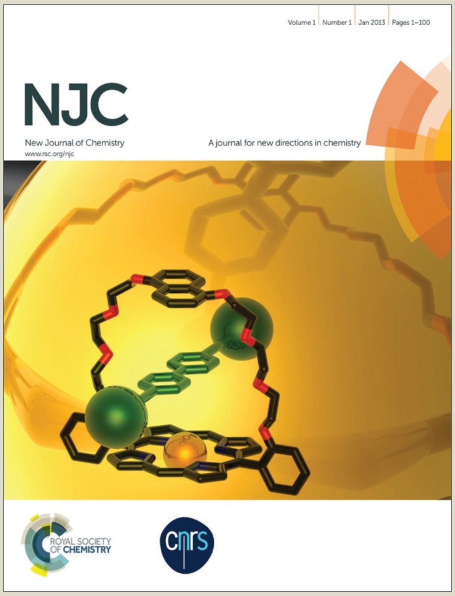
NJC



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/njc

Journal Name

RSCPublishing

ARTICLE

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

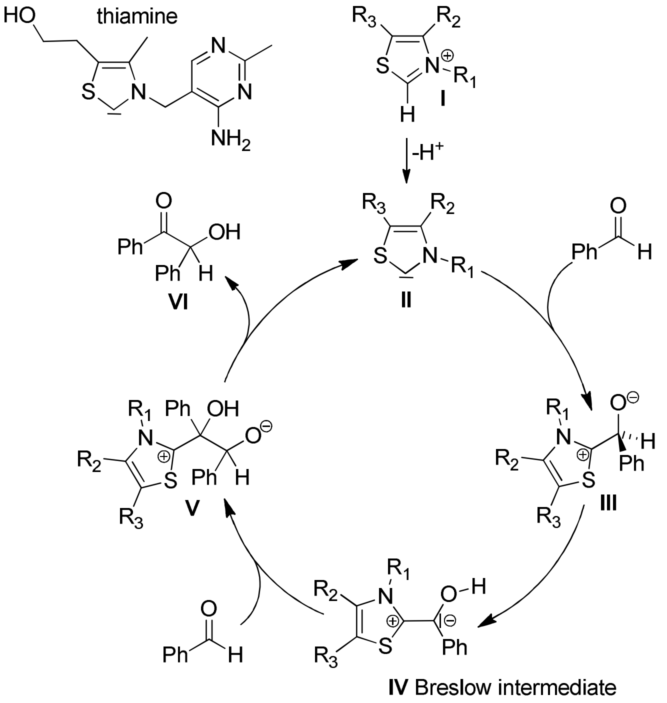
Quantifying N-heterocyclic Carbenes as Umpolung Catalysts in the Benzoin Reaction: Balance between Nucleophilicity and Electrophilicity

Maria Schumacher[a] and Bernd Goldfuss[a]

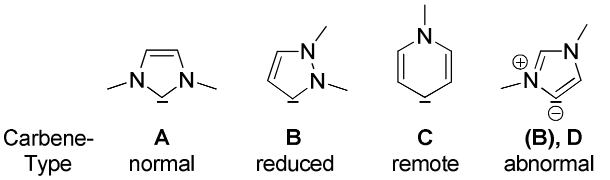
Different types of N-heterocyclic carbenes, i.e. normal, reduced heteroatom stabilized, remote and abnormal carbenes, are computationally studied (THF-CPCM-B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)) in the benzoin reaction to assess their characteristics as umpolung catalysts. Two general trends are apparent with an increasing number of nitrogen atoms in the heterocycles: a) the tendency for the initial addition of the carbenes to the aldehyde decreases, due to decreased nucleophilicity; b) during the umpolung step, the developing negative charge in the Breslow intermediates becomes better stabilized by conjugation with the adjacent, more electrophilic carbene carbon atoms. Relative to the starting reactants, the free energies for the intermediates and the transition structures decrease with more remote positions of the nitrogen atoms to the carbene carbon atoms. Among the normal N-heterocyclic carbenes oxazole-2-ylidene shows the lowest activation barrier for the rate determining umpolung step (E_a = 25.2 kcal mol^{-1}) in the benzoin reaction. The comparison of all computed carbenes points to remote and abnormal pyridyl-3-ylidene as catalyst with the lowest activation energy (E_a = 24.0 kcal mol^{-1}). This abnormal carbene exhibits the best balance between nucleophilic and electrophilic characteristics in the benzoin reaction.

Introduction

N-heterocyclic carbenes (NHCs) are widely employed as ligands and catalysts.[1] An especially prominent application field of such carbenes is umpolung catalysis,[2] used e.g. for C-C couplings, such as the benzoin reaction.[3,4] The ancestor cyanide-catalysed coupling of benzaldehyde to afford benzoin was discovered by Wöhler and Liebig as early as 1832.[5] In this remarkable reaction, a C-C-bond between two inherently electrophilic carbon atoms of the carbonyl groups is formed via umpolung of a formyl function.[6] Lapworth first proposed a stabilized α-hydroxyl carbanion[7] as key intermediate of this reaction. In 1943 Ukai et al. found that thiazolium salts catalyse the benzoin reaction as well.[8] The commonly accepted mechanism has been proposed by Breslow,[9] based on studies of model systems of biochemical reactions catalyzed by thiamine (vitamin B_1, Scheme 1). Deprotonation of the thiazolium salt (**I**) forms the catalytically active carbene (**II**), which adds to an aldehyde to give an oxyanion (**III**). A proton transfer leads to the Breslow intermediate (**IV**)[10], which adds to a second equivalent of aldehyde (**V**). After a further proton transfer, the benzoin product (**VI**) is eliminated and the carbene catalyst (**II**) can re-enter another cycle. Experimentally studies of the kinetics of the benzoin reaction by Leeper et al. showed that the addition of the catalyst to a benzaldehyde molecule, the deprotonation and the addition to a second aldehyde molecule and the following elimination of the catalyst are partially rate-determining.[11] With the introduction of carbenes to the benzoin reaction, the scope of the reaction could be extended to enantioselective acyloin type couplings[12] with an even broader range of substrates[3], particularly the Stetter reaction.[4] Since then, carbenes have been the dominant catalysts in enantioselective umpolung reactions, supplemented by lithio phosphonates as alternative umpolung catalysts for enantioselective acyloin couplings with acylsilanes.[13] Computational assessments of thermodynamic and kinetic characteristics for umpolung steps of aldehyde and acylsilane substrates show that the nucleophilic carbene is by far the strongest umpolung catalyst for the formation of the Breslow intermediate.[14] Nucleophilic N-heterocyclic carbenes (NHCs) can be differentiated in normal heterocyclic carbenes **A**, reduced heteroatom stabilized carbenes **B**[15], remote carbenes **C** and abnormal carbenes **D**[16] (Scheme 2). From the normal heterocyclic carbenes **A**, where the carbene carbon atom is bonded to two heteroatoms, the number of adjacent heteroatoms decreases to one in reduced heteroatom stabilized carbenes **B** and to remote carbenes **C**, which do not have any heteroatom adjacent to the carbene carbon atom.

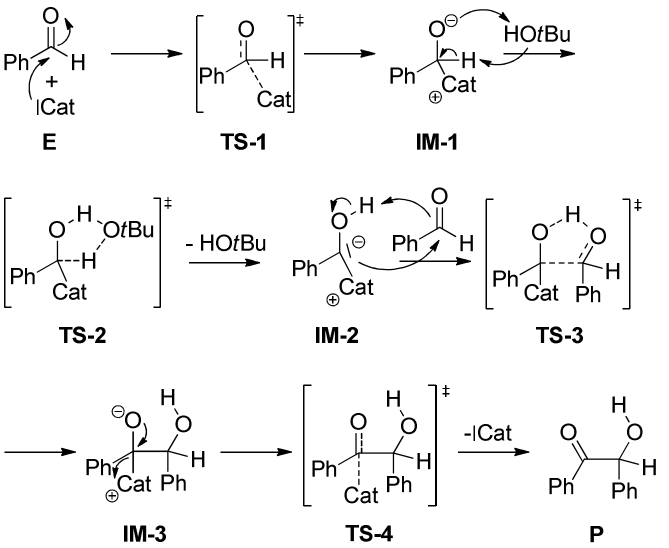


Scheme 1 Catalytic cycle of the benzoin reaction proposed by Breslow, based on studies of biochemical reactions catalyzed by thiamine.



Scheme 2 Types of N-heterocyclic carbenes (NHC): normal **A**, reduced nitrogen atom stabilized **B** (CAAC), remote **C**, abnormal **D**.

The adjacent heteroatoms significantly stabilize the singlet ground state, due to their σ-accepting and π-donating characteristics.[17] A direct consequence of the remote heteroatom position is the weaker stabilization of the free carbene caused by the lower electronegativity of the carbon atom compared to the nitrogen atom and the resulting lower electron withdrawing effect. Furthermore no π-donation into the empty p_z-orbital of the carbene carbon atom occurs.[17g] This leads to more nucleophilic, but also to more electrophilic carbenes. While often requiring the metal carbene complexes,[18] these carbenes are strong donating ligands. Abnormal carbenes **D** (Scheme 2) are compounds that cannot be described by a canonical structure without charges.[19] The immense number of known NHCs includes a catalyst for every given problem. Both electronic and steric factors play a role in the stabilization of carbenes.[20] A comparative assessment of the electronic factor, reflected in the skeletal structures of NHCs, is conducive for the catalyst design. To identify the most efficient type of carbene as umpolung catalyst for the C-C-coupling reactions, we investigated carbenes of type **A**-**D** (Scheme 2) in the elementary reaction steps of a model benzoin reaction (Scheme 3), which is archetypical for these umpolung reactions.



