N–C Bond Activation

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Structural Characterization of N-Alkylated Twisted Amides: Consequences for Amide Bond Resonance and N–C Cleavage

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Abstract: *Herein, we describe the first structural characterization of N-alkylated twisted amides prepared directly by N-alkylation of the corresponding non-planar lactams. This study provides the first experimental evidence that N-alkylation results in a dramatic increase of non-planarity around the amide N–C(O) bond. Moreover, we report a rare example of a molecular wire supported by the same amide C=O-Ag bonds. Reactivity studies demonstrate rapid nucleophilic addition to the N–C(O) moiety of N-alkylated amides, indicating the lack of n_N to $\pi^*_{C=O}$ conjugation. Most crucially, we demonstrate that N-alkylation activates the otherwise unreactive amide bond towards σ N–C cleavage by switchable coordination.*

Over the last three decades, twisted amides have emerged as valuable transition state mimics of numerous biologically relevant enzymatic reactions.[1–4] Studies have implicated N-coordination as a method to disrupt the amide bond resonance, where a suitable ligand activates the amide bond towards isomerization[5] or σ N–C bond cleavage.[6] The characterization of N-protonated amides represents a significant challenge because the O-protonated structure is more thermodynamically stable than the N-protonated one (e.g. formamide, 13.9 kcal mol^{-1});[7] to date only few structural examples of N-protonated amides have been reported (Figure 1 A).[8] There is an intrinsic bias favoring N-alkylation vs. O-alkylation by ca. 2.5 kcal mol^{-1} compared with N-/O-protonation affinities.[9] O-methylation of dimethylacetamide is favored over N-alkylation by ca. 3 kcal mol^{-1}.[9] N-alkylation of amides plays a crucial role in a vast range of biologically relevant mechanisms,[10a–g] including enzymatic N-methylation of carboxamido groups,[10a] enzymatic N-alkylation of toxins,[10b] and N-alkylation of polypeptides;[10c] however, the study of N-alkylation of non-planar amides has been severely limited.[11] Alkyl groups exert a more stabilizing effect on the N–C(O) bond than H due to $\sigma_{C\text{-}H}$ to $\sigma^*_{N\text{-}C}$ hyperconjugation;[12] however, alkyl functions are also more sterically-demanding, which contributed to the formidable challenge in straightforward isolation of N-alkylated species.[11]

Recently, there has been a significant interest in the activation of N–C(O) amide bonds by selective metal insertion into the N–C(O) bond.[13] To date, the vast majority of these transformations involve a ground-state amide distortion[14] such as twisted cyclic imides reported by our group[14a,b,g,h] and acyclic twisted imides reported independently by Zou[14c] and Garg,[14d,e] where N-coordination[7f,g] is believed to activate the amide bond towards metal insertion (Figure 1 B). Moreover, while deuterium labeling has been used to investigate mechanisms of amide bond activation,[6a] the NH proton undergoes exchange. Thus, a straightforward access to N-alkylated amides would shed light on the mechanistic details of the N–C bond activation reactions.

