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Kinetics and mechanism of triethylamine-catalyzed 1,3-proton shift Optimized and substantially improved reaction conditions for biomimetic reductive amination of fluorine-containing carbonyl compounds

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Abstract

Kinetic study of the triethylamine (TEA)-catalyzed isomerization of imine, derived from benzylamine and trifluoroacetophenone to the corresponding *N*-benzylidene-2,2,2-trifluoro-1-(phenyl)ethylamine has revealed concerted nature of the mechanism of this reaction via a virtually unionized transition state. As a synthetic bonus of this kinetic study, we found that application of a polar solvent (acetonitrile) and four equivalents of TEA provide for optimal reaction conditions at high concentrations. We demonstrate that application of these reaction conditions allows to substantially increase the reaction rates, chemical yields and results in cleaner formation of the target products.
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Keywords: 1,3-Proton shift reaction; Kinetics; Mechanism; Biomimetic reductive amination; Fluorinated compounds

1. Introduction

Biological transamination (BTA) [1], constitutes a fundamentally important process in most living organisms as a pathway of α-keto and α-amino acids metabolism. It is therefore not surprising that BTA and its chemical models have been the focus of research activity of numerous research groups from the 1930 [1] to the present [2], generating a great wealth of research data. Interestingly, besides the medicinal, biochemical and synthetic applications, BTA also plays a major role in some theories on the origin of life as the primordial source of α-amino acids [3].

Mechanistically, BTA (Scheme 1) consists of a base-catalyzed 1,3-proton transfer across an azaallyllic anionic intermediate **3** giving rise to Schiff bases of α-keto acids **2** or α-amino acids **4** as precursors of α-amino acids and pyridoxal **5** and α-keto carboxylic acids and pyridoxamine **1**, respectively [4]. In a native, biological system, the 1,3-proton transfer is performed by the ω-amino group of the corresponding enzyme's α,ω-diamino acid. For example, in the transamination reaction catalyzed by aspartate aminotransferase the ω-amino group of lysine 258 selectively transfers a proton within the same face of the delocalized 2-azaallyl anion **3** [5]. Martell's [6], Snell's [7], Casella's [8] and Breslow's [9,2a,b] groups studied the mechanisms and stereochemistry of BTA using native as well as model pyridoxal-based systems. They demonstrated a paramount importance of the metal complex formation in controlling the chemical and stereochemical outcome of BTA. The first systematic investigation of the stereochemical outcome of transamination reaction, on purely chemical, metal-free models, was performed by Cram's group [10]. Using KO*t*Bu-catalyzed azomethine–azomethine isomerization of simple α-(phenyl)ethylamine derived Schiff bases they studied the nature of ion pair formation (contact vs. solvent-separated ion pairs) and the suprafacial/antarafacial character of the proton-transfer step. The major conclusion of their work is that the 1,3-proton shift transfer occurs predominantly within a contact ion pair in a highly stereoselective suprafacial manner. Contributions from other groups demonstrated that: (a) in general, triad prototropy of imines (1,3-proton shift, azomethine–azomethine isomerization) is rather immobile, requiring a strong base for this isomerization

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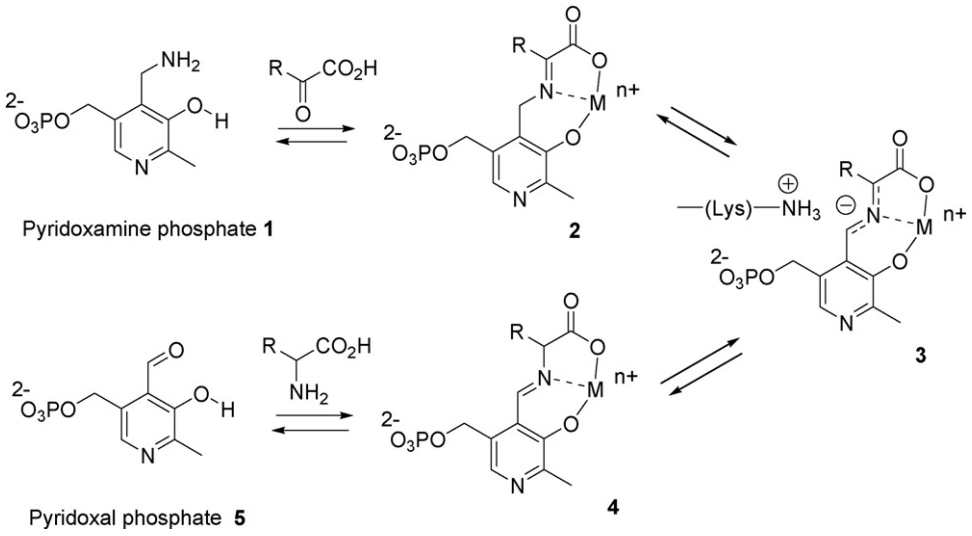


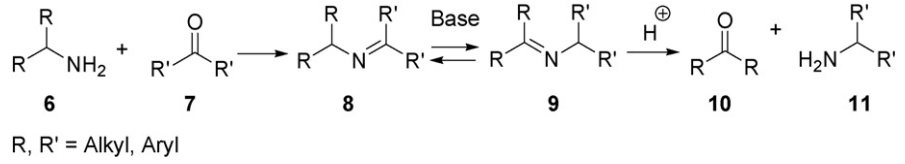
Scheme 1. Biological transamination.

to occur [11] and (b) the equilibrium constants of the 1,3-prototropic shift of imines are adequately correlated by the Hammett equation ($\rho = 0.94$), in other words, the equilibrium shifted towards the more CH acidic isomer [12].