Scheme 3 Model benzoin reaction for computational comparative analyses of different carbenes (**1**-**19**) (THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), results see Tables 1-5).

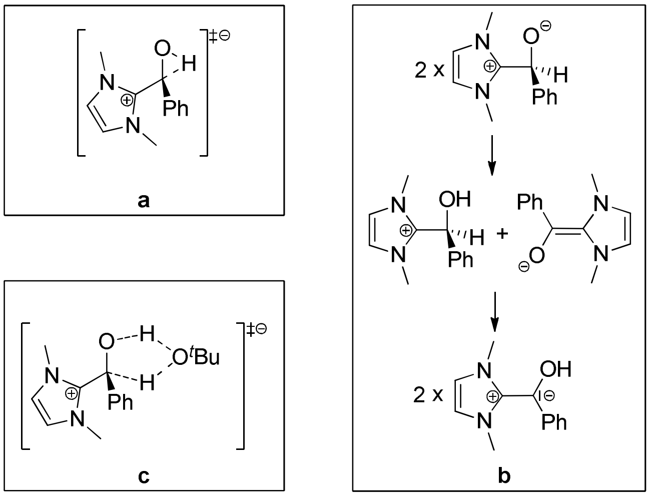
Results and Discussion

A suitable catalyst for the umpolung of aldehydes in the benzoin reaction needs nucleophilic reactivity[21] for the addition to benzaldehyde (**IM-1** via **TS-1**, Scheme 3) as well as electrophilic properties to stabilize the adjacent negative charge in the umpoled aldehyde (**IM-2** via **TS-2**, Scheme 3). Competitive pathways for the proton transfer of the umpolung (**TS-2**, Scheme 3) are the 1,2-H-shift[14] (**a**, Scheme 4), an intermolecular proton transfer between two carbene/aldehyde coupled intermediates[22] (**b**, Scheme 4) and the proton transfer assisted by a corresponding acid (**c**, Scheme 4).[22b,23] We regard the latter mechanism for the umpolung as most feasible due to the work of Xue et al.[22b] Here *t*-BuOH is present in the reaction due to the deprotonation of the salt precatalyst with *t*-BuOK.

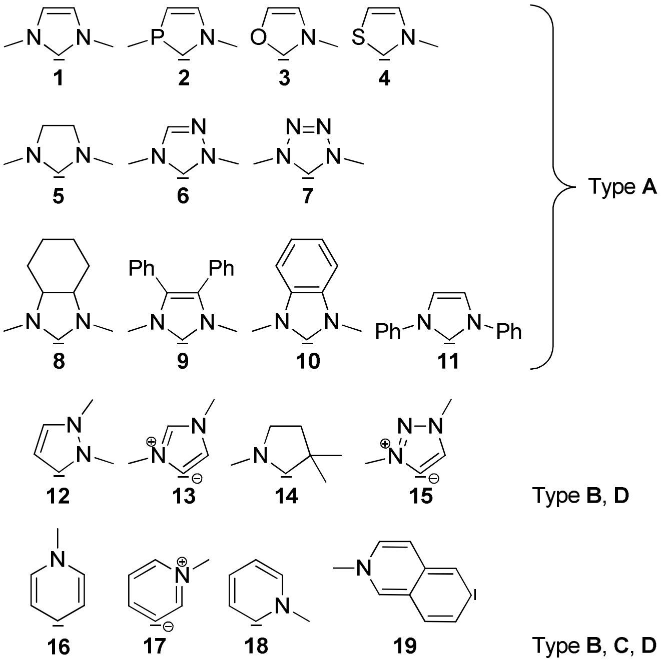
Normal NHCs of type **A** in catalytic acyloin reactions are typically derived from imidazolium or triazolium salts.[3,4] Thus we started our investigations based on imidazole-2-ylidene **1** (Scheme 5).

Different heteroatoms

To investigate the influence of different heteroatoms, carbenes **1**-**4** of type **A** (imidazole-2- **1**, phosphazole-2- **2**, oxazole-2- **3** and thiazole-2-ylidene **4**, Scheme 2 and 5) were chosen. The results of the calculation are depicted in Figure 1 and Table 1.



Scheme 4 Competitive mechanism for the proton transfer of the umpolung step: **a** 1,2-H-shift, **b** intermolecular proton transfer between two carbene/aldehyde coupled intermediates, **c** assisted by a corresponding acid.



Scheme 5 Carbenes of the types **A**-**D** (cf. Scheme 2) studied in the benzoin reaction.

The addition of the carbene to benzaldehyde (**TS-1**, Scheme 3) is favored for phosphazole-2-ylidene **2** (ΔG_{TS-1} = 19.3 kcal mol^{-1}) directly followed by imidazole-2-ylidene **1** (ΔG_{TS-1} = 20.3 kcal mol^{-1}). The relative free energy is slightly higher for oxazole-2- **3** and thiazole-2-ylidene **4** (both ΔG_{TS-1} = 21.5 kcal mol^{-1}). Imidazole-2-ylidene **1** bears two nitrogen atoms with a planar environment which features a σ-electron withdrawing and a π-donating effect. Phosphazole-2-ylidene **2** features a nitrogen atom with planar environment and a phosphorus atom with pyramidal environment which indicates, that only nitrogen is a π-donor.[16] As phosphorus is more electropositive than nitrogen, the donor property of the phosphazole-2-ylidene **2** is superior to imidazole-2-ylidene **1**.

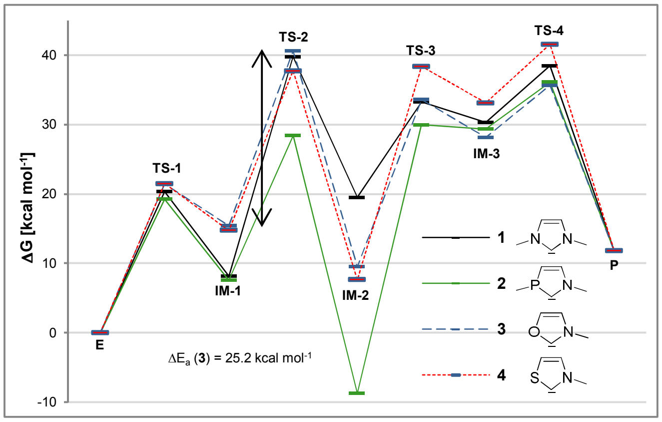


Figure 1 Umpolung of benzaldehyde catalysed by carbenes of Type **A** (Scheme 2) containing different heteroatoms **1**-**4**. (THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), relative free energies referring to isolated reactants). The lowest overall energy difference $\Delta E_{overall}$ is observed for imidazole-2-ylidene **1**.

Table 1 Relative free energies (kcal mol^{-1}) for the benzoin reaction catalysed by carbenes of Type **A** (Scheme 2) containing different heteroatoms **1**-**4** according to Scheme 5.[a]

ΔG[b].	E	TS-1	IM-1	TS-2	IM-2	TS-3	IM-3	TS-4	P .
1	0	20.3	8.1	39.8	19.5	33.3	30.3	38.5	11.8
2	0	19.3	7.6	28.4	-8.7	30.0	29.4	36.1	11.8
3	0	21.5	15.4	40.6	9.5	33.6	28.2	35.7	11.8
4	0	21.5	14.7	37.7	7.6	38.4	33.1	41.6	11.8

a THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d) with ZPE correction, scaled by 0.9806, energies in kcal mol^{-1}; b T = 298.15 K, P = 1.01325$\cdot 10^{5}$ Pa.

Nyulászi et al. showed that heteroatoms have a decreasing stabilization effect on carbenes in the order N > O > S as well as decreased delocalisation of π-electrons in the order N > S > O.[24] Sulfur is also more electropositive than oxygen, hence thiazole-2-ylidene **4** is a stronger donor. The adduct of phosphazole-2-ylidene **2** and benzaldehyde (**IM-1**, Scheme 3) is most favored (ΔG_{IM-1} = 7.6 kcal mol^{-1}) directly followed by imidazole-2-ylidene **1** (ΔG_{IM-1} = 8.1 kcal mol^{-1}) and about 6 kcal mol^{-1} more favored compared to the other carbenes (ΔG_{IM-1} (**4**) = 14.7 kcal mol^{-1}, ΔG_{IM-1} (**3**) = 15.4 kcal mol^{-1}). Phosphazole-2-ylidene **2** has the lowest relative free energy for the transition state of the umpolung (**TS-2**, Scheme 3, ΔG_{TS-2} = 28.4 kcal mol^{-1}), which is 9.3 kcal mol^{-1} lower than the relative free energy with thiazole-2-ylidene **4** (ΔG_{TS-2} = 37.7 kcal mol^{-1}) followed by imidazole-2- **1** and oxazole-2-ylidene **3** (ΔG_{TS-2} (**1**) = 39.8 kcal mol^{-1}, ΔG_{TS-2} (**3**) = 40.6 kcal mol^{-1}). The low relative free energy for the umpolung (ΔG_{TS-2}) with phosphazole-2-ylidene **2** leads to an exergonic Breslow intermediate **IM-2** (Scheme 3, ΔG_{IM-2} = -8.7 kcal mol^{-1}). The phosphorus atom does hardly transfer π-electron density to the carbene carbon atom[16], due to its high s-lone pair character[25] which is apparent from its pyramidal environment (angle sum = 291.8°, Figure 2). Hence the negative charge of the d^{1}-species can be better stabilized by conjugation, which is reflected in the shorter C-C bond (1.361 Å, Figure 2). Similar, sulphur and oxygen in the heterocyclic ring cause a higher electrophilicity of the carbene carbon atom.