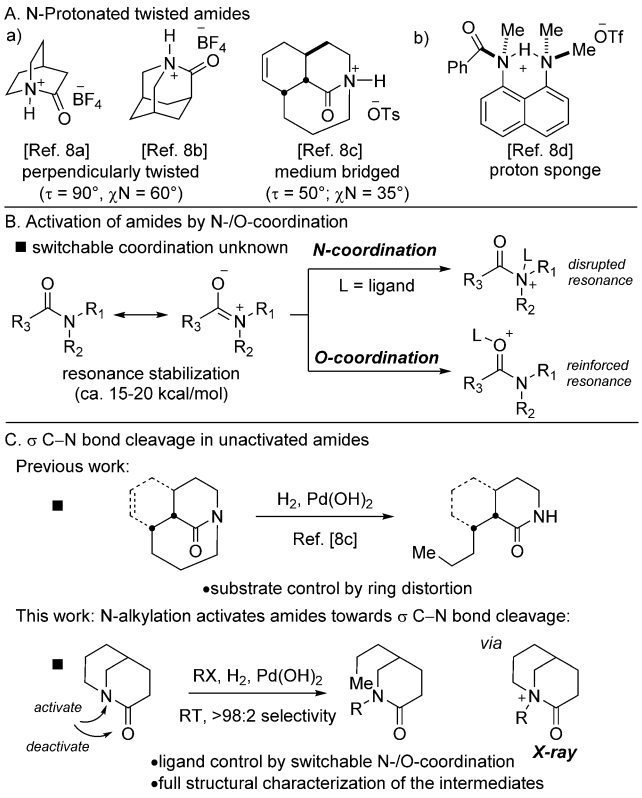

Figure 1. A) Previously reported examples of structurally-characterized N-protonated amides. B) Activation of amides by N-/O-coordination. C) This work: the first structural characterization and N–C cleavage of N-alkylated twisted amides.

Herein, we demonstrate the first structural characterization of N-alkylated twisted amides prepared directly by N-alkylation of the corresponding non-planar lactams. Most crucially, we demonstrate that N-alkylation activates the otherwise unreactive amide bond adjacent to N–C(O) towards amide σ C–N bond cleavage (Figure 1 C). This study provides the first experimental evidence that N-

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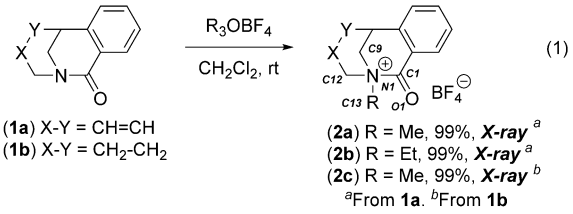
alkylation results in a dramatic increase of non-planarity around the twisted N–C(O) amide bond. A direct comparison of neutral, N-protonated and N-alkylated amides in the same series of compounds is provided. We present a unique example of a molecular wire supported by the amide C=O–Ag bonds in the same amide scaffold. Reactivity studies demonstrate rapid nucleophilic addition to the N–C(O) moiety of N-alkylated amides, indicating the lack of n_N to $\pi^*_{C=O}$ conjugation. The mechanistic details have important implications for the amide bond resonance and the design of catalytic processes involving σ N–C bond activation.

The challenge of isolating N-alkylated non-planar amides is readily evident from the elegant studies by Brown[11] and Aubé[8c] on the reactivity of medium bridged lactams with alkylating reagents, in which susceptibility of the formed ammonium salts towards hydrolysis prevented the successful isolation and/or structural characterization. To begin to understand the role of amide bond twist and structural changes, we screened a series of non-planar amides using various alkylating reagents.[15] We were delighted to discover that twisted amide **1a** readily prepared via the intramolecular Heck reaction,[16] undergoes completely selective (N- vs. O-) alkylation at the nitrogen atom upon treatment with Meerwein's reagent containing a non-nucleophilic counterion, to afford the corresponding salt **2a** in quantitative yield [Eq. (1)].



(1)

The corresponding ethyl salt **2b** was also obtained in excellent yield, while the reaction of the fully saturated analogue **1b** (see below) demonstrated that the internal olefin is not required for the alkylation and stability. The N-alkylated products **2a**–**2c** were crystalline, and their structures could be unambiguously confirmed by X-ray crystallography (Figure 2). Table 1 summarizes the Winkler–Dunitz distortion parameters τ, χ_N and χ_C, and bond lengths of the N-alkylated lactams.[17] Notably, we also solved the crystal structure of the neutral amide **1a** (see Supporting Information (SI)). The availability of this structure allows ready comparison between the neutral amide and its N-alkylated salts. Furthermore, we have succeeded in the synthesis of N-protonated salts of **1a** using HBF_4 and $HSbF_6$. Both of these salts are thermally stable and give crystals suitable for structure determination (**3a**, **3b**, Figure 3, see SI and Table 1).

