Organocatalysis

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Aldehyde Umpolung by N-Heterocyclic Carbenes: NMR Characterization of the Breslow Intermediate in its Keto Form, and a Spiro-Dioxolane as the Resting State of the Catalytic System**

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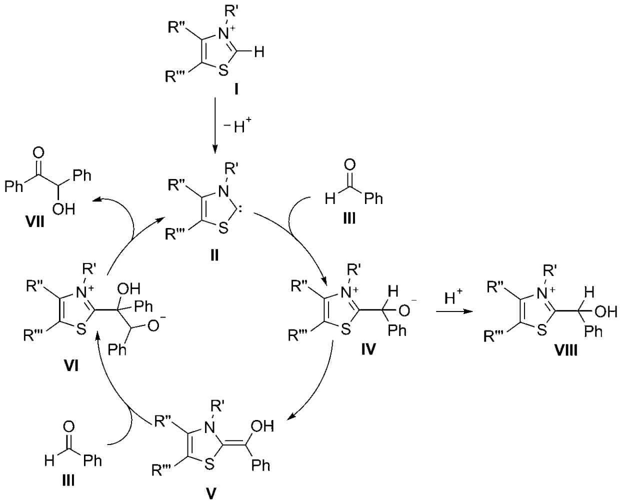
Dedicated to Professor Ronald Breslow

The enormous potential of N-heterocyclic carbenes (NHCs) as organocatalysts has become evident in recent years.[1] Furthermore, NHCs are well-known as excellent ligands in metal-based catalytic reactions.[2] The most intriguing use of NHCs as organocatalysts is based on their ability to render aldehydes nucleophilic, thereby inverting the typical electrophilic nature of aldehydes ("umpolung").[3] A prototypical reaction based on the umpolung of aldehydes is the benzoin condensation. In 1943, Ukai et al. recognized that not only cyanide ions but also thiazolium salts can be used as catalysts for the benzoin condensation.[4] Stetter et al. were among the first to recognize the catalytic potential of 3-alkylthiazolium salts in benzoin-type condensations of aliphatic aldehydes, which cannot be effected by cyanide.[5] Recent years have seen impressive enantioselective variants and versatile homoenolate chemistry resulting from conjugate umpolung of enals or related compounds.[1,6] Similarly, the benzoin condensation is of interest to industry, for example for the catalytic condensation of formaldehyde to glycolaldehyde.[7]

In 1958, Breslow proposed a mechanism for the thiazolium-catalyzed benzoin condensation (Scheme 1).[8] The thiazolium salt **I** is deprotonated at its most acidic position to form the thiazolin-2-ylidene **II**, the catalytically active species. Nucleophilic attack of the carbene **II** onto the aldehyde **III** generates the tetrahedral intermediate **IV**. A subsequent proton shift affords the enaminol **V**, commonly referred to as the Breslow intermediate. This acyl anion equivalent **V** reacts with the carbonyl group of a second aldehyde molecule, generating intermediate **VI**. A second proton transfer follows and the elimination of benzoin **VII** regenerates the carbene catalyst **II.**



Scheme 1. Catalytic cycle of the benzoin condensation as proposed by Breslow.[8]

Several experimental and theoretical investigations have resulted in the identification of intermediates early in the catalytic cycle. The initial adduct **IV** and also its O-protonated form **VIII** have been identified by NMR spectroscopy[9] and mass spectrometry[10] in thiazolium-catalyzed reactions. Enders, Teles and co-workers succeeded in preparing and characterizing a 5-(hydroxymethyl)triazolium salt as a triazolium-based analogue of structure **VIII**, starting from a triazolium salt and formaldehyde.[7]

In contrast, spectroscopic characterization of the Breslow intermediate itself (**V**) is scarce. Jordan et al. studied the reaction of thiazolium salts with benzaldehydes and formulated the 2-(α-hydroxybenzyl)thiazolium ion **VIII** as a likely intermediate.[9b] UV spectroscopy pointed to the presence of the enaminol **V**.[9b] To our knowledge, there has been no unambiguous identification of the key intermediate in NHC umpolung catalysis, namely the Breslow intermediate. We therefore decided to undertake a thorough NMR spectroscopic investigation of the NHC–aldehyde interaction using a stable and readily accessible carbene, 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene **1**, introduced by Enders, Teles and co-workers.[11]