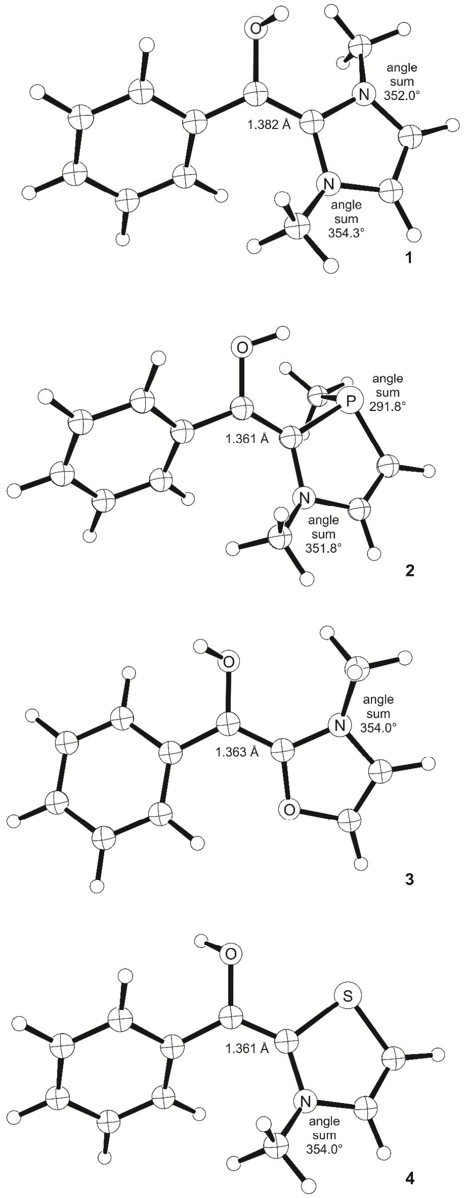


Figure 2 Breslow intermediates **IM-2** of benzaldehyde with imidazole-2- **1**, phosphazole-2- **2**, oxazole-2- **3** and thiazole-2-ylidene **4**.

Hence the Breslow intermediate is more stabilized due to the strong conjugation with the carbene carbon atom (C-C bond: **3**: 1.363 Å, **4**: 1.361 Å, Figure 2) compared to imidazole-2-ylidene **1** (C-C-bond: 1.382 Å, Figure 2; ΔG_{IM-2} (**4**) = 7.6 kcal mol^{-1}, ΔG_{IM-2} (**3**) = 9.5 kcal mol^{-1}, ΔG_{IM-2} (**1**) = 19.5 kcal mol^{-1}). The more stabilized the Breslow intermediate **IM-2** (Scheme 3), the higher the activation energy for the addition of the Breslow intermediate to benzaldehyde (**TS-3**, Scheme 3). Nevertheless the addition is most favored for phosphazole-2-ylidene **2** (ΔG_{TS-3} = 30.0 kcal mol^{-1}) and for imidazole-2- **1** and oxazole-2-ylidene **3** (ΔG_{TS-3} (**1**) = 33.3 kcal mol^{-1}, ΔG_{TS-3} (**3**) = 33.6 kcal mol^{-1}). Only thiazole-2-ylidene **4** has a higher relative free transition state energy (ΔG_{TS-3} = 38.4 kcal mol^{-1}). The following intermediate **IM-3** (Scheme 3) is most favored for oxazole-2- **3** and phosphazole-2-ylidene **2** (ΔG_{IM-3} (**3**) = 28.2 kcal mol^{-1}, ΔG_{IM-3} (**2**) = 29.4 kcal mol^{-1}), followed by imidazole-2- **1** and thiazole-2-ylidene **4** (ΔG_{IM-3} (**1**) = 30.3 kcal mol^{-1}, ΔG_{IM-3} (**4**) = 33.1 kcal mol^{-1}). The recovery of the catalyst and product formation (**TS-4**, Scheme 3) is most favored for oxazole-2- **3** and phosphazole-2-ylidene **2** (ΔG_{TS-4} (**3**) = 35.7 kcal mol^{-1}, ΔG_{TS-4} (**2**) = 36.1 kcal mol^{-1}). The recovery of imidazole-2-ylidene **1** has a slightly higher free energy (ΔG_{TS-4} = 38.5 kcal mol^{-1}) and is followed by thiazole-2-ylidene **4** (ΔG_{TS-4} = 41.6 kcal mol^{-1}). The lowest activation energy for the rate-determining step the is found for oxazole-2-ylidene **3** (E_a = 25.2 kcal mol^{-1}, **IM-1** → **TS-2**) followed by thiazole-2- **4** (E_a = 30.8 kcal mol^{-1}, **IM-2** → **TS-3**) and imidazole-2-ylidene **1** (E_a = 31.7 kcal mol^{-1}, **IM-1** → **TS-2**). The low relative free energy of the Breslow intermediate **IM-2** with phosphazole-2-ylidene **2** leads to a high activation energy E_a = 38.7 kcal mol^{-1} (**IM-2** → **TS-3**).

Different numbers of nitrogen atoms

The influence of delocalisation of π-electrons and the number of nitrogen atoms in the five membered ring was then investigated with imidazole-2- **1**, imidazoline-2- **5**, 1,2,4-triazole-5- **6** and tetrazole-5-ylidene **7** (Type **A**, Scheme 2 and 5). The results of the calculation are depicted in Figure 3 and Table 2. The addition of the carbene to benzaldehyde (**TS-1**, Scheme 3) is most favored for imidazole-2-ylidene **1** (ΔG_{TS-1} = 20.3 kcal mol^{-1}). The addition of tetrazole-5-ylidene **7** is significantly higher (ΔG_{TS-1} = 25.8 kcal mol^{-1}).

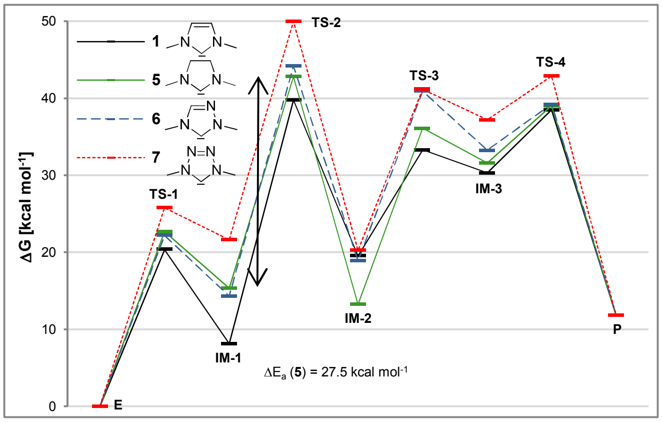


Figure 3 . Umpolung of benzaldehyde catalysed by carbenes of type **A** (Scheme 2) with a different number of nitrogen atoms **1**, **5**-**7**. (THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), relative free energies referring to isolated reactants). The lowest overall energy difference $\Delta E_{overall}$ is observed for imidazole-2-ylidene **1**.

Table 2 Relative free energies (kcal mol^{-1}) for the benzoin reaction catalysed by carbenes of Type **A** (Scheme 2) with a different number of nitrogen atoms **1**, **5**-**7** according to Scheme 5.[a]

ΔG[b].	E	TS-1	IM-1	TS-2	IM-2	TS-3	IM-3	TS-4	P .
1	0	20.3	8.1	39.8	19.5	33.3	30.3	38.5	11.8
5	0	22.7	15.3	42.8	13.2	36.1	31.6	39.0	11.8
6	0	22.2	14.3	44.2	18.9	40.9	33.3	39.2	11.8
7	0	25.8	21.6	50.0	20.2	41.2	37.2	42.9	11.8

a THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d) with ZPE correction, scaled by 0.9806, energies in kcal mol^{-1}; b T = 298.15 K, P = 1.01325·10^{5} Pa.

