delta S^{\ddagger}$  were highly negative for all systems. For the ‘catalyzed’ process [(**E-s-Z-o-Z**) form], the enthalpies varied from positive [83.7 for system (**1c** + **2d**)] to negative [–4.5 for system (**1d** + **2c**)] depending on the nature of the  $\beta$ -substituent, amine and solvent. For all studied systems  $\Delta H^{\ddagger}$  values were higher in acetonitrile than in hexane. The entropies  $\Delta S^{\ddagger}$  also changed in a wide range.

Steady-state treatment of Scheme 1 gave Eqn (4):

$$k_{\text{obsd}} = \frac{k_1 k_2 + k_3 [A]}{k_{-1} + k_2 + k_3 [A]} \quad (4)$$

for the observed second-order rate constant ([A]—amine concentration)<sup>12</sup> according to which  $k_{\text{obsd}} = k_{-1}$  when  $k_{-1} < (k_2 + k_3 [A])$ , and the reaction was overall second order. When the ‘uncatalyzed’ reaction was faster than the catalyzed reaction but slower than the reverse reaction, that is,  $k_{-1} \gg k_2 \gg k_3 [A]$ ,  $k_{\text{obsd}}$  was composite but still a second-order rate constant:  $k_{\text{obsd}} = k_1 k_2 / k_{-1}$ . For the catalyzed reaction, when  $k_{-1} \gg (k_2 + k_3 [A])$ ,  $k_{\text{obsd}}$  was given as the sum of the second- and third order terms and

it would increase linearly with increase in the amine concentration:  $k_{\text{obsd}} = (k_1 k_2 / k_{-1}) + (k_1 k_3 / k_{-1}) [A]$  (see Fig. 4). In this case the reaction followed two competing routes: an ‘uncatalyzed’ route, whose rate constant  $k'$  was given by  $k_1 k_2 / k_{-1}$ , and a ‘catalyzed’ route whose constant  $k''$  was  $k_1 k_3 / k_{-1}$ . The  $k''/k'$  values of Table 1 were identical with  $k_3/k_2$  ratios and hence this ratio was a measure of the relative importance of the two routes starting from a common intermediate (Scheme 1).

The ratios observed were strongly dependent on the bulk of the  $\beta$ -substituent and amine, as well as on the solvent polarity. For systems [(**1b–d**) + (**2c**)] in acetonitrile and for [(**1a**) + (**2c**)] in hexane, the ratio  $k_3/k_2 > 50$  whereas for all the other studied systems, these ratios were smaller but high enough to be regarded as being in the region of a genuine base catalysis.<sup>10,25</sup> Taking into account the above-mentioned kinetic effect of the medium, we came to the conclusion that for  $k_3/k_2 < 5$  the reaction acceleration was caused by amine catalysis in hexane only if the amine concentration was small enough to change noticeably the relative permittivity of the solution, namely [**2a–d**]  $\leq 5 \times 10^{-3}$  M. On the other hand if the amine catalysis was absent in polar acetonitrile, the slope  $k''$  should be zero or even negative due to the relative permittivity decrease induced by the addition of the less polar amine to the highly polar acetonitrile. Hence,  $k_3/k_2 \leq 0$  should be expected. A linear downward dependence,  $\ln k$  versus [amine], was observed exclusively for

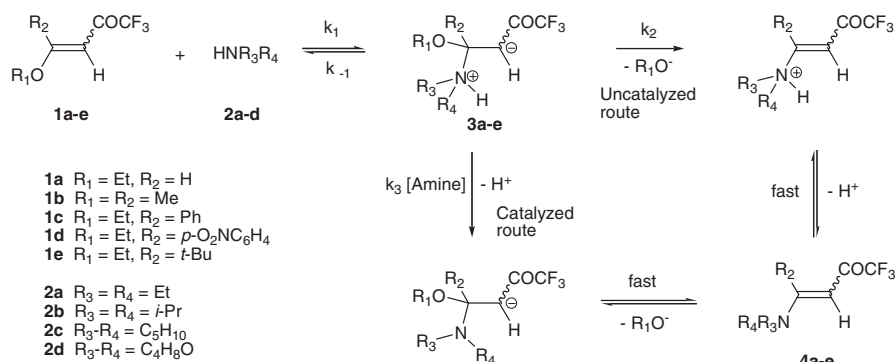
**Table 3.** Activation parameters of the reaction of (1a-e) with amines (2a-d)