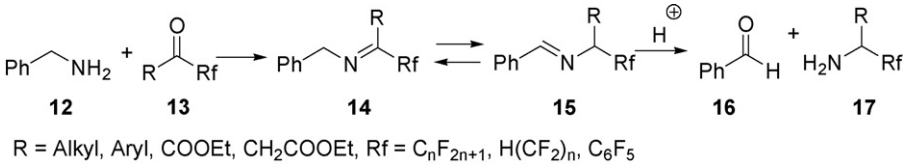
From the synthetic standpoint, BTA is an intramolecular reduction–oxidation process via a base-catalyzed 1,3-proton shift in azaallylic systems of the appropriate imines (Scheme 2). Therefore, if one can control the equilibrium between imines **8** and **9**, then a biomimetic approach for oxidation of amines to carbonyl compounds [13] (from **6** to **10**) and reductive amination of carbonyl compounds to amines [14] (from **7** to **11**) can be developed. The apparent synthetic advantage of this biomimetic approach over the purely chemical methods is that it does not require the application of conventional, external oxidizing or reducing reagents thus allowing for the development of an environmentally benign, metal-free reduction or oxidation processes. Moreover, this biomimetic oxidation/reduction can be conducted under *operationally convenient conditions* without recourse to very low or high temperatures, air/moisture sensitive reagents, dry and degassed solvents. However, for this transformation to be synthetically useful the equilibrium constant between **8** and **9** should be close to 100 or higher [13,14].

2. Results and discussion

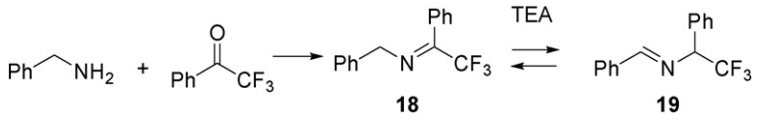
Some time ago, we found ([15], for biomimetic transamination of fluorinated α-keto acids, see: [15p], [16], [17–19]) that Schiff bases **14** (Scheme 3), derived from α-trifluoromethyl-containing carbonyl compounds (aldehydes, ketones, α- and β-keto acids) and benzylamine, or its derivatives or analogs, easily undergo virtually irreversible isomerization to give the corresponding imine **15** under the action of various organic bases. Compounds **15** can be easily hydrolyzed to afford the target fluorinated amine **17** and the corresponding derivative of benzaldehyde. This biomimetic method is general, affordable and truly practical for large-scale preparations of various fluorinated amines, α- and β-amino acids. The difference between isomerization of trifluoromethyl-containing imine **14** to **15** and the literature examples [6–11] is that the former can be effectively catalyzed by triethylamine (TEA) or even pyridine. Typically the reactions are conducted in a TEA solution at ambient or elevated temperatures. Since TEA and pyridine are relatively weak organic bases, formation of ionized species, like an azaallyl anionic intermediate **3** (Scheme 1), as suggested in previous reports [6–11], is highly unlikely. Taking into account the high synthetic value of this biomimetic



Scheme 2. Biomimetic oxidative deamination/reductive amination.



Scheme 3. Biomimetic reductive amination of fluorinated carbonyl compounds.



Scheme 4.

reductive amination for preparation of fluorinated amines and amino acids, we decided to investigate the kinetics and mechanism of the key step in this process, i.e. the organic base-catalyzed isomerization of imine **14** to **15**. Here we describe the corresponding mechanistic study which allowed us to optimize and substantially improve the reaction conditions and the overall outcome of this method.

As a model starting compound we chose imine **18** (Scheme 4) derived from benzylamine and trifluoroacetophenone. In this case there are no protons in the α-position to the Schiff base function and therefore an alternative imine-enamine isomerization is not possible. Imine **18** was distilled several times to provide a sample of 99.9% purity that was suitable for kinetic studies.

The TEA-catalyzed reaction is relatively slow (depending on the applied experimental conditions it takes hours or days for completion) and could easily be followed by ^{19}F and ^{1}H NMR spectroscopy. In all studied systems the equilibrium between species **18** and **19** (Scheme 4) is shifted towards the formation of the *N*-benzylidene (yield of **19** is >99%). Only two peaks were observed by ^{19}F NMR at 90.9 ppm and 87.8 ppm throughout the reaction that were assigned to the reactant **18** and product **19**, respectively (Fig. 1). No intermediates or byproducts were observed either by ^{19}F or by ^{1}H NMR. The width-at-half-height and the chemical shifts of the peaks that correspond to the imine **18** and the *N*-benzylidene **19** were the same regardless of the concentration of the base throughout the reaction. Furthermore cooling the reaction mixture to −40 °C resulted in no peak splitting, which suggests the lack of intermediates or interacting complexes with TEA.