The structure of **2a** (N-Me salt) shows that N-methylation significantly enhances the pyramidal character of nitrogen (χ_N). The resulting change is substantial giving practically pyramidalized nitrogen of $sp^{2.97}$ (**2a**, χ_N increases from 49.7 to 58.3°). This is accompanied by a dramatic increase of N–C bond twist (**2a**, τ changes from 30.7 to 44.0°) and flattening of

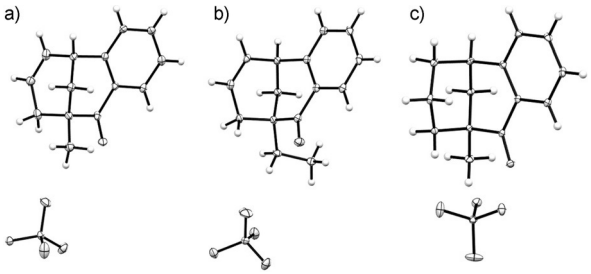


Figure 2. Crystal structures of a) **2a**, b) **2b**, and c) **2c**. Selected bond lengths (Å) and angles (deg) in **2a**: N1–C1 1.554(3), C1–O1 1.192(3), C1–C2 1.466(3), N1–C13 1.503(3); C9-N1-C1-O1 165.7(2), C12-N1-C1-O1 −72.6(3), C9-N1-C1-C2 −15.3(3), C12-N1-C1-C2 106.4(2). **2b**: N1–C1 1.546(2), C1–O1 1.192(2), C1–C2 1.467(2), N1–C13 1.521(2); C9-N1-C1-O1 168.6(1), C12-N1-C1-O1 −71.8(1), C9-N1-C1-C2 −11.6(2), C12-N1-C1-C2 108.0(1). **2c**: N1–C1 1.536(1), C1–O1 1.196(1), C1–C2 1.466(2), N1–C13 1.505(2); C9-N1-C1-O1 156.3(1), C12-N1-C1-O1 −83.0(1), C9-N1-C1-C2 −27.3(1), C12-N1-C1-C2 93.4(1).

Table 1: Summary of structural parameters.[a]

Entry	Amide	N–C(O) [Å]	C=O [Å]	χ_N [deg]	χ_C [deg]	τ [deg]
1	**1a**	1.386	1.226	49.7	7.1	30.7
2	**2a**	1.554	1.192	58.3	1.0	44.0
3	**2b**	1.546	1.192	60.4	0.2	41.7
4	**2c**	1.536	1.196	59.3	3.6	55.2
5	**3a**	1.522	1.201	55.2	0.9	42.8
6	**3b**	1.539	1.196	55.0	0.7	42.0
7	**4**	1.355	1.262	47.7	5.8	33.3
8	**1c**	1.349	1.193	0.0	0.0	0.0

[a] **1c**: Formamide, calculated values (Ref. [7a]).

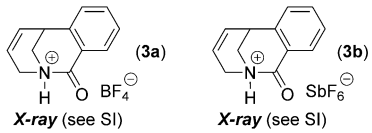


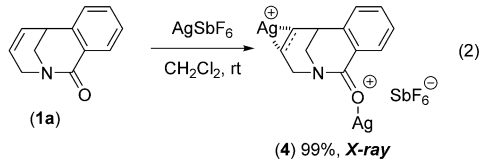
Figure 3. Structures of N-alkylated amides prepared by selective N-protonation of neutral amide **1a**.

the carbon atom (**2a**, χ_C decreases from 7.1 to 1.0°). The observed bond lengths in **2a** are N–CO bond length of 1.554 Å, and C=O bond length of 1.192 Å. This corresponds to a significant N–CO lengthening (by 0.168 Å) and a moderate shortening of the C=O bond (by 0.034 Å). Notably the N–CO amide bond length of 1.554 Å in **2a** is the longest recorded so far for an amide derivative.[18] Overall, the structural changes indicate that the amide bond in **1a** undergoes nitrogen rehybridization and bond rotation upon N-methylation.[8i]