The presence of an unsaturated five membered ring causes increased p_z-population at the carbene carbon atom.[17] More nitrogen atoms increase the group electronegativity of this system which leads to an increasing polarisation of the bond to the carbene carbon atom. This results in a higher p character of this bond and therefore in a higher s character of the lone pair orbital, which is thus stabilized and less donating.[17g] The following intermediate **IM-1** (Scheme 3) is most stabilized by imidzole-2-ylidene **1** (ΔG_{IM-1} = 8.1 kcal mol^{-1}). The least stabilized intermediate is built with tetrazole-5-ylidene **7** (ΔG_{IM-1} = 21.6 kcal mol^{-1}). The transition state of the umpolung (**TS-2**, Scheme 3) is most favored for imidazole-2-ylidene **1** (ΔG_{TS-2} = 39.8 kcal mol^{-1}), directly followed by imidazoline-2- **5** and triazole-5-ylidene **6** (ΔG_{TS-2} (**5**) = 42.8 kcal mol^{-1}, ΔG_{TS-2} (**6**) = 44.2 kcal mol^{-1}). The relative free energy for the umpolung is significantly higher with tetrazole-5-ylidene **7** (ΔG_{TS-2} = 50.0 kcal mol^{-1}). The Breslow intermediate **IM-2** (Scheme 3) is most favored for imidazoline-2-ylidene **5** (ΔG_{IM-2} = 13.2 kcal mol^{-1}), which results in the shortest C-C bond (1.370 Å, Figure 4). The Breslow intermediates are considerably higher in energy with trizaole-2- **6**, imidazole-2- **1** and tetrazole-5-ylidene **7** (ΔG_{IM-2} (**6**) = 18.9 kcal mol^{-1}, ΔG_{IM-2} (**1**) = 19.5 kcal mol^{-1}, ΔG_{IM-2} (**7**) = 20.2 kcal mol^{-1}), accompanied with longer C-C bonds (Figure 4). The delocalization of π-electrons is decreased in the Breslow intermediates with these carbenes. Both nitrogen atoms are located next to the carbene carbon atom. N-lonepair-donation reduces the electrophilicity of the carbene carbon atom. The pyramidality of the nitrogen atoms, given as angle sum, provides a measure for lone pair-conjugation. The higher the angle sum is, the more planar is the nitrogen atom.[22a] The resulting conjugation occurs via p_z orbital and is so much stronger. The lower the angle sum is, the weaker is the conjugation coming from the sp^3 orbital. The higher the electrophilicity of the carbene carbon atom in the umpoled substrate adduct is, the stronger is its stabilization by conjugation. The nitrogen atoms of triazole-2- **6**, imidazole-2- **1** and tetrazole-5-ylidene **7** are no longer planar (Figure 4) in comparison to the other steps in the catalytic cycle. Imidazoline-2-ylidene **5** has a pyramidal geometry of its nitrogen atoms (Figure 4). The more nitrogen atoms are located in the heterocycle the more electron density from the π orbitals is located at the nitrogen atoms and not at the p_z orbital of the carbene carbon atom, resulting in a higher electrophilicity of the carbene carbon atom.[17g] Therefore, the negative charge in the Breslow intermediate is stronger stabilized with tetrazole-5-ylidene **7**. The addition of the Breslow intermediate to the second benzaldehyde molecule (**TS-3**, Scheme 3) is most favored for imidazole-2-ylidene **1** (ΔG_{TS-3} = 33.3 kcal mol^{-1}). The negative charge is less stabilized and the attack to the second benzaldehyde molecule is favored. The following intermediate **IM-3** (Scheme 3) is also most favored for imidazole-2-ylidene **7** (ΔG_{IM-3} = 30.3 kcal mol^{-1}). The relative free energy for the recovery of the catalyst and the product formation (**TS-4**, Scheme 3) is nearly the same for imidazole-2- **1**, imidazoline-2- **5** and 1,2,4-triazole-5-ylidene **6** (ΔG_{TS-4} (**1**) = 38.5 kcal mol^{-1}, ΔG_{TS-4} (**5**) = 39.0 kcal mol^{-1}, ΔG_{TS-4} (**6**) = 39.2 kcal mol^{-1}). For all catalysts the umpolung is the rate-determining step. The lowest activation energy is observed for the saturated imidazoline-2-ylidene **5** with E_a = 27.5 kcal mol^{-1}. Followed by tetrazole-5- **7** (E_a = 28.4 kcal mol^{-1}), 1,2,4-triazole-5- **6** (E_a = 29.9 kcal mol^{-1}) and imidazole-2-ylidene **1** (E_a = 31.7 kcal mol^{-1}) the activation energy becomes lower the less nitrogen atoms are in the ring.

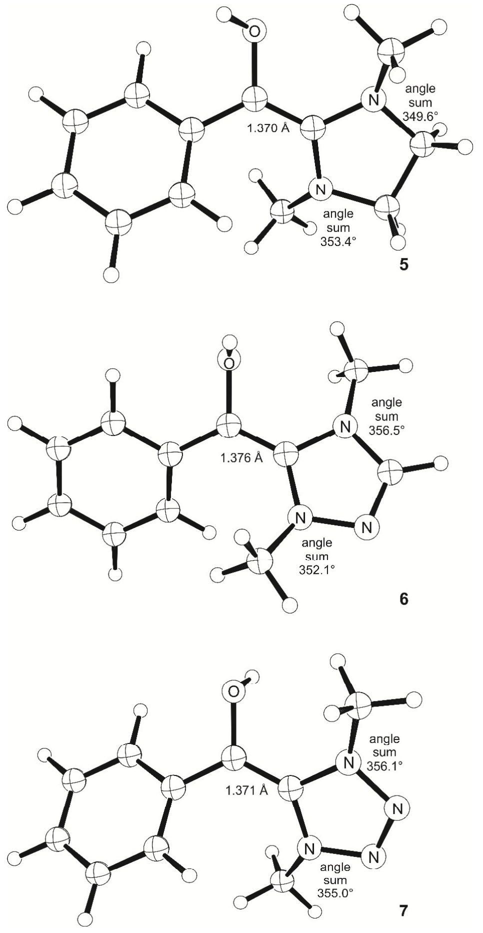


Figure 4 Breslow intermediates **IM-2** of benzaldehyde with imidazoline-2- **5**, 1,2,4-triazole-5- **6** and tetrazole-5-ylidene **4** (imidazole-2-ylidene **1** is depicted in Figure 2).

Position of phenyl rings

The influence of the position of phenyl rings was further investigated with imidazole-2- **1**, perhydrobenzimidazole-2- **8**, 4,5-diphenyl-imidazole-2- **9**, benzimidazole-2- **10** and 1,3-di-phenyl-imidazole-2-ylidene **11** (Type **A**, Scheme 2 and 5). The results of the calculation are depicted in Figure 5 and Table 3. The addition of the catalyst to benzaldehyde (**TS-1**, Scheme 3) has a relative free energy slightly above 20 kcal mol^{-1} for imidazole-2- **1**, perhydrobenzimidazole-2- **8**, 4,5-diphenyl-imidazole-2- **9** and benzimidazole-2-ylidene **10**. The relative free energy is significantly higher for 1,3-diphenyl-imidazole-2-ylidene **11** (ΔG_{TS-1} = 26.4 kcal mol^{-1}). The adduct **IM-1** (Scheme 3) is most stable for imidazole-2-ylidene **1** (ΔG_{IM-1} = 8.1 kcal mol^{-1}).

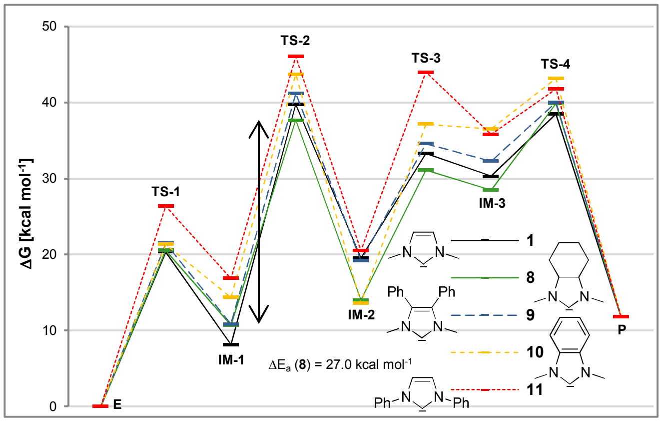


Figure 5 Umpolung of benzaldehyde catalysed by imidazole and imidazoline derivative carbenes **1**, **8**-**11**. (type **A**, Scheme 2; THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), relative free energies referring to isolated reactants). The lowest overall energy difference $\Delta E_{overall}$ is observed for imidazole-2-ylidene **1**.

Table 3 Relative free energies (kcal mol^{-1}) for the benzoin reaction catalysed by imidazole and imidazoline derivative carbenes **1**, **8**-**11** (type **A**, Scheme 2) according to Scheme 5.^{a}

ΔG^{b}	E	TS-1	IM-1	TS-2	IM-2	TS-3	IM-3	TS-4	P .
1	0	20.3	8.1	39.8	19.5	33.3	30.3	38.5	11.8
8	0	20.5	10.7	37.7	14.0	31.1	28.5	39.9	11.8
9	0	21.4	10.8	41.2	19.2	34.6	32.3	40.0	11.8
10	0	21.3	14.3	43.7	13.6	37.2	36.5	43.2	11.8
11	0	26.4	16.8	46.0	20.5	44.0	35.8	41.8	11.8

a THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d) with ZPE correction, scaled by 0.9806, energies in kcal mol^{-1}; b T = 298.15 K, P = $1.01325 \cdot 10^{5}$ Pa.