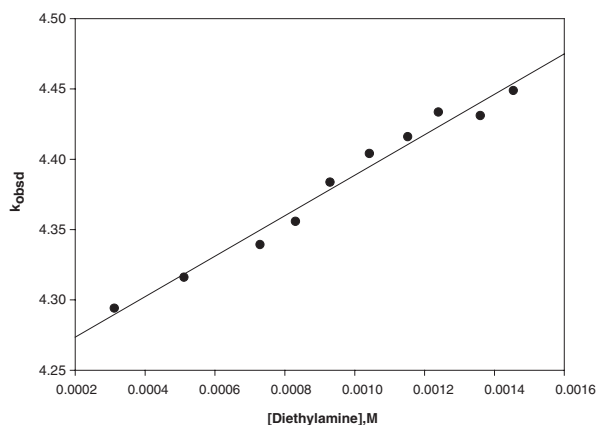
Enone	Amine	Solvent	Stereoisomer	Uncatalyzed reaction		Catalyzed reaction	
				$\Delta H^{\ddagger a}$ kJ mol <sup>-1</sup>	$\Delta S^{\ddagger a}$ kJ mol <sup>-1</sup>	$\Delta H^{\ddagger a}$ JK <sup>-1</sup> mol <sup>-1</sup>	$\Delta S^{\ddagger a}$ JK <sup>-1</sup> mol <sup>-1</sup>
<b>1a</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	21.1 ± 5.5	-161 ± 15	3.6 ± 1.1	-96 ± 10
		<i>n</i> -Hexane	E-s-Z-o-Z	30.8 ± 3.6 <sup>b</sup>	-188 ± 16 <sup>b</sup>	—	—
	<b>2c</b>	Acetonitrile	E-s-Z-o-Z	11.2 ± 2.0 <sup>b</sup>	-222 ± 16 <sup>b</sup>	67.9 ± 2.7 <sup>b</sup>	-17 ± 13 <sup>b</sup>
		<i>n</i> -Hexane	E-s-Z-o-Z	14.8 ± 2.8	-162 ± 14	29.1 ± 2.4	-78 ± 25
<b>1b</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	11.0 ± 3.0	-189 ± 11	—	—
		Acetonitrile	E-s-Z-o-Z	33.7 ± 2.0	-181 ± 12	—	—
	<b>2b</b>	Acetonitrile	E-s-Z-o-Z	31.0 ± 2.1	-167 ± 14	61.6 ± 2.9	-62 ± 12
		<i>n</i> -Hexane	E-s-Z-o-Z	26.0 ± 2.0	-211 ± 18	—	—
	<b>2c</b>	<i>n</i> -Hexane	E-s-Z-o-Z	28.3 ± 2.0	-169 ± 10	9.5 ± 3.0	-211 ± 13
		Acetonitrile	E-s-Z-o-Z	18.8 ± 1.8	-170 ± 15	23.3 ± 2.1	-114 ± 17
<b>1c</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	25.4 ± 1.7	-191 ± 16	5.0 ± 1.3	-246 ± 20
		Acetonitrile	E-s-Z-o-Z	22.8 ± 4.6	-173 ± 15	20.7 ± 2.4	-162 ± 14
	<b>2b</b>	Acetonitrile	E-s-Z-o-Z	32.1 ± 3.7	-178 ± 16	32.2 ± 4.6	-202 ± 19
		Acetonitrile	Z-s-Z-o-Z	35.0 ± 3.4	-159 ± 11	— <sup>c</sup>	— <sup>c</sup>
	<b>2c</b>	<i>n</i> -Hexane	E-s-Z-o-Z	76.0 ± 2.6	-35 ± 18	—	—
		Acetonitrile	E-s-Z-o-E	54.4 ± 2.7	-112 ± 15	57.4 ± 3.8	-85 ± 6
<b>1d</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	15.3 ± 4.0	-263 ± 13	—	—
		Acetonitrile	E-s-Z-o-Z	25.6 ± 2.2	-170 ± 13	—	—
	<b>2c</b>	<i>n</i> -Hexane	E-s-Z-o-Z	20.9 ± 3.2	-178 ± 11	48.5 ± 6.1	-41 ± 13
		Acetonitrile	E-s-Z-o-Z	14.6 ± 3.0	-214 ± 20	27.7 ± 5.7	-173 ± 16
	<b>2d</b>	<i>n</i> -Hexane	E-s-Z-o-Z	27.8 ± 3.0	-169 ± 9	83.7 ± 6.6	32 ± 22
		Acetonitrile	E-s-Z-o-Z	27.8 ± 3.0	-169 ± 9	—	—
<b>1e</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	30.3 ± 3.0	-179 ± 11	—	—
		Acetonitrile	E-s-Z-o-Z	32.7 ± 3.3	-170 ± 13	70.3 ± 5.2	-41 ± 14
	<b>2b</b>	Acetonitrile	E-s-Z-o-Z	19.5 ± 1.9	-250 ± 17	—	—
		<i>n</i> -Hexane	E-s-Z-o-Z	22.8 ± 2.7	-174 ± 15	-4.5 ± 2.7	-229 ± 19
	<b>2c</b>	Acetonitrile	E-s-Z-o-Z	18.6 ± 1.5	-178 ± 18	73.2 ± 4.4	29 ± 19
		<i>n</i> -Hexane	E-s-Z-o-Z	25.1 ± 2.0	-180 ± 14	—	—
<b>1e</b>	<b>2a</b>	<i>n</i> -Hexane	E-s-Z-o-Z	27.3 ± 2.0	-166 ± 14	53.8 ± 3.8	-79 ± 16
		Acetonitrile	E-s-Z-o-Z	25.3 ± 1.7	-218 ± 17	—	—
	<b>2c</b>	Acetonitrile	E-s-Z-o-Z	49.4 ± 3.7	-144 ± 14	—	—
		Acetonitrile	Z-s-Z-o-Z	64.0 ± 3.6	-95 ± 9	—	—
	<b>2d</b>	<i>n</i> -Hexane	E-s-Z-o-Z	43.1 ± 2.5	-168 ± 15	—	—
		Acetonitrile	E-s-Z-o-Z	39.3 ± 2.0	-184 ± 14	—	—
<b>1e</b>	<b>2c</b>	<i>n</i> -Hexane	E-s-Z-o-Z	50.1 ± 2.6	-120 ± 16	—	—
		Acetonitrile	Z-s-Z-o-Z	51.9 ± 2.5	-113 ± 12	—	—
	<b>2d</b>	<i>n</i> -Hexane	Z-s-Z-o-Z	43.4 ± 2.6	-166 ± 15	—	—
		Acetonitrile	E-s-Z-o-Z	23.2 ± 2.2	-235 ± 17	21.7 ± 3.9	-237 ± 13
<b>1e</b>	<b>2d</b>	<i>n</i> -Hexane	E-s-Z-o-Z	42.9 ± 2.2	-155 ± 14	—	—
		Acetonitrile	Z-s-Z-o-Z	13.6 ± 1.4	-237 ± 16	— <sup>c</sup>	— <sup>c</sup>