The X-ray structure of N-protonated **1a** (**3a**, HBF_4 salt, see SI) reveals a N–C(O) bond distance of 1.522 Å and a C=O bond distance of 1.201 Å, which while still exceptional, clearly indicate that the amide bond in **1a** undergoes a smaller amide bond distortion upon N-protonation (cf. N-alkylation, **2a** and **2b**).[8a–d] Other distortion parameters in **3a** ($\tau = 42.8$; $\chi_N =$

55.2; $\chi_C = 0.9$) are in agreement with a less substantial amide bond rehybridization upon N-protonation.

We have also succeeded in the synthesis and full characterization of a rare O-coordinated silver salt of an amide bearing a single coordination site [Eq. (2)].[19]



Ligand coordination increases the rotational barrier (O-coordination) or disrupts the amide bond resonance (N-coordination).[20] Lectka[5a,b] and Bannwarth[5c,d] have reported studies on the role of Cu^{II} on the amide bond resonance with multiple binding sites. To date, the effect of N-/O-switchable metal coordination on the properties of amides has not been documented. The observed lengths of the N–C(O) bond in **4** are 1.355 Å, while the length of the C=O bond is 1.262 Å (Figure 4). Thus, N–C(O) experiences moderate shortening

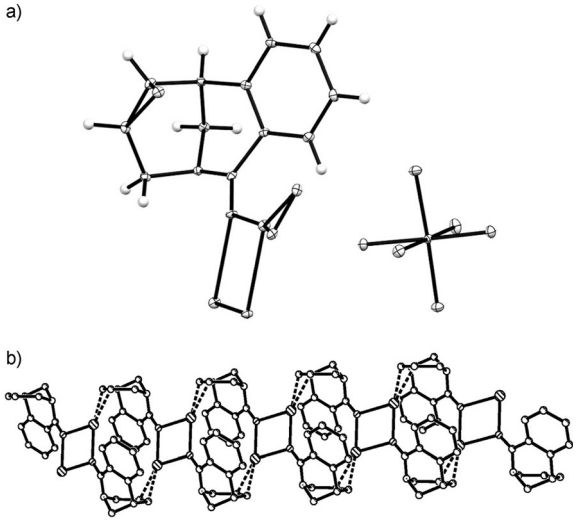
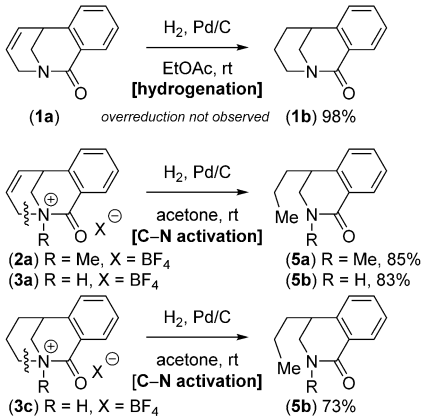


Figure 4. Crystal structure of **4**. a) Single molecule. b) Part of an infinite chain. SbF_6 counterions are not shown. Selected bond lengths (Å) and angles (deg) in **4**: N1–C1 1.355(5), C1–O1 1.262(4), C1–C2 1.475(5), O1–Ag1 2.224(2), C10–Ag2 2.292(3), C11–Ag2 2.463(3), Ag1–F 2.785; C9-N1-C1-O1 173.5(3), C12-N1-C1-O1 −54.3(4), C9-N1-C1-C2 −12.4(5), C12-N1-C1-C2 119.9(3), N1-C1-O1-Ag1 −160.0(2), C2-C1-O1-Ag1 13.8(5), C9-C8-C10-Ag2 116.2(3), N1-C12-C11-Ag2 −68.6(3).