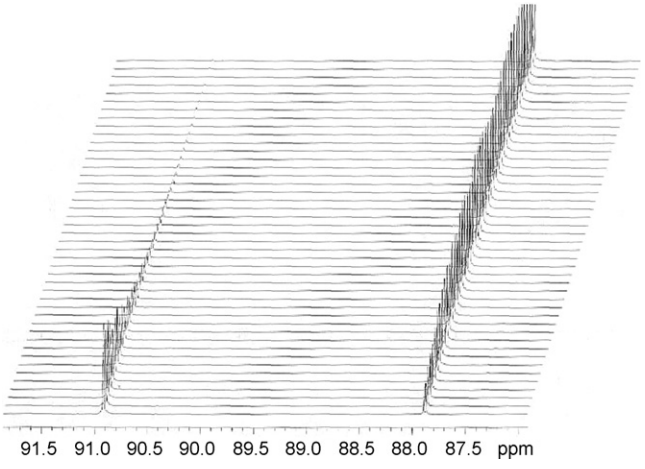


Fig. 1. Time resolved ^{1}H NMR spectra illustrating the depletion of **18** at 90.9 ppm and the formation of **19** at 87.8 ppm. The chemical shifts are referenced to C_6F_6 (0 ppm). The spectra are 1000 s apart. *Conditions*: [Imine]$_0$ = 1 M, [TEA] = 0.25 M, T = 25 °C in acetonitrile.

2.1. Concentration dependencies

Concentration vs. time traces were developed using the relative peak integrals of the time resolved NMR spectra (Fig. 1). The initial rate method was used to determine the concentration and temperature dependencies of the reaction rate and the solvent effects. The reaction exhibits first-order dependence both on [TEA] and [Imine], indicated by the linear fits of the initial rates (v_0) vs. [TEA] (at constant [Imine]$_0$) and v_0 vs. [Imine]$_0$ (at constant [TEA]) plots that are passing through the origins (Fig. 2). The experimentally determined rate law thus can be written in the following form:

$$\text{Rate} = \frac{-\text{d[Imine]}}{\text{d}t} = \frac{\text{d[Benzylidene]}}{\text{d}t} = k[\text{Imine}][\text{TEA}] \qquad (1)$$

When the base and imine concentrations were comparable to each other (i.e. under non-saturating concentrations of either the substrate or the catalyst) the reaction was followed until completion and the observed kinetic traces were well described by a single exponential model (Fig. 2), which corroborates the first-order dependency of the rate law on [Imine] and also indicates that TEA serves as a catalyst (not a reaction partner) in the reaction. The single exponential fits of the kinetic traces for the formation of the product and the depletion of the reactant resulted in similar rate constants (Fig. 3), which also evidences for the presence of no measurable intermediates.

For synthetic purposes the kinetics of the reaction was also investigated at high [TEA] (0.25–4 M) and [Imine]$_0$ (1 M) concentrations. The observed saturation kinetics for the base dependencies under these conditions are explained by the

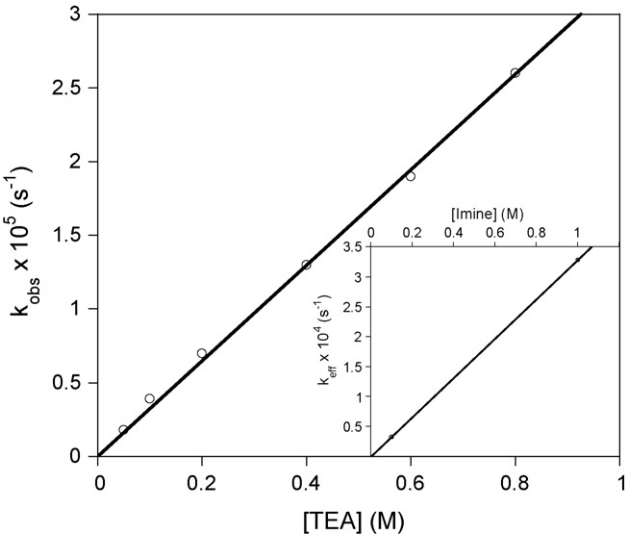


Fig. 2. Effect of [TEA] and [Imine] (inset) on the 1,3-H-shift reaction rate. *Conditions*: [Imine]$_0$ = 0.1 M, [TEA] = 0.05–0.8 M, T = 25 °C in acetonitrile, inset: [Imine]$_0$ = 0.1–1 M, [TEA] = 0.25 M, T = 25 °C in acetonitrile.

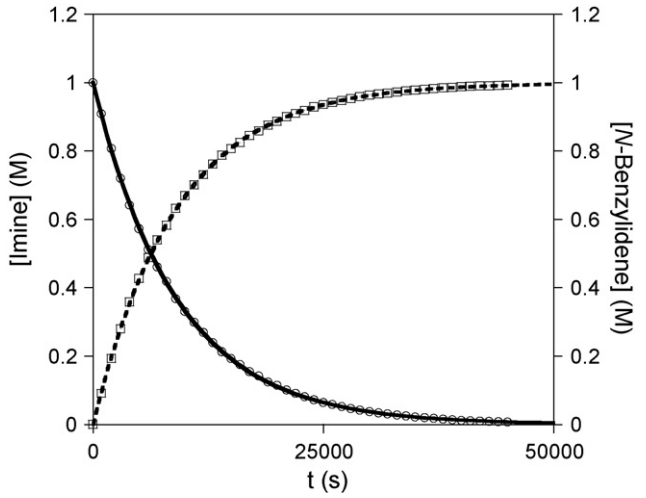


Fig. 3. Typical kinetic traces reflecting the depletion of **18** (circles, left most ordinate), and the formation of **19** (squares, right most ordinate) together with the corresponding exponential fits (solid line: depletion of **18**, dashed line: formation of **19**). The peak integrals of the time resolved ^{19}F NMR spectra developed the traces. *Conditions*: $[Imine]_0 = 1$ M, [TEA] = 0.25 M, $T = 25$ °C in acetonitrile.

change in the relative permittivity of the solvent due to the comparable relative volumes of the reactants and the solvent (Fig. 4) (at lower concentrations strictly linear curves were observed).