<sup>a</sup> The errors in the activation parameters were calculated similarly to authors.<sup>26</sup>

<sup>b</sup> From reference.<sup>10</sup>

<sup>c</sup> Activation parameters are not presented in view of the high errors of estimation.

**Scheme 1.** Mechanism of studied reaction of substituted alkoxyvinyl trifluoromethyl ketones with secondary amines.



**Figure 4.** Dependence  $k_{obsd}$  versus [Diethylamine] of **(1a)** reaction with **(2a)** in hexane at 20°C.

systems [(**1c**) + (**2b**)] and [(**1d**) + (**2d**)] (see Supplementary Data), where the amine concentrations were very high (0.1–1.4 M). A similar decrease in  $k_{obsd}$  with increasing amine concentration in acetonitrile was observed for the reaction of triethylamine with 1-bromo-2,2-dicyano-1-*p*-nitrophenyl-ethylene.<sup>25</sup> Thus,  $k''$  values and  $k''/k'$  ratios in parenthesis (Table 1) were apparent and in fact close or equal to zero. In all other cases,  $k_3/k_2$  ratios increased significantly on going from hexane to acetonitrile, as a sign of genuine base catalysis.

### 'Catalyzed' route

The catalysis mechanism implied necessarily the removal of an ammonium proton from the reaction intermediate which can occur significantly in two different ways (Scheme 1): (a) a *slow*, rate-limiting proton abstraction from the zwitterionic intermediate (**3a–e**) by the base to form the deprotonated intermediate (**5**), from which the leaving group, broke off *rapidly*, and (b) a *rapid* deprotonation of (**3a–e**) followed by a *slow* detachment of the leaving OR<sub>1</sub> group which was general acid-catalyzed by the conjugated acid of the amine (SB-GA, specific base-general acid mechanism). Electrophilic catalysis either via SB-GA mechanism (transition state 6) or via transition state 7 (Fig. 5) seemed unlikely when the reactivities of piperidine and morpholine in their reaction with (**1a–e**) are compared. These amines exhibit identical steric bulk, but the morpholinium ion was 2.3 pK<sub>a</sub> units more acidic in acetonitrile than that of the