(by 0.031 Å), while C=O is significantly lengthened (by 0.036 Å) upon Ag-coordination in **1a**. These structural changes indicate substantial increase in the double bond character in **1a** upon O-coordination. Strikingly, **4** crystallizes as a one-dimensional wire, displaying infinite chain structure.[21] Ag^I bonds to two carbonyl oxygens from two molecules across a center of symmetry forming a planar parallelogram (104.29° (Ag-O-Ag), 75.71° (O-Ag-O)) with the silver atom stabilized by π-donation from the endocyclic olefin.[22] The O–Ag bond distance is 2.571 Å, which is in a good agreement with the previously reported bond distance for Ag–O bond in glycylglycine of 2.494 Å.[23] The C10–Ag and C11–Ag distances are 2.292 Å and 2.463 Å, which corresponds to olefin–Ag complexes (e.g. $[Ag(\eta^2\text{-}C_2H_4)_3]^+$ of 2.396 Å).[24,25] The propensity of amide **1a** to undergo quantitative N- or O-coordination with different ligands suggests that selective modification of the amide bond rotational barrier may be possible by using appropriate ligands.[5]

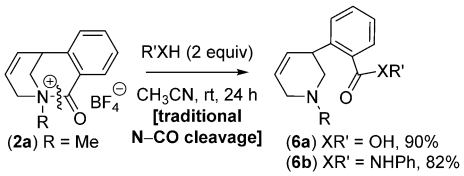
As expected, the chemical reactivity of N-alkylated amides is remarkable. Most notably, although the unactivated neutral precursor **1a** underwent clean hydrogenation under standard catalytic hydrogenation conditions (H_2, Pd/C, EtOAc), subjecting the N-methylated lactam **2a** to identical hydrogenation conditions afforded the sole product resulting from the cleavage of an otherwise unactivated σ C–N bond (Scheme 1).[6a] The reaction was completely regioselective



Scheme 1.

with respect to the C–N bond that is more distorted from the C=O π system. Moreover, the N-protonated lactam **3a** underwent the successful N–C hydrogenolysis, demonstrating that simple protonation is sufficient to trigger the N–C cleavage.[13b] The successful N–C hydrogenolysis of **5a** lacking an olefin, demonstrates that the internal olefin is not required for the reaction. Overall, these results unambiguously demonstrate that activation of the amide bond by N-coordination triggers novel reactivity of amides.

The N-methylated lactams react instantaneously at room temperature with standard nucleophiles resulting in fully regioselective cleavage of the amidic N–CO bond (structure unambiguously confirmed by X-ray crystallography of a derivative, see SI) (Scheme 2). For instance, the reaction of **2a** with 5 equiv of D_2O in CD_3CN gives a $t_{1/2}$ of 15.6 min, while the reaction of **2a** with 2 equiv of $PhNH_2$ in CD_3CN gives a $t_{1/2}$ of 12.5 min. The N-methylated **2a** is unstable to manipulations in common nucleophilic solvents such as DMSO or MeOH. By contrast, boiling of the neutral lactam **1a** in CH_3CN with H_2O (5 equiv, 100 °C, 24 h) or with $PhNH_2$ (2 equiv, 100 °C) affords only recovered starting material. These reactions



Scheme 2.

unambiguously demonstrate that N-coordination activates the amide linkage towards the nucleophilic opening.

In conclusion, the first structural characterization of N-alkylated twisted amides demonstrates that N-alkylation results in a dramatic increase of the amide bond distortion. A unique O-coordinated amide within the same amide provides insights into the effect of switchable N-/O-coordination. N-coordination triggers the amide bond towards catalytic cleavage of unactivated σ N–C bonds, which may find applications in biological contexts and metal catalyzed reactions of amides.

Acknowledgements

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Keywords: amide bonds · N–C activation · N–C cleavage · N-coordination · twisted amides

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Angew. Chem. **2016**, *128*, 5146–5150

[1] Reviews: a) A. Greenberg, C. M. Breneman, J. F. Liebman, *The Amide Linkage: Structural Significance in Chemistry, Biochemistry and Materials Science*, Wiley, New York, **2000**; b) M. Szostak, J. Aubé, *Chem. Rev.* **2013**, *113*, 5701.