2.2. Solvent effect

The TEA-catalyzed proton shift reaction was studied in four different solvents at 25 °C. The rate of the reaction changes only slightly with the polarity of the solvent. The 12-fold change in the rate going from benzene to acetonitrile (i.e. a 16.5-fold increase in the relative permittivity of the solvent) suggests the lack of an ionic intermediate or activated complex (Table 1), which is in contrast to the previous study by Jaeger and Cram [20] where an *inherently symmetrical azaallylic carbanion asymmetrically ion paired with potassium intermediate* was proposed in the potassium *tert*-butoxide-catalyzed transamination reactions of (−)-(*S*)-*N*-(α-methylneopentylidene)-α-phenylethylamine and (+)-(*S*)-*N*-(α-methylbenzylidene)pinacolylamine.

Table 1
TEA-catalyzed proton shift reaction in four different solvents

Solvent	ε_r	k ($\times 10^4$ M^{-1} s^{-1})
C_6H_6	2.27	0.26
C_6H_5Cl	5.65	0.46
Acetone	20.7	1.5
CH_3CN	37.5	3.2

The Kirkwood function of the reaction is shown in Fig. 5. In most cases $(\varepsilon - 1)/(2\varepsilon + 1)$ is proportional to $1/\varepsilon$ except at very low ε. The $\ln k$ vs. $1/\varepsilon$ plot (Fig. 5 inset) shows a moderate negative slope which suggests that the activated complex in the transition state is only slightly more polar than the reagents. These observations are consistent with a concerted mechanism and do not support an ionic transition state. Isopolar transition state reactions with small or negligible solvent effects are often found amongst pericyclic reactions such as the [3,3] sigmatropic rearrangement of an allyl thiobenzoate into an allyl thiolbenzoate [21].

2.3. Temperature effect

The temperature dependency of the second-order rate constants of the reaction was investigated in acetonitrile and chlorobenzene. The data were evaluated using the Eyring equation. The Eyring plots are depicted in Fig. 6 together with

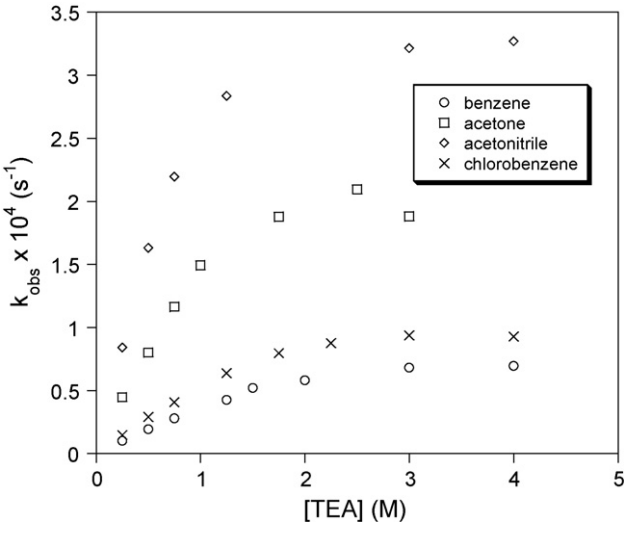


Fig. 4. Effect of [TEA] on the observed pseudo-first-order rate constants at high TEA and imine concentrations. *Conditions*: $[Imine]_0 = 1$ M, [TEA] = 0.25–4 M, $T = 25$ °C in different solvents. *Note*: the deviation of the curves from linearity at high [TEA] is due to the change in the ε of the medium.

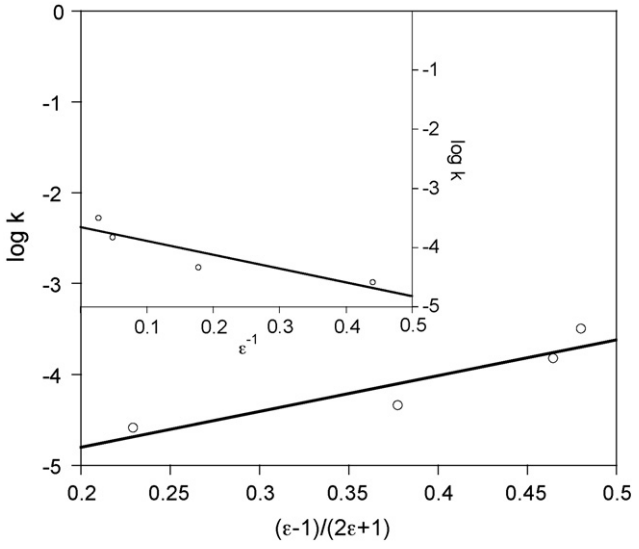


Fig. 5. Kirkwood plot of the calculated second-order rate constants (k) using four different solvents. Inset: log k vs. ε^{-1} plot demonstrating the effect of the polarity of the solvent on the reaction rate. The second-order rate constants were calculated from initial rates based on the [TEA] and [Imine] dependencies of the rate law.

Table 2
Activation parameters of TEA-catalyzed proton shift reaction in two different solvents

Solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})
C_6H_5Cl	37.8 ± 0.036	−198.1 ± 0.12
CH_3CN	32.7 ± 1.43	−200.4 ± 4.48

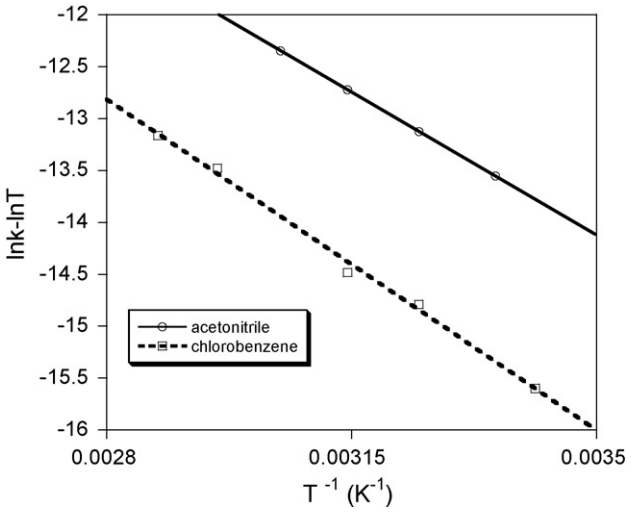
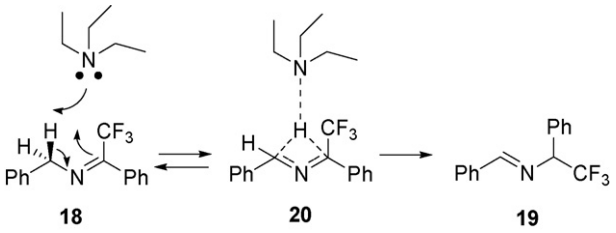


Fig. 6. Eyring plots show the effect of temperature on the rate constant in chlorobenzene and acetonitrile. *Conditions*: squares (dashed line): [Imine]$_0$ = 1 M, [TEA] = 0.25 M, T = 20–75 °C, solvent: chlorobenzene; circles (solid line): [Imine]$_0$ = 1 M, [TEA] = 0.25 M, T = 25–55 °C, solvent: acetonitrile.

the linear fits. The obtained activation parameters are presented in Table 2.

The relatively low values of the activation enthalpies and large negative activation entropies indicate a large entropy barrier and do not support an ionic mechanism. This entropy barrier is explained by both the bimolecularity of the process (i.e. direct participation of the base molecule in the transition state) and a highly ordered activated complex in the transition state with a four-membered ring (Scheme 5). The entropy of activation is similar for the two solvents and only a 1.15-fold decrease in the activation enthalpy was observed with a



Scheme 5. Proposed mechanism for TEA-catalyzed 1,3-proton shift.

significant change in the polarity of the solvent (i.e. going from chlorobenzene to acetonitrile), which also supports a nonionic transition state.

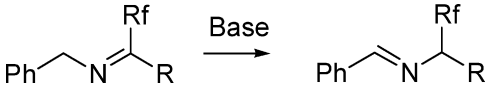
The proposed mechanism for the TEA-catalyzed 1,3-proton shift reaction based on these kinetic data is shown in Scheme 5. The role of a base, such as TEA, is to increase the polarization of one of the benzylic protons bond to the point where it can trigger a concerted shift of the C–H benzylic bond and the π-bond of the C=N moiety through the formation of an unionized transition state **20** with a four-membered ring.

Similar type of intermediate with a four-membered ring was proposed in the base-catalyzed intramolecular 1,3-bis(4-fluorophenyl)triazene by Limbach et al. [22] based on the observed ^{1}H NMR spectra, temperature-dependent H/D isotope effect and their semi-empirical quantum mechanical calculations. The observed convex curvature of the Arrhenius curves is explained by the formation of an interacting complex (hydrogen bond between the triazene and the base) that precedes the proton transfer. In our study no indication of such association was found between either **18** or **19** and TEA.

Taking advantage of the obtained kinetic data, we decided to use them for synthetic purposes and optimize the procedure for isomerization of various imines **21** to Schiff bases **22**. Table 3 summarizes our findings. In all studied cases (entries 2, 4, 6, 8 and 10), the application of acetonitrile as a solvent and only four equivalents of TEA allowed us to substantially reduce the reaction time and, in some cases, increase the chemical yields (entry 2 vs.1, 6 vs. 5, 8 vs. 7 and 10 vs. 9). The representative examples include fluorinated aliphatic aldehydes (entries 2 and 6), aromatic aldehydes (entry 10) and ketones (entries 4 and 8). Thus, in all studied cases, the reaction rates were increased by

Table 3
TEA-catalyzed proton shift reaction of various fluorine-containing imines under the optimized conditions

Run	R	Rf	Base	Solvent	Temperature	~4 $t_{1/2}$ time (h)	Yield (%)
1	H	CF_3	TEA	TEA	rt	90	91 [15g]
2	H	CF^3	TEA (4 equiv.)	MeCN	rt	12	95
3	Me	CF_3	TEA	TEA	50	190	95 [15g]
4	Me	CF_3	TEA (4 equiv.)	MeCN	50	25	95
5	H	C_3F_7	TEA	TEA	rt	90	88 [15g]
6	H	C_3F_7	TEA (4 equiv.)	MeCN	rt	11	93
7	Bn	CF_3	TEA	TEA	78	48	92 [15g]
8	Bn	CF_3	TEA (4 equiv.)	MeCN	78	5	97
9	H	C_6F_5	TEA	TEA	rt	160	92 [15g]
10	H	C_6F_5	TEA (4 equiv.)	MeCN	rt	21	96



5–10 times and generally the purity of the products **22** was substantially higher as no other fluorine peaks were observed in the reaction mixtures. It is important to note that application of acetonitrile, as a polar solvent, did not increase the undesired dehydrofluorination, as no peaks of possible unsaturated products were observed by ^{19}F NMR in the crude reaction mixtures. The data shown in Table 3 clearly demonstrate that the synthetic efficiency of the 1,3-proton shift reaction can be substantially increased by using the optimized reaction conditions reported here.

In summary, kinetic study of the TEA-catalyzed isomerization of imine, derived from benzylamine and trifluoroacetophenone to the corresponding *N*-benzylidene-2,2,2-trifluoro-1-(phenyl)ethylamine has revealed concerted nature of the mechanism of this reaction via an unionized transition state. As a synthetic bonus of the kinetic study, we found that application of a polar solvent and four equivalents of TEA provide optimal reaction conditions at high concentrations in many cases. We demonstrate that application of these reaction conditions substantially increases the reaction rates, chemical yields, facilitate the cleaner formation of the target products.

3. Experimental

3.1. Materials

Triethylamine was doubly distilled. Acetone-D_6 (D, 99.9%), acetonitrile-D_3 (D, 99.8%) and benzene-D_6 (D, 99.5%) were obtained from Cambridge Isotope Laboratories. Chlorobenzene-D_5 (D, 99%) was obtained from Alfa Aesar.

3.2. Synthesis of imine *18*

Imine **18** was prepared as previously reported [15k]. It was doubly distilled (purity was >99.9%) and stored in a refrigerator as 4.0 M solutions of deuterated solvents (CD_3CN, benzene-D_6, acetone-D_6 or chlorobenzen-D_5).

3.3. NMR experiments

NMR spectra were recorded with a Varian XL-400 spectrometer. The ^{19}F NMR chemical shifts (ppm) were referenced to hexafluorobenzene ($\delta = 0$ ppm), the ^{1}H NMR shifts were referenced to TMS ($\delta = 0$ ppm).

3.4. Kinetic study of biomimetic reductive amination (from *18* to *19*)

The purity of the imine **18** was checked by ^{1}H and ^{19}F NMR before each kinetic run after diluting the freshly prepared 4.0 M stock solution with the calculated amount of deuterated solvent (CD_3CN, benzene-D_6, acetone-D_6 or chlorobenzen-D_5) in an NMR tube at rt. The reactions were initiated by adding the calculated amount of TEA (that was incubated at rt) to the NMR tube (the total volume of the solutions were 0.700 mL), and the reactions were monitored by ^{19}F or ^{1}H NMR at various temperatures.

3.5. General procedure for the isomerization of various imines *21* to Schiff base *22*

The reaction conditions for imine **18** (Table 3, run 2) is described here as a representative example: the reactants and solvents were incubated at rt. The reactions were initiated by the addition of 2.12 mL (1.52 mmol) of triethylamine to the flask that contained the imine (1.0 g, 3.80 mmol) and 2 mL of CH_3CN. The reaction mixture was stirred at the temperature indicated in Table 3 and monitored by ^{19}F NMR. After complete consumption of the starting imine, the solvent and triethylamine was removed under vacuum, followed by purification of the residue by a short path silica gel column (hexane/AcOEt = 8/1). Upon removal of the solvent, the Schiff base was obtained with >95% purity.

All the spectra and physical properties of the prepared Schiff bases coincide with the corresponding authentic samples [15g].