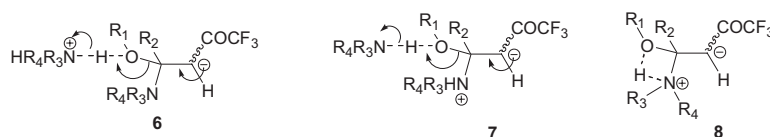
piperidinium ion.<sup>26</sup> It is also likely that morpholine was a stronger proton donor than piperidine owing to the electron withdrawal character of its oxygen atom. If formation of **7** was rate determining, the  $k''/k'$  ratio for morpholine, which was one of the weakest studied bases, should be one of the highest, but instead, it was one of the smallest found. Analyzing the reaction of substituted ethylenes with piperidine and morpholine, Rappoport showed,<sup>26</sup> that if formation of **6** was rate determining the  $k''(2c)/k''(2d)$  ratio was expected to be small. However, the observed ratios of 96÷283 in acetonitrile and 10÷12 in hexane were inconsistent with this expectation. Consequently, rate-determining proton transfer seems the most likely route for all the systems for which the 'catalyzed' process was observed.

### 'Uncatalyzed' route

Characteristic features of the uncatalyzed route involve the sequential cleavage of <sup>+</sup>N—H and C—O bonds. An initial rate-determining or preequilibrium deprotonation of <sup>+</sup>N—H by the solvent cannot compete efficiently with deprotonation by added amine.<sup>26</sup> There were two possible reaction pathways involving a rate determining C<sub>sp</sub><sup>2</sup>—O bond cleavage. Moreover, an unassisted cleavage of C<sub>sp</sub><sup>2</sup>—O bond was unlikely since acetonitrile (and hexane even more so) was not a good solvating agent for anions. On the other hand, the C<sub>sp</sub><sup>2</sup>—O bond cleavage may be assisted electrophilically by a proton of the ammonium moiety (see Fig. 5, structure **8**), as suggested by Rappoport and coworkers<sup>26</sup> for Ad<sub>N</sub>-E vinylic substitution. In transition state **8**, the proton transfer occurs through a structure with an unfavourable geometry, but it has the advantage of a possible internal solvation of the leaving group with consequent charge dispersal. In all studied enones (**1a–e**), conformers (**-o-Z**) dominated<sup>19</sup> thus promoting formation of structure **8** as transition state. Low  $k''/k'$  ratios in most systems (Table 1) confirmed this assumption. Moreover, in system [(**1c**) + (**2c**)] where the rate constants  $k'$  and  $k''$  were estimated for all the existing stereoisomeric forms, the largest  $k''/k'$  ratio was observed for (**-o-E**) conformer (*vide infra*).

### Effect of β-substituent

Replacement of β-H for β—CH<sub>3</sub> caused a 600-times reduction of  $k'$  and 2.8 × 10<sup>3</sup>-times reduction of  $k''$  {for (**E-s-Z-o-Z**) of systems [(**1a**) + (**2c**)] and [(**1b**) + (**2c**)] in



**Figure 5.** Structures **7** and **8**



hexane, 20°C}. This reduction was produced exclusively by an additional shielding of the reaction centre ( $\beta$ -carbon) to the amine nucleophilic attack. A larger  $k''$  reduction as compared to  $k'$  was explained by a retardation of the deprotonation due to additional steric impediment in transition state (**3a**) for the second amine molecule to reach the ammonium proton. A similar effect was observed for (**1c**). In case of replacement of  $\beta$ -CH<sub>3</sub> for  $\beta$ -Ph, it should be expected at least 10<sup>4</sup>-times reduction of  $k_{\text{obsd}}$  in view of ground state stabilization of (**1c**) due to  $\pi(\text{Ph})$ - $\pi(\text{C}=\text{C})$  conjugation.<sup>14</sup> However,  $k'$  of (**1c**) was only 3-fold larger than that of (**1b**). Considering that the nucleophilic attack on C <sub>$\beta$</sub>  of a vinylic system usually occurs in a plane perpendicular to that of the double bond, with an angle  $\approx 90^\circ$ <sup>14</sup>, the steric effect of a phenyl group should increase when Ph ring is out-of the plane of the enone system, as a result of the ring rotation around C<sub>Ph</sub>-C<sub>C=C</sub> bond. Steric repulsion between the hydrogen atoms of the aromatic ring and the carbonyl oxygen favours this rotation, thus disturbing  $\pi(\text{Ph})$ - $\pi(\text{C}=\text{C})$  conjugation. According to quantum chemical calculations, the dihedral angle Ph-C=C was 50–90° in all the isomers of (**1c**).<sup>19</sup> Almost 2-fold reactivity increase for (**1c**) compared with that of (**1b**) was a consequence of -R character of Ph and +R character of CH<sub>3</sub> ( $\sigma_1 = 0.1$  and  $-0.05$ , respectively). In the single isomer of (**1d**), *viz.* (**E-s-Z-o-Z**), the aromatic ring was rotated around C<sub>Ar</sub>-C<sub>C=C</sub> bond by  $\approx 90^\circ$ , breaking the  $\pi(\text{Ar})$ - $\pi(\text{C}=\text{C})$  conjugation almost completely. Hence, here again the electronic influence of *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> substituent was exclusively inductive<sup>19</sup> determining a further increase in enone reactivity.

