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Manuscript Title:

$Zn(OTf)_2$-catalyzed addition of amines to carbodiimides: efficient synthesis of guanidines and unpredicted formation of Zn–N amido species

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Contents:

1) Characterization Data

1. Colorless solid, yield 97%. ^{1}H NMR (400 MHz, C_6D_6): δ 0.91 (d, J = 6.4 Hz, 12H, CH_3), 3.52 (br, 2H, NH), 3.64-3.69 (m, 2H, CH), 6.90 (t, J = 7.6 Hz, 1H, p-C_6H_5), 7.10 (d, J = 7.6 Hz, 2H, o-C_6H_5), 7.25 (t, J = 7.6 Hz, 2H, m-C_6H_5). ^{13}C NMR (100 MHz, C_6D_6): δ 23.4, 43.4, 121.3, 123.7, 129.6, 149.7, 151.6. [1]

2. Colorless solid, yield 96%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.08-2.03 (m, 20H, CH_2), 3.42 (br, 2H, NH), 3.63 (br, 2H. CH), 6.86-7.23 (m, 5H, C_6H_5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.6, 25.3, 33.4, 49.8, 120.9, 123.3, 128.8, 149.6, 150.1. [2]

3. Colorless solid, yield 96%. ^{1}H NMR (400 MHz, C_6D_6): δ 1.20 (s, 18H, CH_3), 3.67 (br, 2H, NH), 6.92-7.25 (m, 5H, C_6H_5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.0, 50.6, 121.4, 123.5, 129.5, 149.9, 151.5. [3]

4. Colorless solid, yield 91%. ^{1}H NMR (300 MHz, C_6D_6): δ 4.37-4.47 (m, 4H, CH_2 and NH), 6.87-7.16 (m, 15H, C_6H_5). ^{13}C NMR (75 MHz, C_6D_6): δ 46.3, 123.0, 124.4, 127.9, 128.9, 129.0, 130.1, 132.1, 132.2, 136.3, 136.4, 154.6, 154.8. [4]

5. Colorless solid, yield 97%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.88 (d, J = 6.3 Hz, 12 H, CH_3), 3.26-3.67 (m, 4H, CH and NH), 6.84-7.16 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 23.2, 43.19, 116.1 (d, J = 21.6 Hz), 124.5 (d, J = 7.43 Hz), 147.6 (d, J = 2.48 Hz), 150.0 (d, J = 1.28 Hz), 160.1. [3]

6. Colorless solid, yield 97%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.78 (d, J = 6.3 Hz, 12H, CH_3), 3.33 (br, 2H, NH), 3.46-3.52 (m, 2H, CH), 6.78-7.11 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 23.3, 43.4, 121.1, 121.9, 123.7, 130.5, 135.0, 149.8, 153.3. [1]

7. Colorless solid, yield 97%. ^{1}H NMR (400 MHz, C_6D_6): δ 0.86 (d, J = 6.4 Hz, 12H, CH_3), 3.37 (br, 2H, NH), 3.55-3.60 (m, 2H, CH), 6.68-7.31 (m, 4H, C_6H_4). ^{13}C NMR (100 MHz, C_6D_6): δ 23.3, 43.4, 113.7, 125.4, 132.5, 149.6, 150.7. [1]

8. Colorless solid, yield 95%. ^{1}H NMR (400 MHz, C_6D_6): δ 0.93 (d, J = 6.8 Hz, 12H, CH_3), 3.32 (br, 2H, NH), 3.59-3.68 (m, 2H, CH), 6.41-7.87 (m, 4H, C_6H_4). ^{13}C NMR (100 MHz, C_6D_6): δ 23.7, 43.5, 97.3, 122.9, 123.1, 129.3, 139.6, 149.3, 152.6. [1]

9. Colorless solid, yield 96%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.91 (d, J = 6.3 Hz, 12 H, CH_3), 1.32 (d, J = 6.9 Hz, 6H, CH_3), 3.36-3.63 (m, 5H, CH and NH), 6.94-7.33 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 23.3, 23.4, 28.6, 43.3, 122.1, 123.0, 126.2, 126.7, 142.2, 148.5, 148.8.[3]