[2] a) B. W. Poland, M. Q. Xu, F. A. Quiocho, *J. Biol. Chem.* **2000**, *275*, 16408; b) A. Romanelli, A. Shekhtman, D. Cowburn, T. W. Muir, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 6397; c) P. Shemella, B. Pereira, Y. M. Zhang, P. Van Roey, G. Belfort, S. Garde, S. K. Nayak, *Biophys. J.* **2007**, *92*, 847; d) D. G. A. Johansson, G. Wallin, A. Sandberg, B. Macao, J. Aqvist, T. Hard, *J. Am. Chem. Soc.* **2009**, *131*, 9475.

[3] a) A. Williams, *J. Am. Chem. Soc.* **1976**, *98*, 5645; b) V. Somayaji, R. S. Brown, *J. Org. Chem.* **1986**, *51*, 2676; c) C. L. Perrin, *Acc. Chem. Res.* **1989**, *22*, 268; d) R. S. Brown, A. J. Bennet, H. Slebocka-Tilk, *Acc. Chem. Res.* **1992**, *25*, 481; e) J. I. Mujika, J. M. Mercero, X. Lopez, *J. Am. Chem. Soc.* **2005**, *127*, 4445; f) B. Wang, Z. Cao, *Chem. Eur. J.* **2011**, *17*, 11919.

[4] a) R. K. Harrison, R. L. Stein, *Biochemistry* **1990**, *29*, 1684; b) J. Liu, M. W. Albers, C. M. Chen, S. L. Schreiber, C. T. Walsh, *Proc. Natl. Acad. Sci. USA* **1990**, *87*, 2304; c) G. Fischer, *Chem. Soc. Rev.* **2000**, *29*, 119; d) C. M. Eakin, A. J. Berman, A. D. Miranker, *Nat. Struct. Mol. Biol.* **2006**, *13*, 202; e) F. X. Schmid, *Adv. Protein Chem.* **2002**, *59*, 243.

[5] a) C. Cox, D. Ferraris, N. N. Murthy, T. Lectka, *J. Am. Chem. Soc.* **1996**, *118*, 5332; b) C. Cox, T. Lectka, *Acc. Chem. Res.* **2000**, *33*, 849; c) U. Jakob, T. O. Petersen, W. Bannwarth, *J. Organomet. Chem.* **2015**, *797*, 46; d) M. C. Bröhmer, S. Mundinger, S. Bräse, W. Bannwarth, *Angew. Chem. Int. Ed.* **2011**, *50*, 6175; *Angew. Chem.* **2011**, *123*, 6299.

[6] a) Y. Lei, A. D. Wrobleski, J. E. Golden, D. R. Powell, J. Aubé, *J. Am. Chem. Soc.* **2005**, *127*, 4552; b) T. Shimada, I. Nakamura, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 10546; c) M. Ito, A. Sakaguchi, C. Kobayashi, T. Ikariya, *J. Am. Chem. Soc.* **2007**, *129*, 290; d) S. Ueno, N. Chatani, F. Kakiuchi, *J. Am. Chem. Soc.* **2007**, *129*, 6098; e) Y. Kajita, S. Matsubara, T. Kurahashi, *J. Am. Chem. Soc.* **2008**, *130*, 6058; f) Y. Yoshino, T. Kurahashi, S. Matsubara, *J. Am. Chem. Soc.* **2009**, *131*, 7494; g) M. Tobisu, K. Nakamura, N. Chatani, *J. Am. Chem. Soc.* **2014**, *136*, 5587.

[7] a) A. Greenberg, C. A. Venanzi, *J. Am. Chem. Soc.* **1993**, *115*, 6951; b) A. Greenberg, D. T. Moore, T. D. DuBois, *J. Am. Chem. Soc.* **1996**, *118*, 8658; c) C. R. Kemnitz, M. J. Loewen, *J. Am. Chem. Soc.* **2007**, *129*, 2521; d) S. A. Glover, A. A. Rosser, *J. Org. Chem.* **2012**, *77*, 5492; e) J. Morgan, A. Greenberg, J. F. Liebman, *Struct. Chem.* **2012**, *23*, 197; f) R. Szostak, J. Aubé, M. Szostak, *Chem. Commun.* **2015**, *51*, 6395; g) R. Szostak, J. Aubé, M. Szostak, *J. Org. Chem.* **2015**, *80*, 7905; h) K. B. Wiberg, *Acc. Chem. Res.* **1999**, *32*, 922.

[8] a) K. Tani, B. M. Stoltz, *Nature* **2006**, *441*, 731; b) I. V. Komarov, S. Yanik, A. Y. Ishchenko, A. J. Davies, J. M. Goodman, A. J. Kirby, *J. Am. Chem. Soc.* **2015**, *137*, 926; c) M. Szostak, L. Yao, V. W. Day, D. R. Powell, J. Aubé, *J. Am. Chem. Soc.* **2010**, *132*, 8336; d) C. Cox, H. Wack, T. Lectka, *Angew. Chem. Int. Ed.* **1999**, *38*, 798; *Angew. Chem.* **1999**, *111*, 864; Hydrated 2-azaadamantanone: e) A. J. Kirby, I. V. Komarov, N. Feeder, *J. Chem. Soc. Perkin Trans. 2* **2001**, 522; *N*-protonation in the 2-qunuclidone series: f) E. I. Levkoeva, E. S. Nikitskaya, L. N. Yakhontov, *Dokl. Akad. Nauk SSSR* **1970**, *192*, 342; g) H. Pracejus, M. Kehlen, H. Kehlen, H. Matschin, *Tetrahedron* **1965**, *21*, 2257; For other selected examples of twisted amides, see: h) C. G. Bashore, I. J. Samardjiev, J. Bordner, J. W. Coe, *J. Am. Chem. Soc.* **2003**, *125*, 3268; i) T. G. Lease, K. J. Shea, *J. Am. Chem. Soc.* **1993**, *115*, 2248; j) B. Sliter, J. Morgan, A. Greenberg, *J. Org. Chem.* **2011**, *76*, 2770.

[9] "The Amide Linkage as a Ligand-Its Properties and the Role of Distortion": A. Greenberg in *The Amide Linkage: Structural Significance in Chemistry, Biochemistry and Materials Science* (Eds.: A. Greenberg, C. M. Breneman, J. F. Liebman), Wiley, New York, **2000**.

[10] a) C. Walsh, *Posttranslational Modifcation of Proteins: Expanding Nature's Inventory*, Roberts & Company, **2005**; b) D. H. Scharf, A. Habel, T. Heinekamp, A. A. Brakhage, C. Hertweck, *J. Am. Chem. Soc.* **2014**, *136*, 11674; c) R. Oliyai, V. J. Stella, *Annu. Rev. Pharmacol. Toxicol.* **1993**, *33*, 521; d) Y. Gao, T. Kodadek, *Chem. Biol.* **2013**, *20*, 360; e) S. Donadio, H. M. Perks, K. Tsuchiya, E. H. White, *Biochemistry* **1985**, *24*, 2447; f) H. Nair, A. Somogyi, V. H. Wysocki, *J. Mass Spectrom.* **1996**, *31*, 1141; g) Y. P. Tu, A. G. Harrison, *J. Am. Soc. Mass Spectrom.* **1998**, *9*, 454; For a leading reference on enzymatic N-dealkylation of amides, see: h) L. R. Hall, R. P. Hanzlik, *J. Biol. Chem.* **1990**, *265*, 12349.

[11] Only few examples of isolated N-alkylated non-planar amides have been reported to date. These compounds contained perfectly perpendicular amide bonds (Refs. [8e–g]), or were stabilized by the transannular effects (Ref. [8c]). For a twist dependent switch of N-/O-alkylation in quinuclidone derivatives, see: N. H. Werstiuk, R. S. Brown, Q. Wang, *Can. J. Chem.* **1996**, *74*, 524.