In an initial experiment, we combined triazolylidene **1** with propionic aldehyde **2** in a 1:1 molar ratio. To our delight, the keto tautomer **3** of the Breslow intermediate formed smoothly and was isolated by column chromatography

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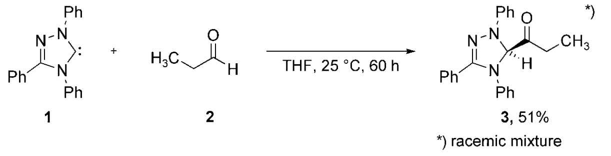
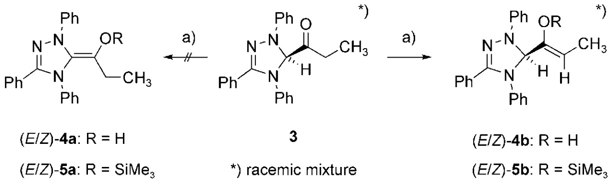


Scheme 2. Synthesis of the 5-propionyl-1,2,4-triazoline **3**.

(Scheme 2). With the ketone **3** in hand, we performed ^{1}H and ^{13}C NMR spectroscopic studies.

In solution (e.g. [D$_8$]THF) the keto form **3** of the Breslow intermediate showed significant oxygen sensitivity, resulting in 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one and propionic acid as the cleavage products, which were identified by NMR spectroscopy.

Under rigorous exclusion of oxygen, treatment of ketone **3** with catalytic amounts of acid (e.g. TFA, *p*-TsOH) did not result in detectable tautomerization to the enaminol (*E*/*Z*)-**4a** or enol (*E*/*Z*)-**4b** (Scheme 3). In the presence of catalytic amounts of NaH and two equivalents of silylating agent BSA (N,O-bis(trimethylsilyl)acetamide), ketone **3** was converted into the silyl enol ether (*Z*)-**5b** (Scheme 3). The *Z*-configuration of **5b** was established by NOE spectroscopy.[12] No evidence for the formation of silyl enol ether (*E*/*Z*)-**5a** was obtained in this study.



Scheme 3. Ketone **3**, potential tautomers and their silylated analogs. a) Base, silylating agent.

The outcome of the above experiments is in accordance with the relative free energies obtained by DFT calculations for the ketone **3** and the enols **4** and **5** (for computed optimized structures see the Supporting Information). According to our calculations, the ketone **3** turned out to be the most stable species, while the *Z*-enol (*Z*)-**4b** and the *E*-enol (*E*)-**4b** are 37.5 and 50.5 kJ mol^{-1} higher in energy, respectively.[13] Most interestingly, the isomeric enaminols (*Z*)-**4a** and (*E*)-**4a** with the hydroxy group *cis* and *trans* to N1 are even higher in energy compared to ketone **3** by as much as 57.2 and 63.3 kJ mol^{-1}, respectively.[14]

Constitutional isomerism as in the case of **4a,b** and **5a,b** (Scheme 3) cannot occur in enols derived from the carbene catalyst and benzaldehyde. When combining the triazolylidene **1** and benzaldehyde in a 1:1 molar ratio, NMR spectroscopy revealed the formation of the ketone **6** with a characteristic resonance at $\delta = 6.10$ ppm (H5) in the ^{1}H NMR spectrum and $\delta = 90.5$ ppm (C5) in the ^{13}C NMR spectrum in [D$_8$]THF (Scheme 4).[15]

Once again, treatment of keto form **6** with acid or base did not result in detectable formation of the enaminol **7a**. Nevertheless, upon addition of base (KO*t*Bu, NaH), loss of the proton resonance at $\delta = 6.10$ ppm (H5 of ketone **6**) was observed, indicating that proton abstraction is possible in this position. After base treatment and addition of two equivalents of silylating agent BSA, a complex mixture resulted, from which, however, the free carbene **1** was clearly discernible due to its carbon resonance at $\delta = 214.8$ ppm in [D$_8$]THF (in situ NMR spectroscopic experiments performed at $T = 253$–298 K). Thus far, attempts to trap a potential enolate intermediate by silylation did not result in unambiguous identification of **7b**.[16] According to our DFT calculations the enol form **7a** of the ketone **6** is disfavored by 55.2 kJ mol^{-1} ((*Z*)-**7a**) and 49.0 kJ mol^{-1} ((*E*))-**7a**) relative to the keto form.[13]

Scheme 4. Ketone **6** derived from triazolylidene **1** and benzaldehyde, enol **7a**, and silyl enol ether **7b**.