The influence of  $\beta$ -CH<sub>3</sub>,  $\beta$ -Ph, and  $\beta$ -(*p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>) on the rate of the 'catalyzed' process was inverse:  $k''(\mathbf{1b}) > k''(\mathbf{1c}) > k''(\mathbf{1d})$  [e.g., 452, 103, and 18.4 in their reaction with (**2c**) in hexane, 20°C, (**E-s-Z-o-Z**)]. The increase in the electron withdrawing effect of  $\beta$ -substituent rises the proton acidity of the ammonium moiety, thus promoting electrophilic assistance through transition state **8** in 'uncatalyzed' route. This phenomenon is accompanied with an appropriate increase in  $k_2$  and a simultaneous decrease in  $k_3$ . The most pronounced steric effect of the  $\beta$ -substituent on  $k''$  rate constants was observed in systems [(**1e**) + (**2a,c,d**)] where the shielding by  $\beta$ -*tert*-butyl group was so strong that the 'catalyzed' process was not observed for every amine (at ambient temperature).

### Steric effects of secondary amines

The steric effects of the studied amines are apparent when the reactivity ratios of (**2c**) and more voluminous (**2a**) are compared. The  $k'(\mathbf{2c})/k'(\mathbf{2a})$  ratio was 10÷44, the smallest ratios, 9.9 and 11.7, being for (**1a**) in hexane, Table 2. An increase in the amine bulk increased  $k_{-1}$  and

$k_2$  due to the destabilization of zwitterion **3**, which increases both terms [ $K(\mathbf{2c})/K(\mathbf{2a})$  and  $k_2(\mathbf{2a})/k_2(\mathbf{2c})$ ] in Eqn (5):

$$\begin{aligned} \frac{k'(\mathbf{2c})}{k'(\mathbf{2a})} &= \left( \frac{k_1(\mathbf{2c})}{k_{-1}(\mathbf{2c})} ; \frac{k_1(\mathbf{2a})}{k_{-1}(\mathbf{2a})} \right) \times \frac{k_2(\mathbf{2a})}{k_2(\mathbf{2c})} \\ &= \frac{K(\mathbf{2c})}{K(\mathbf{2a})} \times \frac{k_2(\mathbf{2a})}{k_2(\mathbf{2c})} \end{aligned} \quad (5)$$

A further increase in the amine bulk made this effect more pronounced: for (**1a**)  $k'(\mathbf{2c})/k'(\mathbf{2b})$  ratio was higher (*cf.*  $1.63 \times 10^4$  in hexane at 20°C) than  $k'(\mathbf{2c})/k'(\mathbf{2a})$  ratio (*vide supra*). The bulkier  $\beta$ -substituent, the higher  $k'(\mathbf{2c})/k'(\mathbf{2a})$  ratio was [*viz.* for (**E-s-Z-o-Z**): 39.0 (**1c**), 40.9 (**1b**) and 44.3 (**1d**), in hexane at 20°C]. The  $\beta$ -substituent introduced an additional steric effect in enones (**1**), which makes the forward rate constant  $k_1$  smaller, and simultaneously  $k_{-1}$  and  $k_2$  larger because of the further increase in the crowding of intermediate (**3**).  $k''(\mathbf{2c})/k''(\mathbf{2a})$  ratios were higher than the associated  $k'(\mathbf{2c})/k'(\mathbf{2a})$ , due to additional steric retardation of the approach of the bulky amine to its ammonium ion, resulting in  $k_3(\mathbf{2c}) > k_3(\mathbf{2a})$ . Again, for (**2b**), this effect was enhanced [ $k''(\mathbf{2c})/k''(\mathbf{2b})$  was  $21.9 \times 10^5$ , for (**1a**) in hexane at 20°C]. Consequently,  $k_3(\mathbf{2c}) \gg k_3(\mathbf{2b})$  so that the 'uncatalyzed' route became the single reaction route at small amine concentrations.