[12] I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, Hoboken, **2010**.

[13] a) A. de Meijere, S. Bräse, M. Oestreich, *Metal-Catalyzed Cross-Coupling Reactions and More*, Wiley, Hoboken, **2014**; b) K. Ouyang, W. Hao, W. X. Zhang, X. Xi, *Chem. Rev.* **2015**, *115*, 12045.

[14] Suzuki reaction: a) G. Meng, M. Szostak, *Org. Lett.* **2015**, *17*, 4364; Heck reaction: b) G. Meng, M. Szostak, *Angew. Chem. Int. Ed.* **2015**, *54*, 14518; *Angew. Chem.* **2015**, *127*, 14726; Suzuki reaction: c) X. Li, G. Zou, *Chem. Commun.* **2015**, *51*, 5089; d) N. A. Weires, E. L. Baker, N. K. Garg, *Nat. Chem.* **2015**, *8*, 75; Esterification: e) L. Hie, N. F. F. Nathel, T. K. Shah, E. L. Baker, X. Hong, Y. F. Yang, P. Liu, K. N. Houk, N. K. Garg, *Nature* **2015**, *524*, 79; Highlight: f) S. Ruider, N. Maulide, *Angew. Chem. Int. Ed.* **2015**, *54*, 13856; *Angew. Chem.* **2015**, *127*, 14062; C–H activation: g) G. Meng, M. Szostak, *Org. Lett.* **2016**, *18*, 796; Suzuki reaction: h) G. Meng, M. Szostak, *Org. Biomol. Chem.* **2016**, *14*, DOI: 10.1039/c6ob00084c.
[15] S. Yamada, *Rev. Heteroat. Chem.* **1999**, *19*, 203.
[16] a) R. Grigg, V. Sridharan, P. Stevenson, T. Worakun, *J. Chem. Soc. Chem. Commun.* **1986**, 1697; For a recent application, see: b) T. P. Ribelin, A. S. Judd, I. Akritopoulou-Zanze, R. F. Henry, J. L. Cross, D. N. Whittern, S. W. Djuric, *Org. Lett.* **2007**, *9*, 5119.
[17] F. K. Winkler, J. D. Dunitz, *J. Mol. Biol.* **1971**, *59*, 169.
[18] R. Hoffmann, H. Hopf, *Angew. Chem. Int. Ed.* **2008**, *47*, 4474; *Angew. Chem.* **2008**, *120*, 4548.
[19] S. Eckhardt, P. S. Brunetto, J. Gagnon, M. Priebe, B. Giese, K. M. Fromm, *Chem. Rev.* **2013**, *113*, 4708.
[20] R. Fussenegger, B. M. Rode, *Chem. Phys. Lett.* **1976**, *44*, 95.
[21] P. F. H. Schwab, M. D. Levin, J. Michl, *Chem. Rev.* **1999**, *99*, 1863.
[22] J. Burgess, P. J. Steel, *Coord. Chem. Rev.* **2011**, *255*, 2094.
[23] T. Shoeib, C. F. Rodriquez, K. W. M. Siu, A. C. Hopkinson, *Phys. Chem. Chem. Phys.* **2001**, *3*, 853.
[24] I. Krossing, A. Reisinger, *Angew. Chem. Int. Ed.* **2003**, *42*, 5725; *Angew. Chem.* **2003**, *115*, 5903.
[25] Computations predict monodentate binding in Ag^{I}/amide complexes: a) V. Romanov, C. K. Siu, U. H. Verkerk, H. El Aribi, A. L. Hopkinson, K. W. M. Siu, *J. Phys. Chem. A* **2008**, *112*, 10912; b) V. Romanov, C. K. Siu, U. H. Verkerk, A. C. Hopkinson, K. W. M. Siu, *J. Phys. Chem. A* **2010**, *114*, 6964.

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