10. Colorless solid, yield 94%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.89 (d, J = 6.0 Hz, 12H, CH_3), 2.82 (s, 1H, CH), 3.54-3.67 (m, 4H, CH and NH), 6.99-7.17 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 23.1, 43.2, 77.2, 84.6, 123.6, 124.6, 125.0, 127.1, 129.6, 150.1, 151.7. [3]

11. Colorless solid, yield 97%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89-1.21 (m, 12H, CH_3), 2.27 (s, 6H, *o*-CH_3), 2.30 (s, 3H, *p*-CH_3), 3.39 (br, 2H, NH), 4.10 (br, 2H, CH), 6.92 (s, 2H, C_6H_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.1, 20.7, 23.5, 43.1, 128.7, 130.7, 143.3, 148.0. [5]

12. Colorless solid, yield 95%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.95 (d, J = 6.3 Hz, 12H, CH_3), 3.45 (s, 3H, CH_3), 3.69-3.74 (m, 4H, CH and NH), 6.74-7.17 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 23.3, 43.4, 55.5, 113.1, 122.0, 122.4, 125.0, 140.2, 150.0, 152.8. [6]

13. Colorless solid, yield 85%, m. p. 125.3~125.8 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12 (d, J = 4.8 Hz, 12H, CH_3), 3.71 (br, 4H, CH and NH), 6.80-8.06 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.7, 43.1, 122.0, 125.2, 139.7, 151.0, 158.4. HRMS calcd. for $C_{14}H_{21}N_4$: 245.1761, found 245.1757. [2]

16. Colorless solid, yield 95%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.87 (d, J = 6.0 Hz, 12H, CH_3), 1.05 (t, J = 7.2 Hz, 3H, CH_3), 3.55-3.64 (m, 4H, CH, NH), 4.13-4.20 (q, J = 6.9 Hz, 2H, CH_2), 7.06-8.27 (m, 4H, C_6H_4). ^{13}C NMR (75 MHz, C_6D_6): δ 14.4, 23.1, 43.3, 60.3, 123.2, 131.7, 149.8, 156.6, 166.6. [2]

17. white solid, yield 94%. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.12 (d, J = 6.6 Hz, 24H, CH_3), 3.46 (br, 4H, CH), 3.78 (br, 4H, NH), 6.67 (s, C_6H_4). ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.8, 42.3, 123.3, 145.7, 150.4. [7]

18. Colorless solid, yield 95%. ^{1}H NMR (300 MHz, C_6D_6): δ 0.99 (d, J = 6.3 Hz, 12H, CH_3), 3.73-3.89 (m, 2H, CH), 6.80-8.29 (m, 3H, C_5H_3N). ^{13}C NMR (75 MHz, C_6D_6): δ 23.3, 42.6, 78.9, 123.3, 144.5, 151.3, 153.9, 162.7. [1]

19. Colorless solid, yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (d, J = 6.4 Hz, 12H, CH_3), 2.22 (s, 3H, CH_3), 3.87 (br, 2H, CH), 6.08 (s, 1H, CH(thiazolyl))). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6, 23.2, 42.6, 102.5, 146.9, 152.4, 175.1. [1]

19a. Colorless liquid, yield 94%. ^{1}H NMR (300 MHz, C_6D_6): δ 1.14 (d, J = 6.3 Hz, 12H, CH_3), 1.48 (t, 4H, CH_2), 3.31 (t, 4H, CH_2), 3.35-3.40 (m, 2H, CH). 7.15 (s, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 24.8, 25.4, 46.9, 48.3, 153.0. [8]

These data of compounds **1-13** and **16-19** are consistent with those reported.

References:

(1) W.-X. Zhang, M. Nishiura and Z. Hou, *Chem. Eur. J.,* 2007, **13**, 4037–4051;

(2) Q. Li, S. Wang, S. Zhou, G. Yang, X. Zhu and Y. Liu, *J. Org. Chem.,* 2007, **72**, 6763–6767.

(3) W.-X. Zhang, D. Li, Z. Wang and Z. Xi, *Organometallics,* 2009, **28**, 882–887.

(4) K. Ramadas, N. Janarthanan and R. Pritha, *Synlett,* 1997, 1053-1054.

(5) F. Montilla, A. Pastor and A. Galindo, *J. Organomet. Chem.,* 2004, **689**, 993–996.