### Solvent effect

Hexane and acetonitrile are aprotic solvents so that the solvent assistance to the leaving-group expulsion was negligible. However, there is a significant change in the dielectric constant on going from hexane (1.89) to acetonitrile (36.2). As it was shown earlier,<sup>10</sup> the polar zwitterion was more readily formed in more polar solvents. The solvent effect on  $k_2$  and  $k_3$  depended on the question whether electrophilic assistance was involved (via transition states **6** and **8**) with a consequent charge dispersal, or whether two separate ions were formed from a zwitterion in an unassisted process. All the studied reactions were accelerated in the more polar solvent. The 'uncatalyzed' reactions of (**2a,c,d**) with (**1b**) at 20°C were 42.8, 44.8, and 25.9 times faster in acetonitrile than in hexane, and the 'catalyzed' processes were 18.3, 376.6, and 38.4 times faster, respectively. Similar trends were observed also for enones (**1c,d**). These values suggested that the transition state was more polar than the ground state and for all amines they agree with a self-assisted route with  $k_2$  via transition state **8**. Moreover, the predominance of the most stable (**E-s-Z-o-Z**) and (**Z-s-Z-o-Z**) forms of enones (**1a-e**) in ground state<sup>19</sup> facilitates the formation of (**8**) as transition state, thus favouring the 'uncatalyzed' route.

## Activation parameters

For all the stereoisomeric forms of enones (**1a–e**), the activation enthalpies of the ‘uncatalyzed’ reactions were positive and the compensating  $\Delta S^\ddagger$  values were highly negative, smaller than  $-95 \text{ J K}^{-1} \text{ mol}^{-1}$ . At the same time,  $\Delta H^{\ddagger'}$  values for the ‘catalyzed’ reaction were small [or close to zero for system [(**1d**) + (**2c**)] in hexane at  $20^\circ\text{C}$ ] and  $\Delta S^{\ddagger'}$  were negative, but highly solvent dependent. In some cases, they were near zero, *cf.*  $\Delta S^{\ddagger'}$  for systems [(**1a**) + (**2b**)] and [(**1d**) + (**2c**)] in acetonitrile. The (**E-s-Z-o-Z**) small or negative  $\Delta H^\ddagger$  values might seem exceptional, but numerous examples<sup>10,26</sup> showed that the same behaviour was the rule, rather than exception, in the reaction of amines with electrophilic olefins in aprotic solvents. Small  $\Delta H^\ddagger$  values should be expected for the reaction of reactive nucleophiles with enones.<sup>10,25</sup> Moreover, the highly negative  $\Delta S^\ddagger$  values were the consequence of the formation of dipolar activated complex from neutral precursors.<sup>10</sup> It was convenient to analyze  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  values as a sum of respective enthalpy and entropy terms for the individual steps of Scheme 1 (Eqn 7–10):<sup>10</sup>

$$\Delta H^{\ddagger'}(\text{uncatalyzed process}) = \Delta H^\circ + \Delta H_2^\ddagger \quad (7)$$

$$\Delta S^{\ddagger'}(\text{uncatalyzed process}) = \Delta S^\circ + \Delta S_2^\ddagger \quad (8)$$

$$\Delta H^\ddagger(\text{catalyzed process}) = \Delta H^\circ + \Delta H_3^\ddagger \quad (9)$$

$$\Delta S^\ddagger(\text{catalyzed process}) = \Delta S^\circ + \Delta S_3^\ddagger \quad (10)$$