Acknowledgments

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References

[1] The term ‘‘transamination’’ was coined in the following paper, A.E. Braunshtein, M.G. Kritsman, Biokhimiya (Moscow) 2 (1937) 859–874.
[2] For review, see:
(a) M.E. Tanner, Acc. Chem. Res. 35 (2002) 237–246;
For recent publications, see:
(b) L. Liu, W. Zhou, J. Chruma, R. Breslow, J. Am. Chem. Soc. 126 (2004) 8136–8137;
(c) L. Liu, R. Breslow, J. Am. Chem. Soc. 125 (2003) 12110–12111;
(d) R.F. Zabinski, M.D. Toney, J. Am. Chem. Soc. 123 (2001) 193–198;
(e) S. Ogo, K. Uehara, T. Abura, S. Fukuzumi, J. Am. Chem. Soc. 126 (2004) 3020–3021.
[3] (a) G. Wachtershauser, Microbiol. Rev. 52 (1988) 452–484;
(b) G. Wachtershauser, Prog. Biophys. Mol. Biol. 58 (1992) 85–201;
(c) C. Huber, G. Wachtershauser, Tetrahedron Lett. 44 (2003) 1695–1697.
[4] A.L. Lehninger, D.I. Nelson, M.M. Cox, Principles of Biochemistry, 2nd ed., Worth Publishers, New York, 1993, pp. 511–514.
[5] M.D. Toney, J.F. Kirsch, Biochemistry 32 (1993) 1471–1479.
[6] A.E. Martell, Acc. Chem. Res. 22 (1989) 115–124.
[7] J.B. Longenecker, E.E. Snell, J. Am. Chem. Soc. 79 (1957) 142–145.
[8] L. Casella, M. Gullotti, J. Am. Chem. Soc. 105 (1983) 803–809.
[9] (a) L. Liu, M. Rozenman, R. Breslow, J. Am. Chem. Soc. 124 (2002) 12660–12661;
(b) L. Liu, R. Breslow, J. Am. Chem. Soc. 124 (2002) 4978–4979;
(c) R. Breslow, J.W. Canary, M. Varney, S.T. Waddell, D. Yang, J. Am. Chem. Soc. 112 (1990) 5212–5219;
(d) R. Breslow, J. Chmielewski, D. Foley, B. Johnson, N. Kumabe, M. Varney, R. Mehra, Tetrahedron 44 (1988) 5515–5524.
[10] D.A. Jaeger, M.D. Broadhurst, D.J. Cram, J. Am. Chem. Soc. 101 (1979) 717–732 (and references therein on previous work reported by Cram’s group).
[11] For review see:
R.W. Layer, Chem. Rev. 63 (1963) 489–510.
[12] (a) P.A.S. Smith, C. Van Dang, J. Org. Chem. 41 (1976) 2013–2015;
(b) H. Brandenberger, P.P. Cohen, Helv. Chim. Acta 36 (1953) 549–554.

[13] For examples of synthetic application of biomimetic oxidative deamination of primary amines, see:
(a) E.J. Corey, K. Achiwa, J. Am. Chem. Soc. 91 (1969) 1429–1432;
(b) V. Calo, L. Lopez, P.E. Todesco, J. Perkin Trans. 1 (1972) 1652–1653;
(c) S. Ohta, M. Okamoto, Synthesis (1982) 756–758;
(d) J.H. Babler, B.J. Invergo, J. Org. Chem. 46 (1981) 1937–1938;
(e) T.F. Buckley, H. Rapoport, J. Am. Chem. Soc. 104 (1982) 4446–4450;
(f) F.G. Baddar, Z. Iskander, Nature 167 (1951) 1069–1070;
(g) F.G. Baddar, J. Chem. Soc. (1950) 136–139;
(h) F.G. Baddar, Z. Iskander, J. Chem. Soc. (1954) 203–209;
(j) F.G. Baddar, Z. Iskander, J. Chem. Soc. (1954) 209–213.

[14] For examples of synthetic application of biomimetic reductive amination of carbonyl compounds, see:
(a) G. Cainelli, D. Giacomini, A. Trere, P.P. Boyl, J. Org. Chem. 61 (1996) 5134–5139;
(b) M. Ando, H. Kuzuhara, Bull. Chem. Soc. Jpn. 63 (1990) 1925–1928 (references therein on previous publications);
(c) J.G.H. Willems, J.G. de Vries, R.J.M. Nolte, B. Zwanenburg, Tetrahedron Lett. 36 (1995) 3917–3920;
(d) A. Hjelmencrantz, U. Berg, J. Org. Chem. 67 (2002) 3585–3594;
(e) S. Bachmann, K.R. Knudsen, K.A. Jørgensen, Org. Biomol. Chem. 2 (2004) 2044–2049;
(f) S. Zimmerman, R. Breslow, J. Am. Chem. Soc. 106 (1984) 1490–1491;
(g) Y. Wu, P. Ahlberg, J. Org. Chem. 57 (1992) 6324–6327;
(h) Y. Wu, P. Ahlberg, Acta Chem. Scand. 46 (1992) 60–72;
(j) K. Bernauer, R. Deschenaux, T. Taura, Helv. Chim. Acta 66 (1983) 2049–2058;
(k) R. Deschenaux, K. Bernauer, Helv. Chim. Acta 67 (1984) 373–377.