We then studied the time dependence of the reaction of propionic aldehyde **2** with the triazolylidene **1**. To this end, the triazolylidene **1***, labeled with ^{13}C at the carbene carbon C5, was employed to trace the fate of the carbene carbon atom. The course of the reaction was monitored by broadband proton-decoupled ^{13}C NMR, using the DEPTQ pulse sequence.[17] The time course of a typical experiment, using [5-^{13}C]triazolylidene **1*** and unlabeled propionic aldehyde **2** in a 1:1 molar ratio, is shown in Figure 1. When the system reaches equilibrium (92 h reaction time; trace e), the spectrum is dominated by just one species, namely the keto tautomer **3** of the Breslow intermediate ($\delta = 88.9$ ppm). Recording the spectra at shorter reaction times reveals the occurrence of an intermediate that has not yet been invoked in mechanistic discussions. Immediately after mixing of triazolylidene **1*** and propionic aldehyde **2**, the ^{13}C NMR spectrum is dominated by the signals from the free carbene **1*** ($\delta = 214.8$ ppm) and a hitherto unknown intermediate with a quaternary carbon

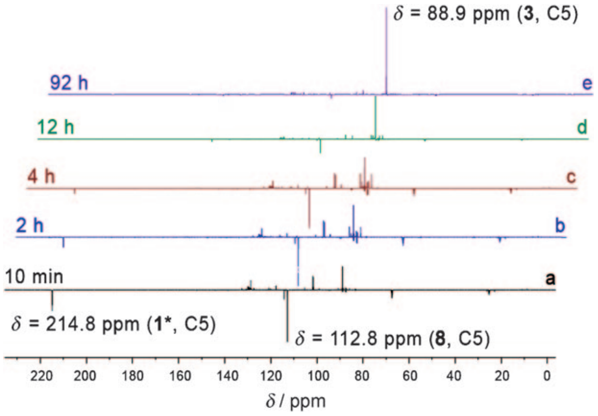


Figure 1. Multiplicity-edited ^{13}C DEPTQ NMR spectra of a reaction mixture containing [5-^{13}C]triazolylidene **1*** and unlabeled propionic aldehyde **2** in a 1:1 molar ratio, recorded at different times after mixing ([D$_8$]THF, 298 K, 150 MHz). Chemical shifts of the intensive signals caused by the labeled carbon atom are given once.

($\delta = 112.8$ ppm; Figure 1, trace a). Applying the [5-^{13}C]triazolylidene **1*** revealed the expected C–H/C couplings and thus additionally confirmed the chemical shift assignments of the ketone **3**: $\delta = 5.62$ ppm (d, $^1J_{CH} = 156.8$ Hz, H5) and $\delta = 208.0$ ppm (d, $^1J_{CC} = 49.2$ Hz, C=O).

Upon analyzing the system under conditions that closely resemble catalytic conditions, that is, in a 10:1 molar ratio of aldehyde to carbene, the carbene was exclusively converted into the species having the quaternary carbon resonance at $\delta = 112.8$ ppm (for spectra, see the Supporting Information). No further transformation to the keto form **3** of the Breslow intermediate was observed under these conditions. In other words, the newly found species (with $\delta = 112.8$ ppm) is not the thermodynamic minimum of the 1:1 carbene–aldehyde system, but it represents the resting state of the system under catalytic conditions, that is, in the presence of large excess of the carbonyl component with respect to the triazolylidene catalyst. The question then arises as to the identity of the structure of this new species with a quaternary carbon resonance at $\delta = 112.8$ ppm.

We reasoned that a signal from a quaternary carbon atom at about 110 ppm points to an orthoamide-like structure.[18] Based on 2D correlation NMR experiments, we propose structure **8**, a spirocyclic orthoamide and 1,3-dioxolane, for this newly found resting state of the catalytic system (Figure 2; for spectra, see the Supporting Information). Its formation can be explained by the addition of a second molecule of aldehyde **2** to the initial zwitterionic carbene–aldehyde adduct **9** (Scheme 5).