The umpolung of benzaldehyde (**TS-2**, Scheme 3) is most stabilized in the order of 2-perhydro-benzimidazole-2- **8**, imidazole-2- **1**, 4,5-diphenyl-imidazole-2- **9**, benzimidazole-2- **10** and 1,3-diphenyl-imidazole-2-ylidene **11**. The Breslow intermediate (**IM-2**, Scheme 3, Figure 6) is most favored for benzimidazole-2- **10** and perhydrobenzimidazole-2- ylidene **8** ($\Delta G_{IM\text{-}2}$ (**10**) = 13.6 kcal mol^{-1}, $\Delta G_{IM\text{-}2}$ (**8**) = 14.0 kcal mol^{-1}). The addition of the Breslow intermediate to the second benzaldehyde (**TS-3**, Scheme 3) takes place in the same order as before. The resulting intermediate (**IM-3**, Scheme 3) is most stabilized with perhydrobenzimidazole-2-ylidene **8** ($\Delta G_{IM\text{-}3}$ = 28.5 kcal mol^{-1}). For the recovery of the catalyst and the product formation (**TS-4**, Scheme 3) the energy intervals are very small in the order of imidazole-2- **1**, perhydrobenzimidazole-2- **8**, 4,5-diphenyl-imidazole-2- **9**, 1,3-diphenyl-imidazole-2- **11** and benzimidazole-2-ylidene **10**. For all catalysts the umpolung is the rate-determining step. The lowest activation energy is observed for the saturated perhydrobenzimidazole-2- **8** (E_a = 27.0 kcal mol^{-1}) followed by 1,3-diphenyl-imidazole-2-ylidene **11** (E_a = 29.2 kcal mol^{-1}), benzimidazole-2- **10** (E_a = 29.4 kcal mol^{-1}), 4,5-diphenyl-imidazole-2- **9** (E_a = 30.4 kcal mol^{-1}) and imidazole-2-ylidene **1** (E_a = 31.7 kcal mol^{-1}).

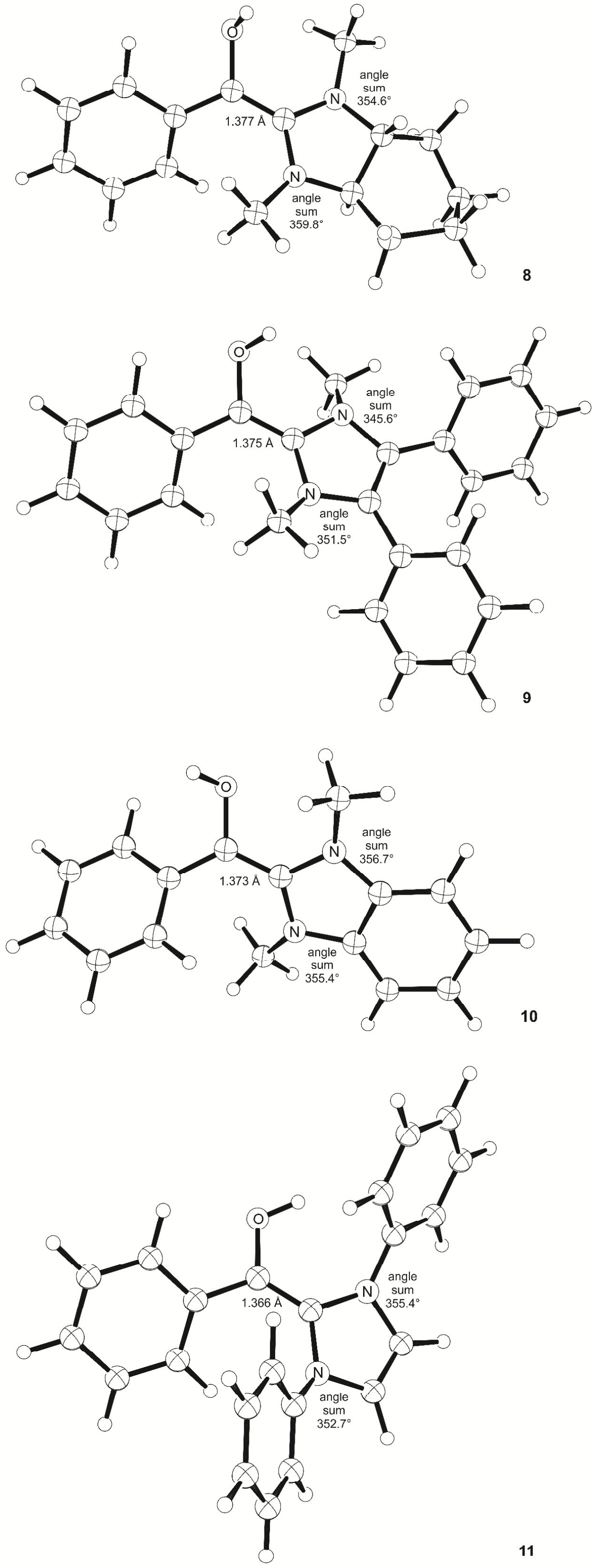


Figure 6 Breslow intermediates **IM-2** of benzaldehyde with perhydrobenzimidazole-2- **8**, 4,5-diphenyl-imidazole-2- **9**, benzimidazole-2- **10** and 1,3-diphenyl-imidazole-2-ylidene **4** (imidazole-2-ylidene **1** is depicted in Figure 2).

Reduced heteroatom stabilized and abnormal carbenes

Different reduced heteroatom stabilized and abnormal five-membered ring carbenes (cyclic (alkyl)(amino)carbenes, CAACs[15], Type **B** and **D**, Scheme 2 and 5), represented by pyrazoline-3- **12**, imidazole-5- **13**, pyrrolidine-2- **14** and 1,2,3-triazole-5-ylidene **15** were computed. The results of the calculation are depicted in Figure 7 and Table 4. Remarkably the relative free energies for the intermediates and the transition structures decrease in comparison to the normal carbenes.

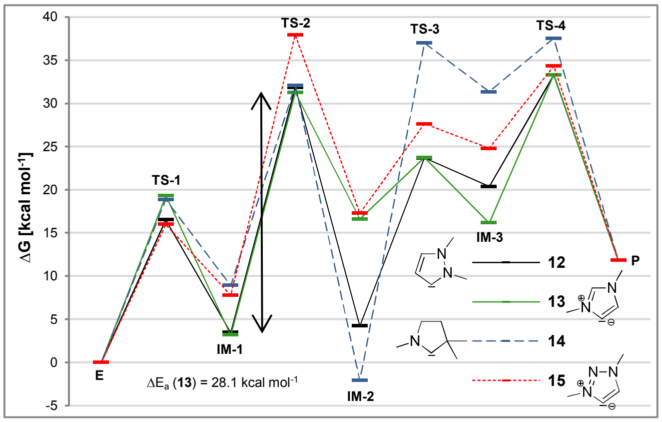


Figure 7 Umpolung of benzaldehyde catalysed by different reduced heteroatom stabilized (**B**) and abnormal (**C**, Scheme 2) five ring carbenes **12**-**15**. (THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), relative free energies referring to isolated reactants). The lowest overall energy difference $\Delta E_{overall}$ is observed for pyrazoline-3- **12** and imidazole-5-ylidene **13**.

Table 4 Relative free energies (kcal mol^{-1}) for the benzoin reaction catalysed by different reduced heteroatom stabilized (**B**) and abnormal (**C**, Scheme 2) five ring carbenes **12**-**15** according to Scheme 5.[a]

ΔG^b	E	TS-1	IM-1	TS-2	IM-2	TS-3	IM-3	TS-4	P .
12	0	16.5	3.4	31.9	4.2	23.7	20.4	33.3	11.8
13	0	19.3	3.2	31.3	16.6	23.7	16.1	33.3	11.8
14	0	18.8	8.9	32.1	-2.1	37.0	31.3	37.5	11.8
15	0	16.0	7.8	37.9	17.3	27.6	24.8	34.3	11.8

a THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d) with ZPE correction, scaled by 0.9806, energies in kcal mol^{-1}; b T = 298.15 K, P = $1.01325\cdot10^5$ Pa.

The addition of the carbene to benzaldehyde (**TS-1**, Scheme 3) is below 20 kcal mol^{-1} for all catalysts with pyrazoline-3- **12** and 1,2,3-triazole-5-ylidene **15** slightly favored (ΔG_{TS-1} (**12**) = 16.5 kcal mol^{-1}, ΔG_{TS-1} (**15**) = 16.0 kcal mol^{-1}). The relative free energy for the adduct **IM-1** (Scheme 3) is only around 3 kcal mol^{-1} for pyrazoline-3- **12** and imidazole-5-ylidene **13**. As mentioned before the less nitrogen atoms are introduced the less the group electronegativity of this system increases which is thus destabilized and more donating. Also the umpolung step **TS-2** (Scheme 3) for these carbenes is more favored than for the normal carbenes. The relative free energy for the umpolung with pyrazoline-3- **12**, imidazole-5- **13** and pyrrolidine-2-ylidene **14** amount to 32 kcal mol^{-1}. Only 1,2,3-triazole-5-ylidene **15** has a higher relative free energy for the umpolung (ΔG_{TS-2} = 37.9 kcal mol^{-1}). The only exergonic Breslow intermediate **IM-2** (Scheme 3) is formed with pyrrolidine-2-ylidene **14** (ΔG_{IM-2} = -2.1 kcal mol^{-1}), which can be explained by the absence of delocalization of π-electrons and can be seen in the strong stabilization by conjugation of the negative charge with a very short C-C bond (1.358 Å, Figure 8). Also pyrazoline-3-ylidene **12** is endergonic, the relative free energy is only slightly increased (ΔG_{IM-2} = 4.2 kcal mol^{-1}, C-C bond: 1.367 Å, Figure 8). Again the more nitrogen atoms are in the heterocycle, the more electron density from the π orbitals is located at the nitrogen atoms and not at the p_z orbital of the carbene carbon atom. Thus the negative charge in the Breslow intermediate can be better stabilized. Pyrazoline-2-ylidene **12** has a lower electron density in the p_z orbital of the carbene carbon atom than imidazole-5- **13** and 1,2,3-triazole-5-ylidene **15**.[17g]