[15] For biomimetic transamination of fluorinated aldehydes and ketones, see:
(a) V.A. Soloshonok, I.L. Gerus, Y.I. Yagupolskii, V.P. Kukhar, Zh. Org. Khim. 23 (1987) 2308–2313;
V.A. Soloshonok, I.L. Gerus, Y.I. Yagupolskii, V.P. Kukhar, Chem. Abstr. 109 (1987) 55185p;
(b) V.A. Soloshonok, I.L. Gerus, Y.I. Yagupolskii, V.P. Kukhar, Zh. Org. Khim. 24 (1988) 993–997;
V.A. Soloshonok, I.L. Gerus, Y.I. Yagupolskii, V.P. Kukhar, Chem. Abstr. 110 (1988) 134824v;
(c) V.A. Soloshonok, Y.I. Yagupolskii, V.P. Kukhar, Zh. Org. Khim. 24 (1988) 1638–1644;
V.A. Soloshonok, Y.I. Yagupolskii, V.P. Kukhar, Chem. Abstr. 110 (1988) 154827b;
(d) A.B. Khotkevich, V.A. Soloshonok, Y.I. Yagupolskii, Zh. Obshch. Khim. 60 (1990) 1005–1008;
A.B. Khotkevich, V.A. Soloshonok, Y.I. Yagupolskii, Chem. Abstr. 113 (1990) 171274y;
(e) V.A. Soloshonok, A.G. Kirilenko, V.P. Kukhar, G. Resnati, Tetrahedron Lett. 35 (1994) 3119–3122;
(f) V.A. Soloshonok, T. Ono, Synlett (1996) 919–921;
(g) V.A. Soloshonok, T. Ono, Tetrahedron 52 (1996) 14701–14712;
(h) H. Ohkura, D.O. Berbasov, V.A. Soloshonok, Tetrahedron Lett. 44 (2003) 2417–2420;
(j) H. Ohkura, D.O. Berbasov, V.A. Soloshonok, Tetrahedron 59 (2003) 1647–1656;
(k) D.O. Berbasov, I.D. Ojemaye, V.A. Soloshonok, J. Fluorine Chem. 125 (2004) 603–607;
(l) T. Ono, V.P. Kukhar, V.A. Soloshonok, J. Org. Chem. 61 (1996) 6563–6569;
(m) V.A. Soloshonok, H. Ohkura, M. Yasumoto, Mendeleev Commun. (2006) 165–167;
(n) V.A. Soloshonok, H. Ohkura, M. Yasumoto, J. Fluorine Chem. 127 (2006) 708–711;
(o) V.A. Soloshonok, M. Yasumoto, J. Fluorine Chem. 127 (2006) 889–893;
(p) V.A. Soloshonok, D.O. Berbasov, J. Fluorine Chem. 125 (2004) 1757–1763;
(r) M. Yasumoto, H. Ueki, V.A. Soloshonok, J. Fluorine Chem. 128 (2007) 736–739.

[16] V.A. Soloshonok, V.P. Kukhar', Tetrahedron 53 (1997) 8307–8314 (for biomimetic transamination of fluorinated α-keto acids).

[17] For biomimetic transamination of fluorinated β-keto acids, see:
(a) V.A. Soloshonok, A.G. Kirilenko, V.P. Kukhar, G. Resnati, Tetrahedron Lett. 34 (1993) 3621–3624;
(b) V.A. Soloshonok, A.G. Kirilenko, N.A. Fokina, I.P. Shishkina, S.V. Galushko, V.P. Kukhar, V.K. Svedas, E.V. Kozlova, Tetrahedron: Asymmetr. 5 (1994) 1119–1126;
(c) V.A. Soloshonok, A.G. Kirilenko, N.A. Fokina, S.V. Galushko, V.P. Kukhar, V.K. Svedas, G. Resnati, Tetrahedron: Asymmetr. 5 (1994) 1225–1228;
(d) V.A. Soloshonok, V.P. Kukhar, Tetrahedron 52 (1996) 6953–6964.

[18] For double biomimetic transamination of fluorinated acids to amines, see: V.A. Soloshonok, H. Ohkura, K. Uneyama, Tetrahedron Lett. 43 (2002) 5449–5452.

[19] For asymmetric version of the biomimetic transamination, see:
(a) V.P. Kukhar, V.A. Soloshonok, S.V. Galushko, A.B. Rozhenko, Dokl. Akad. Nauk SSSR 310 (1990) 886–889;
V.P. Kukhar, V.A. Soloshonok, S.V. Galushko, A.B. Rozhenko, Chem. Abstr. 113 (1990) 78920w;
(b) V.A. Soloshonok, T. Ono, J. Org. Chem. 62 (1997) 3030–3031;
(c) V.A. Soloshonok, T. Ono, I.V. Soloshonok, J. Org. Chem. 62 (1997) 7538–7539;
(d) V.A. Soloshonok, A.G. Kirilenko, S.V. Galushko, V.P. Kukhar, Tetrahedron Lett. 35 (1994) 5063–5064;
(e) V.A. Soloshonok, I.V. Soloshonok, V.P. Kukhar, V.K. Svedas, J. Org. Chem. 63 (1998) 1878–1884;
(f) V.A. Soloshonok, H. Ohkura, M. Yasumoto, J. Fluorine Chem. 127 (2006) 924–929;
(g) V.A. Soloshonok, H. Ohkura, M. Yasumoto, J. Fluorine Chem. 127 (2006) 930–935;
(h) V.A. Soloshonok, Angew. Chem. Int. Ed. Engl. 45 (2006) 766–769;
(j) V.A. Soloshonok, D.O. Berbasov, J. Fluorine Chem. 127 (2006) 597–603;
(k) V.A. Soloshonok, M. Yasumoto, J. Fluorine Chem. 128 (2007) 170–173.

[20] D.A. Jaeger, D.J. Cram, J. Am. Chem. Soc. 93 (1971) 5153–5161.

[21] S.G. Smith, J. Am. Chem. Soc. 83 (1961) 4285–4287.

[22] H.H. Limbach, F. Maennle, C. Detering, G.S. Denisov, Chem. Phys. 319 (2005) 69–92.