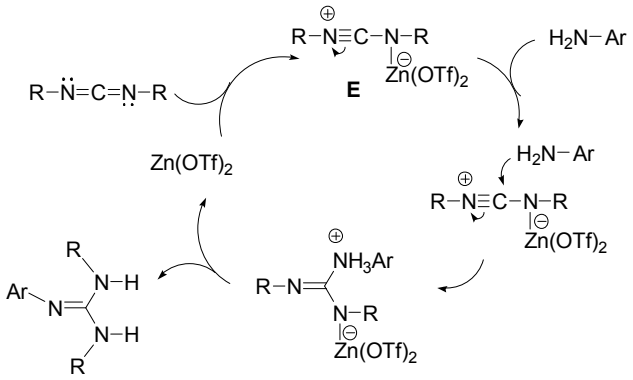
(6) Z. Du, W. Li, X. Zhu, F. Xu, and Q. Shen, *J. Org. Chem.,* 2008, **73**, 8966–8972.

(7) T.-G. Ong, G. P. A. Yap and D. S. Richeson, *J. Am. Chem. Soc.,* 2003, **125**, 8100–8101.

(8) X. Zhu, Z, Du, F. Xu and Q. Shen, *J. Org. Chem.,* 2009, **74**, 6347–6349.

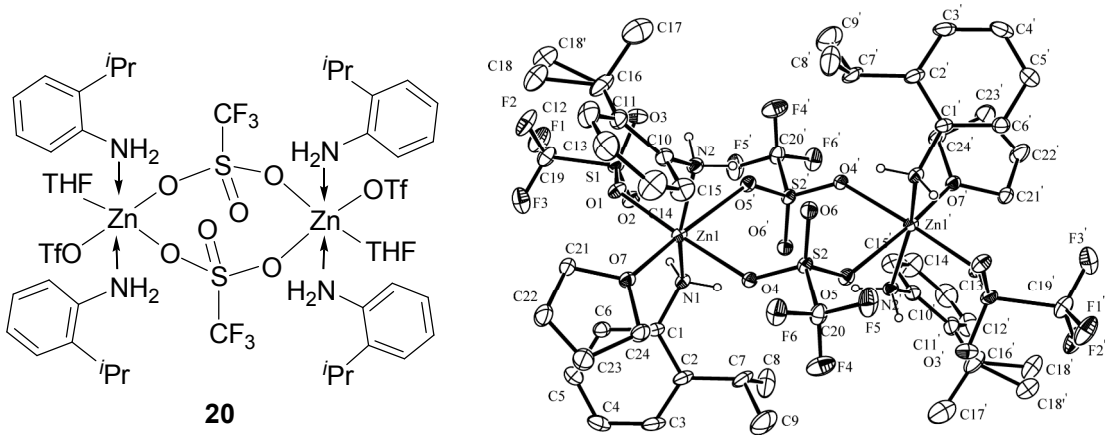
2) An alternative mechanism for the formation of guanidines

$Zn(OTf)_2$ acted as Lewis acid catalyst to activate a carbodiimide yielding the intermediate $RN^{\oplus}{\equiv}C{-}NR{-}Zn^{\ominus}(OTf)_2$ (**E**). Nucleophilic addition of an amine to **E** and proton transfer gave rise to the guanidine and regenerated $Zn(OTf)_2$. see: N. Yamamoto and M. Isobe, *Chem. Lett.,* 1994, 2299–2302.