For system [(**1a**) + (**2c**)] in hexane,  $\Delta H^{\ddagger_3} > \Delta H^{\ddagger_2}$  [ $(\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2}) = (\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2}) = 14.3 \text{ kJ mol}^{-1}$ ] and  $\Delta S^{\ddagger_3} > \Delta S^{\ddagger_2}$  [ $(\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}) = 84 \text{ J K}^{-1} \text{ mol}^{-1}$ ], therefore in this case, the catalysis was due to both activation enthalpic and entropic terms favouring the catalyzed route. As it was shown for the reaction of 1,1-dicyano-2-*p*-di-methylaminophenyl-2-trifluoroethoxyethylene with amines,<sup>25</sup> ( $\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2}$ ) values were positive or close to zero (changed from  $-10$  to  $149 \text{ kJ mol}^{-1}$ ) as a result of an intramolecular assistance by an ammonium proton to the leaving group expulsion, which reduced sufficiently  $\Delta H^{\ddagger_2}$  term and made it smaller than  $\Delta H^{\ddagger_3}$ . The negative values of the activation entropies can be easily explained since two charges in (**3**) were created from the neutral starting species, whereas the positive difference of  $\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}$  was not obvious. Small positive ( $\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}$ ) values ( $29\text{--}32 \text{ J K mol}^{-1}$ ) were also observed for the reaction mentioned above.<sup>25</sup> The  $\Delta S^{\ddagger_3}$  term was negative in view of the loss of translational and rotational degrees of freedom in the termolecular intermediate (**3**). The corresponding entropy loss in  $\Delta S^{\ddagger_2}$  term should be smaller, unless the intramolecular assistance to the departure of the leaving group reduced  $\Delta S^{\ddagger_2}$  due to the constrained geometry in transition state (**8**). According to the authors,<sup>26</sup> the loss of

entropy in the four-membered ring (**8**) should be perceptible.

For the reaction of the bulky amine (**2a**) with enone (**1a**) in hexane,  $\Delta H^{\ddagger'}$  value increased,  $\Delta H^{\ddagger''}$  value decreased and the activation enthalpy became higher for the uncatalyzed reaction ( $\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2} = -17.5 \text{ kJ mol}^{-1}$ ) with  $(\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}) = 65 \text{ J K}^{-1} \text{ mol}^{-1}$ . Consequently for this reaction, the catalysis was due to a favourable activation entropy. Further increase in bulk as in diisopropylamine (**2b**) resulted in negative ( $\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2}$ ) and ( $\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}$ ) values ( $-9.8 \text{ kJ mol}^{-1}$  and  $-39 \text{ J K}^{-1} \text{ mol}^{-1}$  in hexane, respectively) making obvious the predominance of the uncatalyzed reaction ( $k_3/k_2 = 0.39\text{--}0.51$  at  $20\text{--}40^\circ\text{C}$ ). In the more polar acetonitrile, the situation was reversed due to additional stabilization of transition state (**3**):  $\Delta H^{\ddagger_3} > \Delta H^{\ddagger_2}$  and  $\Delta S^{\ddagger_3} > \Delta S^{\ddagger_2}$  [ $(\Delta H^{\ddagger_3} - \Delta H^{\ddagger_2}) = 56.7 \text{ J K}^{-1} \text{ mol}^{-1}$  and  $(\Delta S^{\ddagger_3} - \Delta S^{\ddagger_2}) = 205 \text{ J K}^{-1} \text{ mol}^{-1}$ ]. Hence, the ‘catalyzed’ route dominated ( $k_3/k_2 = 4\text{--}18$  at  $20\text{--}40^\circ\text{C}$ ). The same trends were inherent for (**1b–d**) enones.

Again according to Eqns (7 and 9), experimental  $\Delta H^{\ddagger'}$  and  $\Delta H^{\ddagger''}$  values were the sums of  $\Delta H^\circ$  and  $\Delta H^{\ddagger_2}$  or  $\Delta H^{\ddagger_3}$ , respectively. In the case of  $\pi(\text{Ph})\text{--}\pi(\text{C}=\text{C})$  conjugation [enones (**1c**) and (**1d**)], the  $\Delta H^\circ$  term should be strongly decreased by the additional stabilization of the enone ground state with consequent decrease in  $\Delta H^{\ddagger'}$  and  $\Delta H^{\ddagger''}$  (and therefore with tremendous decrease in  $k'$  and  $k''$ ). Contrary to this assumption, enthalpies  $\Delta H^{\ddagger'}$  and  $\Delta H^{\ddagger''}$  of systems [(**1c,d**) + (**2a–d**)] were very similar to those for (**1b**), thus corroborating deconjugation in Ar–C=C moiety of (**1c**).

## Spatial configuration and reactivity

Enones (**1a**) and (**1b**) were exclusively (**E**) isomers in all the studied solvents, whereas for (**1c**) and (**1e**), we observed the presence of (**Z**) form.<sup>19</sup> It is necessary to note that earlier<sup>21</sup> enone (**1c**) was erroneously reported to be exclusively in (**E**) stereoisomeric form. For enone (**1a**) three possible conformers were identified, (**E-s-Z-o-Z**) form being the most populated (71% in hexane and 72% in acetonitrile).<sup>19</sup> Despite the relatively large percentage of (**E-s-E-o-Z**) (23%) it was impossible to evaluate the reaction rate of this form, in view of the fact that  $k_{\text{obsd}}(\text{E-s-E-o-Z}) \gg k_{\text{obsd}}(\text{E-s-Z-o-Z})$ .