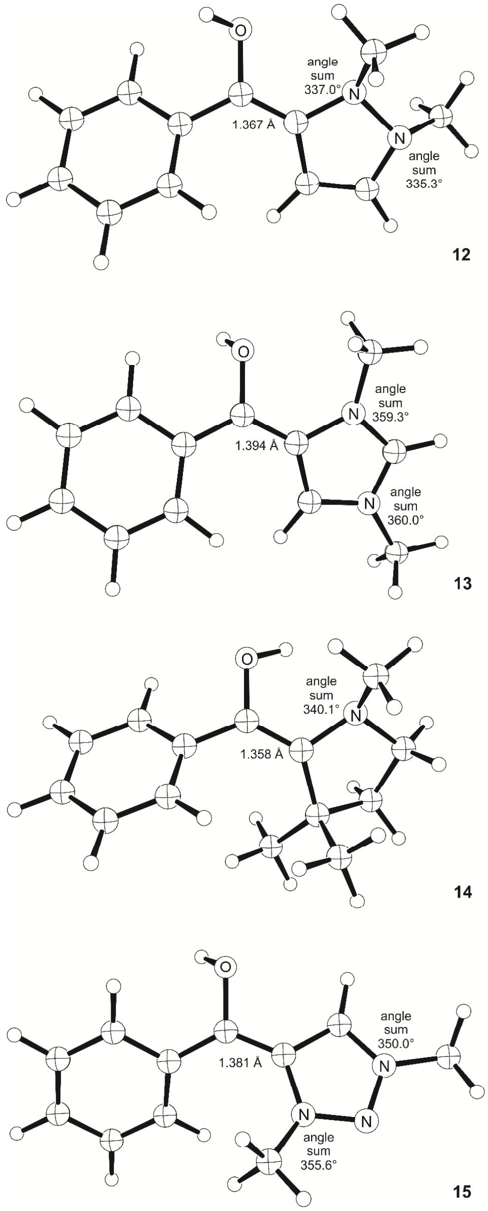


Figure 8 Breslow intermediates **IM-2** of benzaldehyde with pyrazoline-3- **12**, imidazole-5- **13**, pyrrolidine-2- **14** and 1,2,3-triazole-5-ylidene **15**.

The relative free energy of **IM-2** for imidazole-5- **13** and 1,2,3-triazole-5- ylidene **15** is about 12 kcal mol^{-1} higher (ΔG_{IM-2} (**13**) = 16.6 kcal mol^{-1}, ΔG_{IM-2} (**15**) = 17.3 kcal mol^{-1}). The addition of the Breslow intermediate to benzaldehyde (**TS-3**, Scheme 3) is most favored for pyrazoline-3- **12** and imidazole-5-ylidene **13** (both ΔG_{TS-3} = 23.7 kcal mol^{-1}). The lower the relative free energy of the Breslow intermediate is, the higher is the activation energy for the addition to the second benzaldehyde. The following intermediate **IM-3** (Scheme 3) is formed most favored for imidazole-5-ylidene **13** (ΔG_{IM-3} = 16.1 kcal mol^{-1}). The recovery of the catalyst and product formation (**TS-4**, Scheme 3) is most favored for pyrazoline-3- **12** and imidazole-5-ylidene **13** (both ΔG_{TS-4} = 33.3 kcal mol^{-1}). The lowest activation energy is observed for imidazole-5-ylidene **13** (E_a = 28.1 kcal mol^{-1}, **IM1** → **TS2**) followed by pyrazoline-3- **12** (E_a = 28.5 kcal mol^{-1}, **IM1** → **TS2**), 1,2,3-triazole-5- **15** (E_a = 30.1 kcal mol^{-1}, **IM1** → **TS2**) and pyrrolidine-2-ylidene **14** (E_a = 39.1 kcal mol^{-1}, **IM2** → **TS3**).

Distance of the heteroatom

Finally the influence of the distance of the heteroatom to the carbene carbon atom was computed with different pyridyl derivatives, pyridyl-4- **16**, pyridyl-3- **17**, pyridyl-2- **18** and isoquinoline-6-ylidene **19** (Type **B**, **C** and **D**, Scheme 2 and 5). The results of the calculation are depicted in Figure 9 and Table 5.

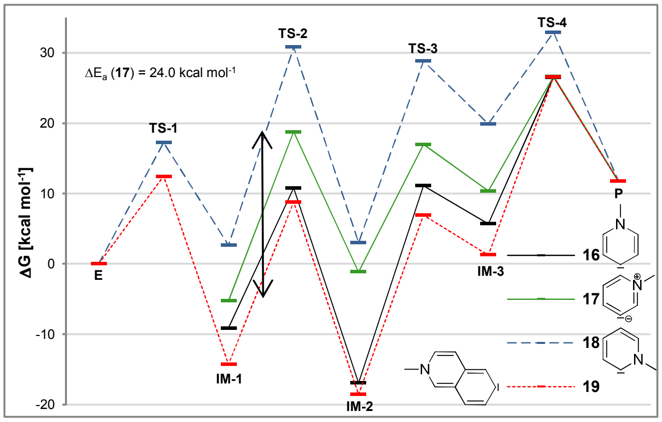


Figure 9 Umpolung of benzaldehyde catalysed by different reduced heteroatom stabilized (**B**), remote (**C**) and abnormal (**D**, Scheme 2) pyridyl ylidenes **16**-**19**. (THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d), relative free energies referring to isolated reactants). The lowest overall energy difference $\Delta E_{overall}$ is observed for pyridyl-3-ylidene **17**.

Table 5 Relative free energies (kcal mol^{-1}) for the benzoin reaction catalysed by different reduced heteroatom stabilized (**B**), remote (**C**) and abnormal (**D**, Scheme 2) pyridyl ylidenes **16**-**19** according to Scheme 5.[a]

ΔG^b.	E	TS-1	IM-1	TS-2	IM-2	TS-3	IM-3	TS-4	P .
16	0	c	-9.2	10.8	-16.9	11.1	5.7	26.5	11.8
17	0	c	-5.2	18.8	-1.2	17.0	10.4	26.7	11.8
18	0	17.3	2.7	30.8	3.0	28.8	19.9	32.9	11.8
19	0	12.5	-14.3	8.8	-18.6	6.9	1.2	26.6	11.8

a THF solvent, CPCM-B3LYP/6-311G+(d,p)//B3LYP/6-31G(d) with ZPE correction, scaled by 0.9806, energies in kcal mol^{-1}; b T = 298.15 K, P = 1.01325·10^5 Pa; c barriereless.

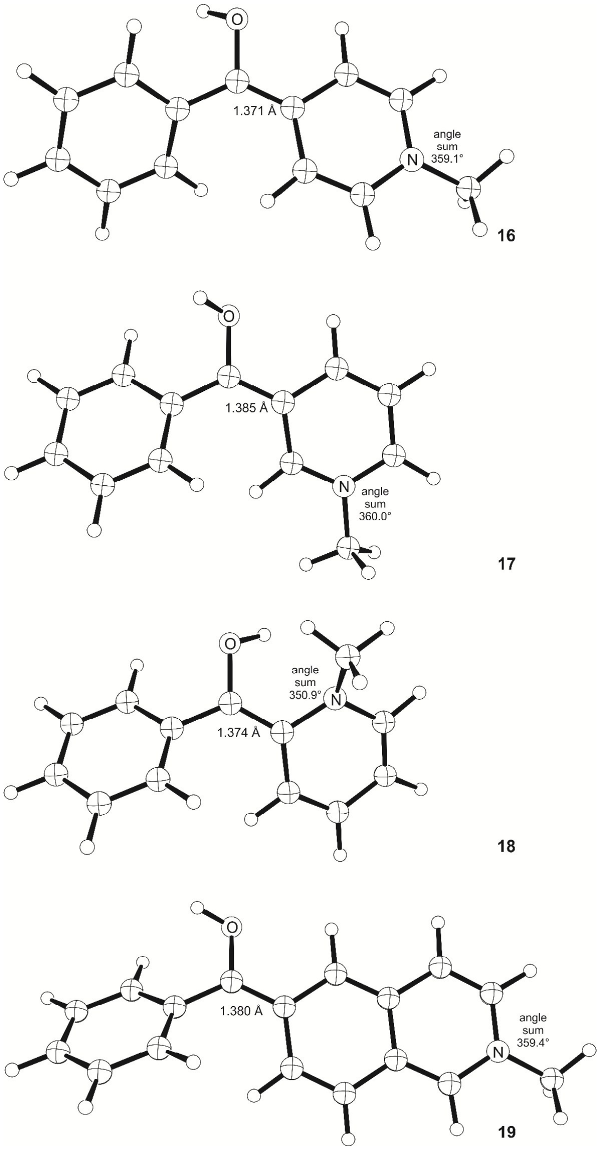


Figure 10 Breslow intermediates **IM-2** of benzaldehyde with pyridyl-4- **16**, pyridyl-3- **17**, pyridyl-2- **18** and isoquinoline-6-ylidene **19**.