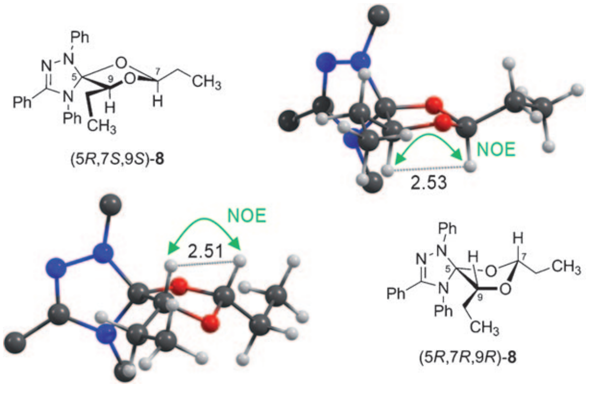
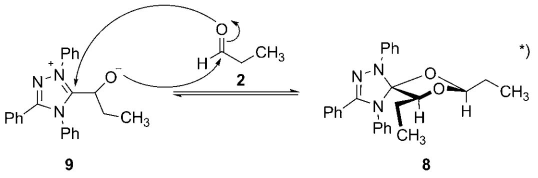


Figure 2. Computed optimized structures of the *cis* isomers of the 5*R* series of possible diastereomers of **8**. Phenyl groups are drawn as single carbon atoms for clarity. H,H distances are given in [Å]. *Trans* isomers are not shown (see the Supporting Information).



*) racemic mixture

Scheme 5. Reversible formation of spirocyclic dioxolane *rac*-**8**.

The composition of the new intermediate *rac*-**8** is further supported by a strong signal at *m*/*z* 414 in the ESI-MS spectrum of the reaction mixture.[19]

In principle, spirocycle **8** can exist as four diastereomeric pairs of enantiomers. However, according to our in situ NMR spectroscopic analysis, only one diastereomeric form is produced exclusively. To aid the assignment of relative configuration by NMR, we undertook a configurational analysis of the spiro-dioxolanes **8** with DFT methods.

From the optimized geometries of the series of diastereomers with 5*R* configuration of the spirocenter (arbitrarily assigned), we obtained the dioxolane H,H distances, which are significantly shorter in the *cis* isomers (2.53 and 2.51 Å; Figure 2) compared to the *trans* isomers (3.74 and 3.75 Å; see the Supporting Information). Based on the strong NOE between the protons H7 and H9 (1D NOE experiments[12]), a *cis* configuration was assigned to the spirocycle **8**. In the *trans* isomers, no NOEs are expected, as the distance between the interacting nuclei is almost 4 Å.

We also calculated ^{1}H and ^{13}C NMR chemical shifts for the isomers of **8** with DFT using the GIAO method (Table 1). For the *cis*-(5*R*,7*R*,9*R*) isomer, the proton H7 is expected to appear approximately 1.2 ppm downfield compared to proton H9, which was not observed experimentally. Therefore, we reason that the *cis*-(5*R*,7*S*,9*S*) diastereomer of **8** is exclusively formed under the reaction conditions (as a racemic mixture). This assumption is further supported by the free relative energies obtained from our DFT calculations, which indicate that (5*R*,7*S*,9*S*)-**8** is the most stable diastereomer of the 5*R* series (Table 2).

Table 1: Selected experimental and computed ^{1}H and ^{13}C NMR chemical shifts for possible diastereomers of dioxolane **8**.[13]

	δ_{exp}[a] [ppm]	*cis*[b] 5*R*,7*R*,9*R*	*cis*[b] 5*R*,7*S*,9*S*	*trans*[b] 5*R*,7*R*,9*S*	*trans*[b] 5*R*,7*S*,9*R*
C5	112.8	119.8	119.2	121.1	120.8
C7	105.3	110.2	110.9	114.8	113.0
C9	83.3	84.5	89.8	86.9	80.0
H7	4.45	5.49	4.16	5.25	4.67
H9	4.15	4.33	4.19	4.24	4.39

[a] Measured in [D$_8$]THF (600 MHz, 298 K). [b] Computed NMR chemical shifts δ_{DFT} in ppm (GIAO-DFT).