The rotation around the  $\text{C}_{\text{sp}}^2\text{--}\text{C}_{\text{sp}}^3$  single bond (**-s-E** and **-s-Z** forms) did not affect the conjugation of C=C and C=O, thus the negative charge of  $\text{C}_\alpha$  was equally dispersed onto  $\text{COCF}_3$  of these forms but negatively charged oxygen of carbonyl in (**E-s-Z-o-Z**) was closer to  $\text{C}_\beta$  than in (**E-s-E-o-Z**) and, thus, reduces  $k_1$  because of the repulsion of the oncoming nucleophile. Of all the stereoisomeric forms in enone (**1c**), isomer (**Z-s-Z-o-Z**) possessed the highest  $k'$  due to a  $k_1$  increase as a result of the reaction centre more accessible to the nucleophile in (**Z**) than in (**E**). Nevertheless, the highest  $k''$  and  $k_3/k_2$

were for (**E-s-Z-o-E**) (see Table 1), a indicating drastic increase in  $k_3$  for (**E-s-Z-o-E**) in comparison with both (**E-s-Z-o-Z**) and (**Z-s-Z-o-Z**). These forms were non-equivalent thermodynamically, (**-o-Z**) being more favoured than (**-o-E**) [(**E-s-Z-o-Z**) conformer was  $9.1 \text{ kJ mol}^{-1}$  more stable than (**E-s-Z-o-E**), and  $4.9 \text{ kJ mol}^{-1}$  more stable than (**Z-s-Z-o-Z**)]<sup>19</sup> with different ability to intramolecular H-bonding in the transition state. Stereoisomeric form (**-o-Z**) promoted the formation of structure (**8**), whereas (**-o-E**) reduced the probability of generation of H-bonded structure similar to (**8**) due to steric interactions between  $\text{H}^+$  and  $\text{R}_1$ . Consequently (**-o-Z**) form assisted 'uncatalyzed' route decreasing the ( $\Delta S^\ddagger_3 - \Delta S^\ddagger_2$ ) difference, whereas (**-o-E**) form promoted 'catalyzed' route, rising ( $\Delta S^\ddagger_3 - \Delta S^\ddagger_2$ ) (vide supra).

In enone (**1e**) the stereoisomer (**Z-s-Z-o-Z**) prevailed over (**E-s-Z-o-Z**) (74 and 26% in hexane, respectively)<sup>19</sup> but the 'catalyzed' route was observed for none of these forms at ambient temperature whereas at higher temperatures  $k''$  was perceptible {e.g.,  $k''/k'$  was 2300 for system [(**1e**) + (**2c**)] in acetonitrile at  $55^\circ\text{C}$ } probably due to H-bond weakening in structure (**8**) as the temperature raised. For the studied amines,  $k'$  (**Z-s-Z-o-Z**) were 10–100 times higher than  $k'$  (**E-s-Z-o-Z**), thus once again illustrating the shielding of the reaction centre greater in (**E**) isomer than in (**Z**).

## CONCLUSION

Reaction of enones (**1a–e**) with secondary amines was a multi-step process with formation of a polar zwitterion as an intermediate, decomposition of which was a limiting step of the process. Notwithstanding the fact that this decomposition occurred predominantly via an 'uncatalyzed' route, the contribution of a 'catalyzed' route was significant in many cases and a rate-determining proton transfer was the most likely 'catalyzed' route for all these systems.  $\beta$ -Substituents diminished the contribution of the 'catalyzed' route in overall processes, not only by steric hindrance to the approach of a second amine molecule to a proton of the ammonium ion but also by stabilizing the (**-o-Z**) conformers due to inductive electron withdrawal which assisted the 'uncatalyzed' route through transition state (**8**). Thus, the phenyl ring in

(**1c,d**) was out of the  $\text{C}=\text{C}$  plane, disturbing  $\pi\text{Ar}-\pi\text{C}=\text{C}$  conjugation. As a result the  $\beta$ -Ar substituent affected enone reactivity predominantly by inductive effect and, to a lesser degree, by steric interactions. (**E-s-Z-o-Z**) form, which predominates in enones (**1a–d**) exhibited a reactivity far weaker than **Z-s-Z-o-Z** form, which was the most populated in (**1e**).

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