The replacement of the second electronegative nitrogen atom with a σ-donor carbon atom leads to even more electron-rich carbenes. The greater the distance between the nitrogen atom and the carbene carbon atom the lower is the relative free energy for the intermediates and the transition structures. The addition of pyridyl-4- **16** and pyridyl-3-ylidene **17** to benzaldehyde (**TS-1**, Scheme 3) is barriereless. The relative free energies for isoquinoline-6- **19** and pyridyl-2-ylidene **18** are 12.5 and 17.3 kcal mol^{-1} respectively. The most favored and exergonic adduct **IM-1** (Scheme 3) is built with isoquinoline-6-ylidene **19** (ΔG_{IM-1} = -14.3 kcal mol^{-1}). Also for the other remote carbenes **IM-1** is exergonic. The relative free energy rises the closer the nitrogen atom is to the carbene carbon atom. The umpolung **TS-2** (Scheme 3) is most favored for isoquinoline-6-ylidene **19**, the relative free energy is even below 10 kcal mol^{-1} (ΔG_{TS-2} = 8.8 kcal mol^{1}) directly followed by pyridyl-4-ylidene **16** (ΔG_{TS-2} = 10.8 kcal mol^{-1}). The relative free energy for the umpolung with pyridyl-3-ylidene **17** is still below 20 kcal mol^{-1}. The introduction of a nitrogen atom adjacent to the carbene carbon atom in pyridyl-2-ylidene **18** results in a relative free energy above 30 kcal mol^{-1}. The Breslow intermediate **IM-2** (Scheme 3) is strongly exergonic for isoquinoline-6- **19** and pyridyl-4-ylidene **16** (ΔG_{IM-2} (**19**) = -18.6 kcal mol^{-1}, ΔG_{IM-2} (**16**) = -16.9 kcal mol^{-1}). The Breslow intermediate with pyridyl-3-ylidene **17** is barely exergonic (ΔG_{IM-2} = -1.3 kcal mol^{-1}) followed by pyridyl-2-ylidene **18** (ΔG_{IM-2} = 3.0 kcal mol^{-1}). The π-population at the carbene carbon atom increases in the order **16** < **18** << **17**.[17f] Pyridyl-3-ylidene **17** has the highest π-population due to its abnormal character. Therefore its stabilization of the Breslow intermediate is poor (C-C bond: 1.385 Å, Figure 10). The same tendency is apparent for the addition to the second benzaldehyde. Isoquinoline-6-ylidene **19** is also favored for this transition state (ΔG_{TS-3} = 6.9 kcal mol^{-1}). Regarding the activation energy for this transition state the addition is most favored for the less stabilized Breslow intermediate with pyridyl-3-ylidene **17**. The same property is reflected for **IM-3**. The recovery of the catalyst and the product formation (**TS-4**, Scheme 3) is similarly favored for pyridyl-4- **16**, isoquinoline-6- **19** and pyridyl-3-ylidene **17** around 26 kcal mol^{-1}. The lowest activation energy is observed for pyridyl-3-ylidene **17** (ΔE_a = 24.0 kcal mol^{-1}, **IM1** → **TS2**) followed by isoquinoline-6- **19** (ΔE_a = 25.5 kcal mol^{-1}, **IM2** → **TS3**), pyridyl-4- **16** (ΔE_a = 28.0 kcal mol^{-1}, **IM2** → **TS3**) and pyridyl-2-ylidene **18** (ΔE_a = 28.1 kcal mol^{-1}, **IM1** → **TS2**).

Conclusions

To fulfil the requirements for a suitable umpolung catalyst in the benzoin reaction, the carbene has to feature both, nucleophilic reactivity for the addition to the aldehyde as well as electrophilic properties to stabilise a developing negative charge for the umpolung step which yields in the Breslow intermediate.

Among the studied normal N-heterocyclic carbenes oxazole-2-ylidene **3** exhibits the lowest activation energy for the rate-determining step E_a (**3**) = 25.2 kcal mol^{-1} (**IM-1** → **TS-2**, Figure 1, Table 1), which coins it as the best normal NHC-catalyst, among the analyzed carbenes. For the phosphazole-2-ylidene **2**, the umpolung step is exergonic, as with less delocalisation of adjacent π-electrons the negative charge is better stabilized. Hence the activation energy is increased (E_a (**2**) = 38.7 kcal mol^{-1}, **IM-2** → **TS-3**, Figure 1, Table 1). With increasing number of nitrogen atoms in the heterocycle, the nucleophilicity of the carbene decreases and lowers the tendency for addition to the aldehyde. However, during the umpolung step, the developing negative charge in the Breslow intermediates becomes better stabilized by conjugation with the adjacent, more electrophilic carbene carbon atom. Not only are the numbers of nitrogen atoms in the heterocycle crucial, but also the position of the nitrogen atoms. Relative to the starting materials, the relative free energies for both the intermediates and the transition structures are decreased for reduced heteroatom stabilized NHCs. This type of NHCs is both more nucleophilic and electrophilic. The nucleophicity of the carbene carbon atom is increased due to lower electronegativity and hence less inductive electron withdrawal from the adjacent carbon atom. Its electrophilicity is also increased due to the lack of π-donation.[17e,f] For the same reasons, the free energies, relative to the starting compounds, of remote NHCs are even more decreased with more remote positions of the nitrogen atoms relative to the carbene carbon atom. The comparison of all computed carbenes points to remote and abnormal pyridyl-3-ylidene **17** as catalyst with the lowest activation energy E_a (**17**) = 24.0 kcal mol^{-1} (**IM-1** → **TS-2**, Figure 9, Table 5). With this remote and abnormal NHC, the developing negative charge in the Breslow intermediates becomes less stabilized by conjugation, because abnormal NHCs have a higher p_z-population at the carbene carbon atom.[17g] Furthermore an increasing exergonic character of the Breslow intermediate results in a higher activation energy E_a for the addition to the second aldehyde molecule so this step becomes rate-determining. Hence, the remote and abnormal pyridyl-3-ylidene **17** exhibits the best balance between nucleophilicity and electrophilicity, among the assed carbene catalysts in the benzoin coupling reaction.

Computational details

In this work the geometry optimizations of minima and transition structures (Berny algorithm) and frequency calculations were performed using GAUSSIAN09[26] at the B3LYP/6-31G(d)[27,28] level of theory. Frequency calculations have been performed to characterise the nature of the stationary points. Ground states are characterised by real frequencies while transition states are characterised by one negative frequency. The frequency calculations provided the thermal correction for free energies at a temperature of 298.15 K and a pressure of 1.01325.105 Pa. The thermochemical analyses were scaled by 0.9806.[29] Higher level single point calculations in THF (ε = 7.58) were performed (CPCM-B3LYP/6-311+G(d,p)).[30] Energies from these single point calculations were combined with the thermodynamic corrections at the lower level of theory to obtain the relative free energy ΔG.

Acknowledgements

We are grateful to the Fonds der Chemischen Industrie for financial support. We especially also thank the Deutsche Forschungsgemeinschaft for funding (GO-930/9-1). Bayer AG, BASF AG, Wacker AG, Evonic AG, Raschig GmbH, Symrise GmbH, Solvay GmbH and the OMG group are thanked for generous support. We are also grateful to the computing centre of the University of Cologne (RRZK).

Notes and references

[a] Department of Chemistry, University of Cologne, Greinstr. 4, 50939 Köln, Germany.
E-mail: goldfuss@uni-koeln.de; Fax: +49-221-470-5057

† Electronic Supplementary Information (ESI) available: See DOI: 10.1039/b000000x/

1 For selected reviews see: (a) H. Clavier and S. P. Nolan, *Annu. Rep. Prog. Chem., Sect. B*, 2007, **103**, 193; (b) M. N. Hopkinson, C. Richter, M. Schedler and F. Glorius, *Nature*, 2014, **510**, 485.

2 For selected reviews see: (a) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.* 2007, **107**, 5606; (b) N. Marion, S. Díez-González and S. P. Nolan, *Angew. Chem.* 2007, **119**, 3046; *Angew. Chem. Int. Ed.* 2007, **46**, 2988; (c) F. Glorius and K. Hirano, *Ernst Schering Foundation Symposium Proceedings*; Springer-Verlag: Berlin, 2008; Vol.2, 159; (d) K. Zeitler, *Ernst Schering Foundation Symposium Proceedings*; Springer-Verlag: Berlin, 2008; Vol.2, 183; (e) X. Bugaut and F. Glorius, *Chem. Soc. Rev.* 2012, **41**, 3511.

3 Carbenes in acyloin-type couplings: (a) T. Dudding and K. N. Houk, *Proc. Natl. Acad. Sci. USA* 2004, **101**, 5770; (b) A. Berkessel and H. Gröger in *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, 2005, 227; (c) D. Enders, T. Balensiefer, O. Niemeier and M. Christmann in *Enantioselective Organocatalysis* (Eds. P. I. Dalko), Wiley-VCH, Weinheim, 2007, 331; d) D. Enders, A. Grossmann, J. Fronert and G. Raabe, *Chem. Commun.* 2010, **46**, 6282; (e) D. A. DiRocco, T. Rovis in *Science of Synthesis: Stereoselective Synthesis Vol.2* (Eds. G. A. Molander, J. G. de Vries, P. A. Evans), Georg Thieme Verlag KG, 2010, 835; (f) P.-C. Chiang and J. W. Bode, *TCI MAIL* 2011, **149**, 2; (g) S. E. O`Toole, C. A. Rose, S. Gundala, K. Zeitler and S. J. Connon, *J. Org. Chem.* 2011, **76**, 347; h) D. T. Cohen, B. Cardinal-David and K. A. Scheidt, *Angew. Chem.* 2011, **123**, 1716; *Angew. Chem Int. Ed.* 2011, **50**, 1678; (i) J. Mahatthananchai and J. W. Bode, *Chem. Sci.* 2012, **3**, 192; (j) H. U. Vora, P. Wheeler and T. Rovis, *Adv. Synth. Catal.* 2012, **354**, 1617; k) M. Schedler, D.-S. Wang and F. Glorius, *Angew. Chem.* 2013, **125**, 2645; *Angew. Chem. Int. Ed.* 2013, 52, 2585; l) X. Bugaut in *Comprehensive Organic Synthesis* 2^{nd} *Edition* (Eds. G. A. Molander, P. Knochel), Elsevier, Oxford, 2014, 424.

4 Carbenes in the Stetter reaction: (a) H. Stetter and M. Schreckenberg, *Angew. Chem.* 1973, **85**, 89; *Angew. Chem. Int. Ed.* 1973, **12**, 81; (b) H. Stetter, *Angew. Chem.* 1976, **88**, 695; *Angew. Chem. Int. Ed.* 1976, **15**, 639; (c) H. Stetter and H. Kuhlmann, *Org. React.* 1991, **40**, 407; (d) A. Berkessel and H. Gröger in *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, 2005, 227; (e) D. A. DiRocco, E. L. Noey, K. N. Houk and T. Rovis, *Angew. Chem.* 2012, **124**, 2441; *Angew. Chem. Int. Ed.* 2012, **51**, 2391.

5 F. Wöhler, J. Liebig, *Ann. Pharm.* 1832, *3*, 24.

6 D. Seebach, *Angew. Chem.* 1979, **91**, 259; *Angew. Chem. Int. Ed.* 1979, **18**, 239; T. A. Hase, *Umpoled Synthons*, Wiley, New York, 1987.

7 A. Lapworth, *J. Chem. Soc.* 1903, **83**, 995.

8 T. Ukai, R. Tanaka and T. A. Dokawa, *J. Pharm. Soc. Jpn.* 1943, **63**, 296.

9 R. Breslow, *J. Am. Chem. Soc.* 1958, **80**, 3719.

10 A. Berkessel, S. Elfert, V. R. Yatham, J.-M. Neudörfl, N. E. Schlörer and J. H. Teles, *Angew. Chem.* 2013, **125**, 11364; *Angew. Chem. Int. Ed.* 2013, **52**, 11158.

11 M. J. White and F. J. Leeper, *J. Org. Chem.* 2001, **66**, 5124.

12 (a) J. C. Sheehan and D. H. Hunneman, *J. Am. Chem. Soc.* 1966, **88**, 3666; (b) J. C. Sheehan and T. Hara, *J. Org. Chem.* 1974, **39**, 1196; (c) D. Enders, K. Breuer and J. H. Teles, *Helv. Chim. Acta*, 1996, **79**, 1217; (d) R. L. Knight and F. J. Leeper, *J. Chem. Soc., Perkin Trans. 1* 1998, 1891; .

13 (a) X. Linghu, J. R. Potnick and J. S. Johnson, *J. Am. Chem. Soc.* 2004, **126**, 3070; (b) M. R. Nahm, J. R. Potnick, M. Yates, P. S. White and J. S. Johnson, *J. Am. Chem. Soc.* 2006, **128**, 2751; (c) M. R. Garrett, J. C. Tarr and J. S. Johnson, *J. Am. Chem. Soc.* 2007, **129**, 12944; (d) A. Gliga, M. Schumacher, H. Klare, F. Soki, J. M. Neudörfl and B. Goldfuss, *Eur. J. Org. Chem.* 2011, 256; (e) M. Schumacher and B. Goldfuss, *New Journal of Chemistry* 2014, **38**, 1040.

14 (a) B. Goldfuss and M. Schumacher, *J. Mol. Model.* 2006, **12**, 591; (b) M. Schumacher and B. Goldfuss, *Tetrahedron* 2008, **64**, 1648.

15 (a) M. Melaimi, M. Soleilhavoup and G. Bertrand, *Angew. Chem.* 2010, **122**, 8992; *Angew. Chem. Int. Ed.* 2010, **49**, 8810; (b).M. Z. Kassaee, F. A. Shakib, M. R. Momeni, M. Ghambarian and S. M. Musavi, *J. Org. Chem.* 2010, **75**, 2539.

16 (a) E. Aldeco-Perez, A. J. Rosenthal, B. Donnadieu, P. Parameswaran, G. Frenking and G. Bertrand, *Science* 2009, **326**, 556; (b) G. Guisado-Barrios, J. Bouffard, B. Donnadieu and G. Bertrand, *Angew. Chem.* 2010, **122**, 4869-4872; *Angew. Chem. Int. Ed.* 2010, **49**, 4759.

17 (a) C. Heinemann and W. Thiel, *Chem. Phys. Lett.* 1994, **217**, 11; (b) C. Heinemann, T. Müller, Y. Apeloig and H. Schwarz, *J. Am. Chem. Soc.* 1996, **118**, 2023; (c) C. Boehme and G. Frenking, *J. Am. Chem. Soc.* 1996, **118**, 2039; (d) W. A. Herrmann and C. Köcher, *Angew. Chem.* 1997, **109**, 2256; *Angew. Chem. Int. Ed.* 1997, **36**, 2162; (e) D. J. Nelson and S. P. Nolan, *Chem. Soc. Rev.* 2013, **42**, 6723; (f) H. V. Huynh and G. Frison, *J. Org. Chem.* 2013, **78**, 328; (g) J. C. Bernhammer, G. Frison and H. V. Huynh, *Chem. Eur. J.* 2013, **19**, 12892.

18 A. Krüger and M. Albrecht, *Aust. J. Chem.* 2011, **64**, 1113.

19 O. Schuster, L. Yang, H. G. Raubenheimer and M. Albrecht, *Chemical Reviews* 2009, **109**, 3445.

20 (a) D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.* 2000, **100**, 39; (b) A. Poater, F. Ragone, S. Giudice, C. Costabile, R. Dorta, S. P. Nolan and L. Cavallo, *Organometallics* 2008, **27**, 2679.

21 (a) B. Maji, M. Breugst and H. Mayr, *Angew. Chem.* 2011, **123**, 7047; *Angew. Chem. Int. Ed.* 2011, **50**, 6915; (b) H. Mayr, S. Lakhdar, B. Maji and A. R. Ofial, *Beilstein J. Org. Chem.* 2012, **8**, 1458; (c) B. Maji, M. Baidya, J. Ammer, S. Kobayashi, P. Mayer, A. R. Ofial and H. Mayr, *Eur. J. Org. Chem.* 2013, 3369.

22 (a) K. J. Hawkes, B. F. Yates, *Eur. J. Org. Chem.* 2008, 5563; (b) Y. He and Y. Xue, *J. Phys. Chem. A* 2011, **115**, 1408.

23 (a) S. Yamabe, S. Yamazaki, *Org. Biomol. Chem.* 2009, **7**, 951; (b) Y. He and Y. Xue, *J. Phys. Chem. A* 2010, **114**, 9222; (c) M. J. Ajitha and C. H. Suresh, *Tetrahedron Letters* 2013, **64**, 7144.

24 Z. Kelemen, O. Hollóczki, J. Oláh and L. Nyulászi, *RSC Adv.* 2013, **3**, 7970.

25 Y. Naruse and Y. Kugiya, *Tetrahedron: Asymmetry*, 2013, **24**, 169.

26 Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji,

M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian, Inc., Wallingford CT, 2010.

27 (a) R. Ditchfield, W. J. Hehre and J. A. Pople, *J. Chem. Phys.* 1971, **54**, 724; (b) V. A. Rassolov, M. A. Ratner, J. A. Pople, P. C. Redfern and L. A. Curtiss, *J. Comp. Chem.* 2001, **22**, 976.

28 (a) A. D. Becke, *J. Chem. Phys.* 1993, **98**, 5648; Implementation: (b) P. J. Stephens, F. J. Devlin, C. F. Chabalowski and M. J. Frisch, *J. Phys. Chem.* 1994, **98**, 11623; (c) C. Lee, W.Yang and R. G. Parr, *Phys. Rev. B.* 1988, **37**, 785; (d) B. Miehlich, A. Savin, H. Stoll and H. Preuss, *Chem. Phys. Lett.* 1989, **157**, 200.

29 A. P. Scott and L. Radom, *J. Phys. Chem.* 1996, **100**, 16502.

30 (a) V. Barone, M. Cossi, *J. Phys. Chem. A.* 1998, **102**, 1995; (b) M. Cossi, N. Rega, G. Scalmani and V. Barone, *J. Comp. Chem.* 2003, **6**, 669.

Different types of N-heterocyclic carbenes, i.e. normal, reduced heteroatom stabilized, remote and abnormal carbenes, are computationally assessed (THF-CPCM-B3LYP/6-311+G(d,p)//B3LYP/6-31G(d)) in the benzoin reaction to study their characteristics as umpolung catalysts.