Table 2: Relative free energies of the possible diastereomers of **8**.[13]

	cis 5*R*,7*R*,9*R*	*cis* 5*R*,7*S*,9*S*	*trans* 5*R*,7*R*,9*S*	*trans* 5*R*,7*S*,9*R*
ΔG[a]	+1.8	0.0[b]	+8.3	+7.6

[a] kJ mol^{-1}. [b] Taken as the zero point.

For a deeper insight into the formation of the dioxolane intermediate **8**, this reaction step was analyzed using DFT methods. Figure 3 shows the structures at the calculated stationary points involved in the formation of dioxolane (5*R*,7*S*,9*S*)-**8** and their relative free energies. Together with the zwitterionic adduct of triazolylidene **1** and propionic

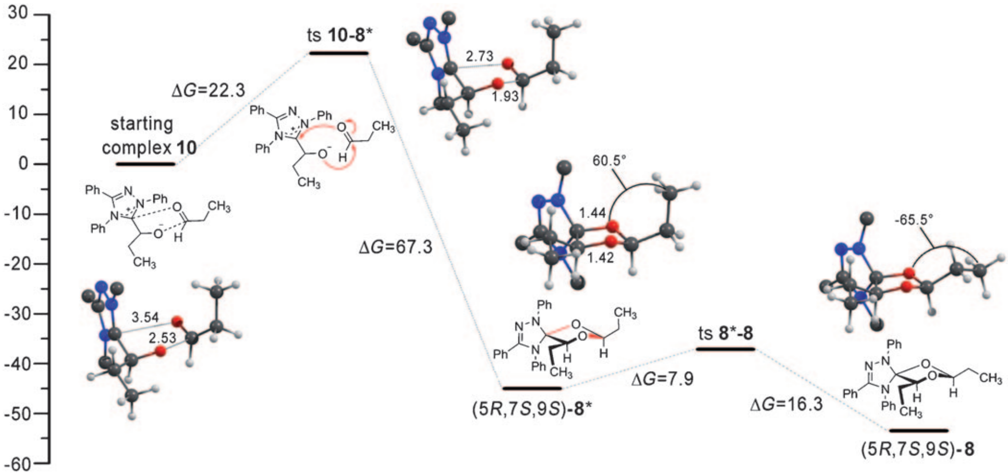


Figure 3. Relative free energies (ΔG, in kJ mol^{-1}) of the stationary points involved in the formation of dioxolane (5*R*,7*S*,9*S*)-**8**.[13] Phenyl groups are drawn as single carbon atoms for clarity. Selected bond lengths are given in [Å] and dihedral angles in [°].

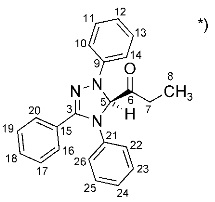
aldehyde **2**, a second molecule of aldehyde **2** forms the starting complex **10**. Our calculations indicate that the nucleophilic attack of the zwitterion on the carbonyl carbon atom of the second aldehyde **2** and the attack of the carbonyl oxygen atom at atom C5 of the triazolium proceed in a concerted but asynchronous manner. Overall, the ring formation requires an activation energy of 22.3 kJ mol^{-1} and should therefore proceed readily at room temperature, at which the reaction was followed by NMR spectroscopy. The spirocyclic dioxolane (5*R*,7*S*,9*S*)-**8*** formed is a rotational isomer with respect to the ethyl group compared to the minimum structure (5*R*,7*S*,9*S*)-**8** (see the Supporting Information). The energy barrier for the interconversion of these two rotamers is very small (7.9 kJ mol^{-1}).

Upon using [5-^{13}C]triazolylidene **1*** and propionic aldehyde **2** in a 1:1 molar ratio, we observed further transformation of the initially formed dioxolane **8** to the keto form **3** (Figure 1), which indicates that the dioxolane formation is reversible. The activation energy for the reverse reaction is calculated to be 67.3 kJ mol^{-1}. Thus, the cleavage of the spirocyclic ring and the release of the second aldehyde molecule **2** to regenerate the initial adduct **9** is feasible under the reaction conditions (room temperature).

In summary, we have discovered novel features of the mechanism of benzoin-type condensations.[8] Under catalytic conditions (i.e. excess of aldehyde substrate with respect to carbene catalyst), the spirocyclic orthoamide **8** turned out to be the resting state of the catalytic system for aliphatic aldehydes. Retro-cleavage of the spirocycle **8** affords the keto form **3** of the Breslow adduct, which represents the thermodynamic minimum of the 1:1 carbene–aldehyde system. The sluggish reactivity of aliphatic aldehydes in carbene-catalyzed Umpolung reactions can be attributed to the following effects: 1) aliphatic aldehydes form a spiro-dioxolane as the resting state of the catalytic system. Retro-cleavage of this 1:2 carbene–aldehyde adduct is necessary for entering the catalytic cycle. 2) In the proton abstraction from competing α-positions of the keto form of the Breslow adduct, enaminol formation is disfavored.

Experimental Section

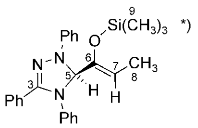
All reactions were performed under inert gas atmosphere using Schlenk and glovebox techniques. THF was dried over Na/benzophenone and distilled prior to use. NMR spectra were recorded on a Bruker Avance II 600 instrument (^{1}H: 600.20 MHz, ^{13}C: 150.92 MHz) except for 1D NOE spectra, which were obtained on a Bruker DRX 500 instrument (^{1}H: 500.13 MHz, ^{13}C: 125.76 MHz). Spectra were recorded at room temperature unless otherwise stated. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS).



3

*) racemic mixture

3: Triazolylidene **1** (500 mg; 1.7 mmol, 1.0 equiv) was dissolved in THF (10 mL) and propionic aldehyde **2** (147 μL; 2.0 mmol, 1.2 equiv) was added. The reaction mixture was stirred at room temperature for 60 h. The solvent was removed in vacuo and ketone **3** was isolated by column chromatography on silica gel (dichloromethane, $R_f = 0.75$) as a yellow oil. Yield: 305 mg (51%). ESI-MS: *m/z* 354 $[M-H_2+H]^+$, 356 $[M+H]^+$, 378 $[M+Na]^+$; HR-ESI-MS: exact mass for $C_{23}H_{21}N_3O_5H$ $[M+H]^+$: 356.1763, found: 356.176 ($\Delta u = 0.0015$); ^{1}H NMR (600 MHz, [D$_8$]THF): $\delta = 7.63$ (d, $^3J_{HH} = 6.8$ Hz, 2H; H16–H20), 7.32 (m, 3H), 7.22 (m, 4H), 7.09 (t, $^3J_{HH} = 7.3$ Hz, 1H; H24), 7.02 (d, $^3J_{HH} = 7.3$ Hz, 2H; H10–H14), 6.95 (d, $^3J_{HH} = 7.3$ Hz, 2H; H22–H26), 6.81 (t, $^3J_{HH} = 7.3$ Hz, 1H; H12), 5.62 (s, 1H; H5), 2.80 (dq, $^2J_{HH} = 18.4$, $^3J_{HH} = 7.4$ Hz, 1H; H7), 2.57 (dq, $^2J_{HH} = 18.4$, $^3J_{HH} = 7.4$ Hz, 1H; H7), 0.99 ppm (dd (“t”), $^3J_{HH} = {}^3J_{HH} = 7.4$ Hz, 3H; H8); ^{13}C NMR (150 MHz, [D$_8$]THF): $\delta = 208.0$ (1C; C6), 149.2 (1C; C3), 145.4 (1C; C9), 143.8 (1C; C21), 130.4 (1C; C18), 130.0 (2C; C11–C13), 129.9 (2C; C23–C25), 129.6 (2C; C17–C19), 129.1 (1C; C15), 128.5 (2C; C16–C20), 126.1 (1C; C24), 124.7 (2C; C22–C26), 120.5 (1C; C12), 113.4 (2C; C10–C14), 88.9 (1C; C5), 29.7 (1C; C7), 7.5 ppm (1C; C8); FT-IR (ATR): $\tilde{\nu} = 3058$ (w), 3030 (w), 2976 (w), 2935 (w), 2354 (w), 1718 (s), 1594 (s), 1491 (s), 1446 (m), 1398 (m), 1345 (s), 1286 (m), 1249 (m), 1177 (w), 1144 (m), 1099 (w), 1066 (m), 1031 (m), 904 (w), 763 (s), 748 (s), 692 cm^{-1} (s).

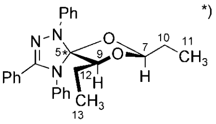


(*Z*)-**5b**

*) racemic mixture

(*Z*)-**5b**: Ketone **3** was dissolved in [D$_8$]THF in the glovebox and 0.2 equiv of NaH were added. The mixture was stirred for 4 h and then transferred to a NMR tube. After addition of 2.0 equiv of BSA, the NMR tube was sealed under rigorous exclusion of oxygen. ^{1}H NMR (600 MHz, [D$_8$]THF): $\delta = 7.58$–7.55 (m, 2H; H$_{arom}$), 7.29–7.20 (m, 10H; H$_{arom}$), 7.12–7.08 (m, 1H; H$_{arom}$), 7.07–7.04 (m, 2H, H$_{arom}$), 5.72 (s, 1H; H5), 5.17 (q, $^3J_{HH} = 6.8$ Hz, 1H; H7), 1.63 (d, $^3J_{HH} = 6.8$ Hz, 3H; H8), 0.06 ppm (s, 9H; H9); ^{13}C NMR (150 MHz, [D$_8$]THF): $\delta = 149.5$ (1C; C6), 149.0 (1C; C3), 147.0 (1C;

C_{arom}), 143.8 (1C; C_{arom}), 129.9 (1C; C_{arom}), 129.7 (1C; CH_{arom}), 129.5 (2C; CH_{arom}), 129.4 (2C; CH_{arom}), 128.9 (2C; CH_{arom}), 128.5 (2C; CH_{arom}), 126.1 (2C; CH_{arom}), 125.9 (1C; CH_{arom}), 119.6 (1C; CH_{arom}), 113.9 (2C; CH_{arom}), 108.7 (1C; C7), 88.6 (1C; C5), 11.3 (1C; C8), 0.9 ppm (3C; C9).



8

*) racemic mixture

8: NMR tubes were charged with 0.1 equiv of labeled triazolylidene **1*** in [D$_8$]THF in a glovebox and sealed with a septum. 1.0 equiv of propionic aldehyde **2** was added with a syringe and the reaction was followed by NMR. ^{1}H NMR (600 MHz, [D$_8$]THF): $\delta = 4.45$ (t, $^3J_{HH} = 5.5$ Hz, 1H; H7), 4.15 (dt, $^3J_{HH} = 7.2$ (t), $^2J_{CH} = 1.8$ Hz (d), 1H; H9), 1.98 (m, 2H; H12), 1.68 (m, 2H; H10), 1.07 (t, $^3J_{HH} = 7.5$ Hz, 3H; H13), 0.86 ppm (t, $^3J_{HH} = 7.6$ Hz, 3H, H11); ^{13}C NMR (150 MHz, [D$_8$]THF): $\delta = 112.8$ (1C; C5), 105.3 (1C; C7), 83.3 (dispersion signal, 1C; C9), 26.3 (1C; C10), 22.6 (1C; C12), 11.0 (1C; C13), 8.8 ppm (1C; C11). When the experiment is carried out with non-labeled carbene **1**, proton H9 appears as simple triplet (owing to non-detectable $^2J_{CH}$ coupling). Aromatic resonances could not be assigned with certainty.

Computational details and references are included in the Supporting Information.

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Keywords: carbenes · NMR spectroscopy · organocatalysis · reaction mechanisms · umpolung

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[1] a) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, **2005**. For selected reviews, see: b) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606–5655; c) N. Marion, S. Diez-Gonzalez, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046–3058; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988–3000; d) D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534–541.

[2] For selected reviews, see: a) D. Bourissou, O. Guerret, F. P. Gabbaï, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39–91; b) W. A. Herrmann, *Angew. Chem.* **2002**, *114*, 1342–1363; *Angew. Chem. Int. Ed.* **2002**, *41*, 1290–1309.

[3] D. Seebach, *Angew. Chem.* **1979**, *91*, 259–278; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239–258.

[4] T. Ukai, R. Tanaka, T. Dokawa, *J. Pharm. Soc. Jpn.* **1943**, *63*, 296–300 (*Chem. Abstr.* **1951**, *45*, 5148).

[5] H. Stetter, R. Y. Rämsch, H. Kuhlmann, *Synthesis* **1976**, 733–735.

[6] Selected recent examples and surveys: a) D. Enders, J. Han, A. Henseler, *Chem. Commun.* **2008**, 3989–3991; b) D. Enders, O. Niemeier, T. Balensiefer, *Angew. Chem.* **2006**, *118*, 1491–1495; *Angew. Chem. Int. Ed.* **2006**, *45*, 1463–1467; c) J. Read deAlaniz, T. Rovis, *Synlett* **2009**, 1189–1207; d) J. Read deAlaniz, M. S. Kerr, J. L. Moore, *J. Org. Chem.* **2008**, *73*, 2033–2040; e) V. Nair, C. R. Sinu, B. P. Babu, V. Varghese, A. Jose, E. Suresh, *Org. Lett.* **2009**, *11*, 5570–5573; f) V. Nair, S. Vellalath, B. P. Babu, *Chem. Soc. Rev.* **2008**, *37*, 2691–2698; g) K. Hirano, A. T. Biju, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 14190–14191; h) C. Burstein, S. Tschan, X. Xie, F. Glorius, *Synthesis* **2006**, 2418–2439; i) Y. Kawanaka, E. M. Phillips, K. A. Scheidt, *J. Am. Chem. Soc.* **2009**, *131*, 18028–18029; j) B. E. Maki, A. Chan, E. M. Phillips, K. A. Scheidt, *Tetrahedron* **2009**, *65*, 3102–3109; k) P.-C. Chiang, Y. Kim, J. W. Bode, *Chem. Commun.* **2009**, 4566–4568; l) P.-C. Chiang, M. Rommel, J. W. Bode, *J. Am. Chem. Soc.* **2009**, *131*, 8714–8718.

[7] J. H. Teles, J.-P. Melder, K. Ebel, R. Schneider, E. Gehrer, W. Harder, S. Brode, D. Enders, K. Breuer, G. Raabe, *Helv. Chim. Acta* **1996**, *79*, 61–83.

[8] R. Breslow, *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726.

[9] a) R. Breslow, R. Kim, *Tetrahedron Lett.* **1994**, *35*, 699–702; b) Y.-T. Chen, G. L. Barletta, K. Haghjoo, J. T. Cheng, F. Jordan, *J. Org. Chem.* **1994**, *59*, 7714–7722; c) M. J. White, F. J. Leeper, *J. Org. Chem.* **2001**, *66*, 5124–5131.

[10] W. Schrader, P. P. Handayani, C. Burstein, F. Glorius, *Chem. Commun.* **2007**, 716–718.

[11] D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J.-P. Melder, K. Ebel, S. Brode, *Angew. Chem.* **1995**, *107*, 1119–1122; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1021–1023.

[12] K. Stott, J. Keeler, Q. N. Van, A. J. Shaka, *J. Magn. Reson.* **1997**, *125*, 302–324.

[13] Gibbs free energies at 298 K in the gas phase.

[14] The same order in energy was found for the four corresponding silyl enol ethers (*Z*)-**5b**, (*E*)-**5b**, (*Z*)-**5a**, and (*E*)-**5a** (see the Supporting Information).

[15] B. Alcaide, G. Escobar, R. Perez-Ossorio, J. Plumet, *Anal. Quim. Ser. C* **1985**, *81*, 85–87.

[16] For an alternative approach to the silylated enaminol form, resulting in decomposition, see: a) A. E. Mattson, A. R. Bharadwaj, A. M. Zuhl, K. A. Scheidt, *J. Org. Chem.* **2006**, *71*, 5715–5724; b) A. E. Mattson, K. A. Scheidt, *Org. Lett.* **2004**, *6*, 4363–4366.

[17] P. Bigler, R. Kümmerle, W. Bermel, *Magn. Reson. Chem.* **2007**, *45*, 469–472.

[18] I. Wawer, J. Osek, *J. Chem. Soc. Perkin Trans. 2* **1985**, 1669–1671.

[19] *m*/*z* 414 could also be assigned to an intermediate later in the catalytic cycle (analogous to **VI**, Scheme 1), but such a structure would not match the quarternary carbon resonance at $\delta = 112.8$ ppm observed for the labeled [5-^{13}C] atom in the ^{13}C NMR spectra.