3) X-ray crystallographic studies for 20 and 22

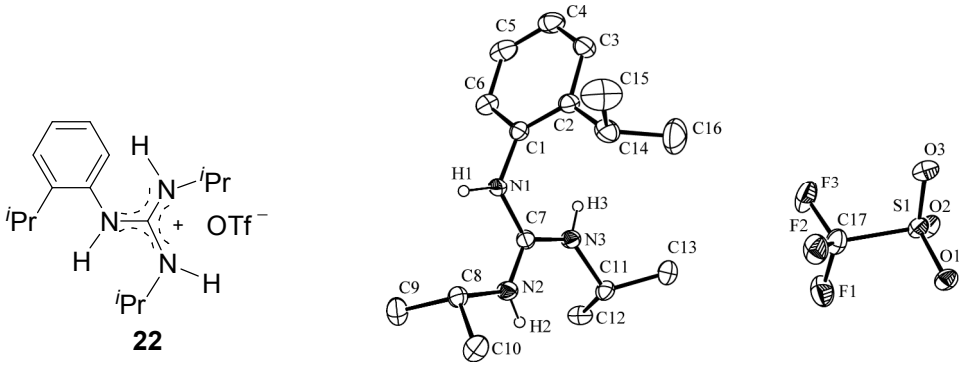
Crystals for X-ray analyses of **20** and **22** were obtained as described in the preparations. Data collections were performed at –100 °C on a Rigaku SATURN 724+ CCD diffractometer, using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The determination of crystal class and unit cell parameters was carried out by the CrystalClear (Rigaku Inc., 2008) program package. The raw frame data were processed using the CrystalClear (Rigaku Inc., 2008) to yield the reflection data file. The structure was solved by use of SHELXTL program. Refinement was performed on F^2 anisotropically for all the non-hydrogen atoms by the full-matrix least-squares method. The hydrogen atoms were placed at the calculated positions and were included in the structure calculation without further refinement of the parameters. Crystal data, data collection and processing parameters for **20** and **22** were given only in Supporting Information. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-741356 (**20**), and CCDC-741355 (**22**). Copies of these data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



SFig. 1 ORTEP drawing of **20** with 30% thermal ellipsoids. Hydrogen atoms, except those on the nitrogen atoms, are omitted for clarity.

STable 1. Crystal data and structure refinement for **20**.

Identification code	**20**	
Empirical formula	$C_{48}\ H_{68}\ F_{12}\ N_4\ O_{14}\ S_4\ Zn_2$	
Formula weight	1412.04	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	I4(1)/a	
Unit cell dimensions	a = 35.199(5) Å	α = 90 °
	b = 35.199(5) Å	β = 90 °
	c = 11.268(2) Å	γ = 90 °
Volume	13960(4) Å^3	
Z	8	
Density (calculated)	1.344 Mg/m^3	
Absorption coefficient	0.894 mm^{-1}	
F(000)	5824	
Crystal size	0.35 x 0.25 x 0.10 mm^3	
Theta range for data collection	1.16 to 25.00 °.	
Index ranges	-41<= h <= 41, -41<= k <= 41, -13 <= l <= 13	
Reflections collected	62839	
Independent reflections	6130 [$R_{(int)}$ = 0.0623]	
Completeness to theta = 25.00 °	99.7 %	
Absorption correction	Numerical	
Max. and min. transmission	0.9160 and 0.7450	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6130 / 21 / 391	
Goodness-of-fit on F^2	1.067	
Final R indices [I>2sigma(I)]	R_1 = 0.0644, wR_2 = 0.1956	
R indices (all data)	R_1 = 0.0681, wR_2 = 0.1999	
Largest diff. peak and hole	0.649 and -0.693 e. Å^{-3}	



SFig. 2 ORTEP drawing of **22** with 30% thermal ellipsoids. Hydrogen atoms, except those on the nitrogen atoms, are omitted for clarity.

STable 2. Crystal data and structure refinement for **22.**

Identification code	**22**
Empirical formula	$C_{17}H_{28}F_3N_3O_3S$
Formula weight	411.48
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, Pna2(1)
Unit cell dimensions	a = 16.419(3) Å α = 90 °.
	b = 12.458(3) Å β = 90 °.
	c = 10.520(2) Å γ = 90 °.
Volume	2151.8(7) Å^3
Z, Calculated density	4, 1.270 Mg/m^3
Absorption coefficient	0.196 mm^{-1}
F(0 0 0)	872
Crystal size	0.30 x 0.29 x 0.13 mm
Theta range for data collection	2.82 to 27.49 °.
Limiting indices	-14 <= h <= 21, -16 <= k <= 16, -13 <= l <= 12
Reflections collected / unique	16883 / 4604 [$R_{(int)}$ = 0.0369]
Completeness to theta = 27.49 °	99.7 %
Absorption correction	Numerical
Max. and min. transmission	0.9749 and 0.9435
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4604 / 1 / 244
Goodness-of-fit on F^2	1.082
Final R indices [I>2sigma(I)]	R_1 = 0.0441, wR_2 = 0.0945
R indices (all data)	R_1 = 0.0482, wR_2 = 0.0977
Absolute structure parameter	0.00(8)
Largest diff. peak and hole	0.185 and -0.200 e. Å^{-3}

4) Copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds