Organic Process Research & Development **2010,** *14,* 1299–1303

Scaleable Preparation of Sensitive Functionalized Aromatics and Heteroaromatics via Directed Metalation Using tmpZnCl · LiCl

Tomke Bresser, Gabriel Monzon, Marc Mosrin, and Paul Knochel*

Ludwig-Maximilians-Universität München, Department Chemie, Butenandtstrasse 5-13, Haus F, 81377 München, Germany

Abstract:

A range of functional aryl and heteroaryl zinc reagents were prepared in THF via directed zincation using the previously reported amide base tmpZnCl·LiCl. These metalation reactions were carried out on 50 mmol scale. Diverse sensitive functional groups such as a nitro group, an aldehyde, an ester, and a nitrile are tolerated. Furthermore, the resulting zinc intermediates show excellent reactivity towards various classes of electrophiles, e.g. Pd-catalyzed cross-coupling reactions or Cu-catalyzed acylations and allylations. In all cases, the metalation rates have been compared with those of the corresponding small-scale reactions (1−2 mmol). Moreover, the recovery of the valuable tmp-H from the aqueous phase has been demonstrated.

Introduction

Directed metalation reactions of unsaturated substrates have become more significant since they facilitate the functionalization of these scaffolds and provide important intermediates in organic synthesis.[1] Functional group tolerance is still a challenge and makes the preparation of functionalized organometallic compounds more complicated. For the performance of such transformations, the use of lithium bases has been carefully investigated, although the functional group tolerance is only modest.[2] In addition to the pioneering work of Snieckus and Beak,[3] a number of new selective bases for achieving regio- and chemoselective metalations have already been reported by Kondo, Uchiyama, Mongin, and Mulvey; especially, mixed -ate bases have found useful applications.[4] Recently, we have shown that magnesium bases such as tmpMgCl·LiCl[5] (tmp = 2,2,6,6-tetramethylpiperidyl) or $tmp_2Mg \cdot 2LiCl$[5h,6] proved to be highly active and selective magnesium bases even though highly sensitive functionalities such as an aldehyde or a nitro group are not tolerated with such bases. Additionally, we have also prepared the chemoselective base $tmp_2Zn \cdot 2MgCl_2 \cdot 2LiCl$[7] that allows the directed zincation of more sensitive aromatics and heteroaromatics. However, using this reagent with some electron-poor aromatic and heterocyclic compounds still gives unsatisfactory results in terms of yields and regioselectivity. Moreover, several activated aromatics bearing a nitro group or heterocycles such as pyridazines require metalation temperatures below −50 °C, which is not convenient for reaction upscaling.[8] Therefore, we have studied the preparation of a more selective zinc base, tmpZnCl·LiCl[9] (**1**), that undergoes the directed regio- and chemoselective zincation of sensitive aryl and heteroaryl

* Author for correspondence. Fax: (+49) 089 2180 77680. E-mail: paul.knochel@cup.uni-muenchen.de.

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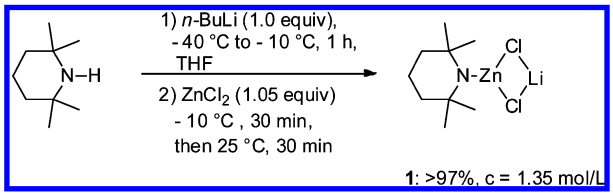
10.1021/op1001935
Published on Web 10/04/2010

Scheme 1. **Preparation of tmpZnCl·LiCl 1**



substrates containing functional groups such as an aldehyde or a nitro group at 25 °C. Its higher selectivity is due to the absence of magnesium salts ($MgCl_2$) and to the nature of the resulting zinc organometallic produced: ArZnX instead of Ar_2Zn (with $tmp_2Zn \cdot 2MgCl_2 \cdot 2LiCl$). The mild base tmpZnCl·LiCl (**1**) is quantitatively prepared by a one-pot procedure, and the THF solution can be stored under an inert gas atmosphere for several weeks at 25 °C. The zincations with this base usually proceed at room temperature. For moderately activated substrates, increased temperatures have to be used (up to 160 °C). Such high reaction temperatures are compatible with the stability of the zinc intermediates and do not reduce the tolerance towards functional groups.[10] Usually, the optimization of these metalation procedures was performed with 1−2 mmol scale. Herein, we report the extension of this commercially available metalation reagent to larger-scale experiments (50 mmol).

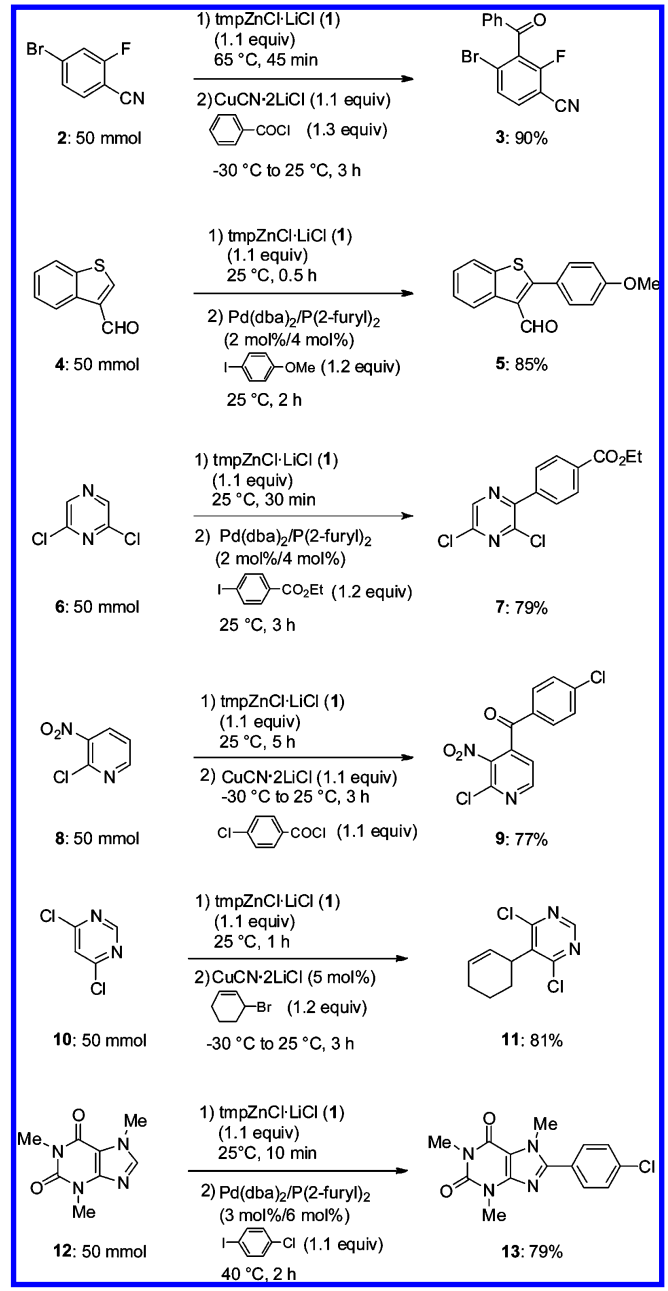
Results and Discussion

For the experiments described in this contribution, the zinc base **1** was prepared in a larger scale than previously described in the literature.[9] Therefore, a dry and argon-flushed 1.0-L Schlenk flask, equipped with a magnetic stirring bar and a rubber septum, was charged with freshly distilled tmp-H (59.5 mL, 350 mmol) dissolved in THF (350 mL). This solution was cooled to −40 °C, and *n*-BuLi (2.3 M in hexane, 152.2 mL, 350 mmol) was dropwise added. After the addition was complete, the reaction mixture was allowed to warm up slowly to −10 °C for 1 h. Then, $ZnCl_2$ (1.0 M in THF, 368 mL, 368 mmol) was dropwise added, and the resulting solution was stirred for 30 min at −10 °C and then for 30 min at 25 °C. The solvents were then removed under high vacuum, affording a yellowish solid. Freshly distilled THF was then slowly added under vigorous stirring until the salts were completely dissolved. The freshly prepared tmpZnCl·LiCl (**1**) solution was titrated prior to use at 0 °C with benzoic acid using 4-(phenylazo)-diphenylamine as indicator.[11] A concentration of 1.35 M in THF was obtained (Scheme 1).

We have carried out several large-scale experiments using tmpZnCl·LiCl (**1**) and further reactions with electrophiles (Scheme 2).

Thus, 2-bromo-4-fluorobenzonitrile (**2**; 9.95 g, 50 mmol) dissolved in THF (50 mL) is reacted with tmpZnCl·LiCl (**1**; 40.7 mL, 1.1 equiv) at 25 °C, and the resulting mixture is warmed to 65 °C for 45 min (same metalation rate as for reactions performed at 1 mmol scale; metalation progress checked by iodolysis of reaction aliquots and gas chromatographical analysis). Quenching with benzoyl chloride (9.1 g, 1.3 equiv) (after the addition of CuCN·2LiCl[12] (55 mL, 1.1 equiv)) furnishes the new substituted benzonitrile **3** in 90% yield. Smooth zincations of arenes and heteroarenes bearing sensitive functionalities such as aldehydes or nitro groups can also be tolerated on larger scales. Thus, the metalation of benzothiophene-3-carbaldehyde (**4**; 8.1 g, 50 mmol) is complete within 30 min at 25 °C using tmpZnCl·LiCl (**1**; 40.7 mL, 1.1 equiv). The corresponding zinc derivative undergoes a Pd-catalyzed cross-coupling reaction[13] with 4-iodoanisole (14.0 g, 1.2 equiv) using $Pd(dba)_2$ (565 mg, 2 mol %) and $P(2\text{-furyl})_3$ (465 mg, 4 mol %)[14] to give after 2 h the corresponding functionalized aldehyde **5** in 85% yield. Similarly, 2,6-dichlo-

Scheme 2. **Zincation of aromatics and heteroaromatics 2, 4, 6, 8, 10, and 12 using tmpZnCl·LiCl (1) and subsequent reactions with electrophiles**



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ropyrazine (**6**; 7.45 g, 50 mmol) is converted into the zincated species within 30 min at 25 °C (same metalation rate compared to 1 mmol scale reactions) using tmpZnCl·LiCl (**1**; 40.7 mL, 1.1 equiv). The trisubstituted pyrazine **7** is obtained in 79% yield after a Neghishi cross-coupling reaction with ethyl 4-iodobenzoate[13] (16.5 g, 1.2 equiv) using $Pd(dba)_2$ (565 mg, 2 mol %) and P(2-furyl)$_3$ (465 mg, 4 mol %).[14] The metalation of 2-chloro-3-nitropyridine (**8**; 7.91 g, 50 mmol) is complete within 5 h at 25 °C. Quenching with 4-chlorobenzoyl chloride (9.63 g, 1.1 equiv) at −30 °C (after transmetalation with CuCN·2LiCl[12] (55 mL, 1.1 equiv) at −30 °C) provides the ketone **9** in 77% yield. Although this yield was not quantitative, the crude GC analysis indicates a clean reaction with few side products, small amounts of pyridine **8**, and acid chloride. The unreacted pyridylzinc reagent gives the chloropyridine **8** back after workup. No attempts were made to recover the starting material to improve the reaction yield further. Other sensitive heterocycles such as pyrimidines or caffeine are zincated at 25 °C. Thus, the metalation of 2,4-dichloropyrimidine (**10**; 7.45 g, 50 mmol) is achieved within 1 h at 25 °C. Trapping with 3-bromocyclohexene (9.7 g, 1.2 equiv) provides after the addition of a catalytic amount of CuCN·2LiCl[12] (5.0 mL, 10 mol %), the allylated pyrimidine **11** in 81%. Remarkably, the full zincation of caffeine (**12**; 9.7 g, 50 mmol) is obtained within 10 min at 25 °C. A Pd(0)-catalyzed cross-coupling reaction[13] with 4-chloro-iodobenzene (13.1 g, 1.1 equiv) using $Pd(dba)_2$ (850 mg, 3 mol %) and P(2-furyl)$_3$ (700 mg, 6 mol %)[14] as catalytic system furnishes the new functionalized purine **13** in 79% yield. The regeneration of 2,2,6,6-tetramethylpiperidine (tmp-H) was carried out as was published recently.[15]

Summary and Outlook

In conclusion, we have shown that regioselective zincations of highly sensitive arenes and heteroaromatics using the mild base tmpZnCl·LiCl (**1**) can safely be carried out on multigram scales with yields comparable to those obtained for small scales. Remarkably, chemoselective zincations can be performed at room temperature and higher temperatures (65 °C), tolerating sensitive functions such as an aldehyde, a nitro group, an ester, or a nitrile.

Experimental Section

General Considerations. All reactions were carried out under air and moisture exclusion. All glassware was oven-dried (80 °C) overnight (minimun of 12 h), evacuated in high vacuum (1×10^{-3} mbar) and backfilled with argon (this procedure was repeated three times). Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under argon. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H NMR (25 °C) and capillary GC analysis. NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (δ 7.25 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR). Column chromatographical purifications were performed using SiO_2 (0.040−0.063 mm, 230−400 mesh ASTM) from Merck. tmp-H, liquid aldehydes, and acid chlorides were distilled prior to use. The completion of the metalation reaction was checked by GC analysis of reaction aliquots (reaction aliquots were quenched with 0.2 mL of a 0.5 M I_2 solution in dry THF, then shaked NH_4Cl (1 mL) and sat. aq $Na_2S_2O_3$ solution (1 mL) and extracted with diethyl ether (1 mL).

Preparation of tmpZnCl·LiCl (1). A dry and argon-flushed 1.0-L Schlenk flask, equipped with a magnetic stirring bar and a rubber septum, was charged with 2,2,6,6-tetramethylpiperidine (59.5 mL, 350 mmol) freshly dissolved in THF (350 mL). This solution was cooled to −40 °C, and *n*-BuLi (2.3 M in hexane, 152.2 mL, 350 mmol) was dropwise added. After the addition was complete, the reaction mixture was allowed to warm up slowly to −10 °C for 1 h. $ZnCl_2$ (1.0 M in THF, 368 mL, 368 mmol, 1.05 equiv) was dropwise added, and the resulting solution was stirred for 30 min at −10 °C and then for 30 min at 25 °C. The solvents were then removed under vacuum, affording a yellowish solid. Freshly distilled THF was then slowly added under vigorous stirring until the salts were completely dissolved. The freshly prepared tmpZnCl·LiCl (**1**) solution was titrated prior to use at 25 °C with benzoic acid using 4-(phenylazo)diphenylamine as indicator. A concentration of 1.35 M in THF was obtained.

Preparation of 3-Benzoyl-4-bromo-2-fluorobenzonitrile (3). To a solution of 2-bromo-4-fluorobenzonitrile (**2**; 9.95 g, 50 mmol) dissolved in THF (50 mL) was added tmpZnCl·LiCl (**1**; 1.35 M in THF, 40.7 mL, 55 mmol) at 25 °C, and the resulting mixture was heated for 45 min at 65 °C. The reaction mixture was then cooled to −30 °C, and CuCN·2LiCl (1 M solution in THF, 55 mL, 55 mmol) was added. After 30 min of stirring at the same temperature, benzoyl chloride (9.1 g, 65 mmol) was added, and the resulting mixture was allowed to warm up slowly to 25 °C within 3 h. The reaction mixture was then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (diethyl ether/pentane, 1:4) furnished the compound **3** (13.6 g, 90%) as a colourless solid. **Mp**: 97.5−98.9 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ: 7.81−7.79 (m, 2 H), 7.70−7.62 (m, 1 H), 7.60−7.59 (m, 2 H), 7.54−7.48 (m, 2 H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ: 189.2, 159.5 (d, J = 263.7 Hz), 135.0, 134.9, 134.3, 130.7 (d, J = 21.0 Hz), 129.7, 129.6, 129.2, 126.4 (d, J = 5.2 Hz), 112.7, 101.3 (d, J = 6.1 Hz). **MS (70 eV, EI)** *m*/*z*: 303 (28) [M^+], 105 (100), 77 (33), 51 (11). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3090, 3073, 2240, 1928, 1740, 1681, 1594, 1578, 1564, 1456, 1449, 1422, 1313, 1284, 1272, 1248, 1171, 1125, 1077, 1001, 987, 966, 938, 886, 832, 789,

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715, 688, 673. **HRMS (EI) Calcd for $C_{14}H_7BrFNO$**, 302.9695; Found, 302.9689.

Preparation of 2-(4-Methoxyphenyl)-1-benzothiophene-3-carbaldehyde (5). To a solution of benzothiophene-3-carbaldehyde (**4**; 8.1 g, 50 mmol) dissolved in THF (50 mL) was added tmpZnCl·LiCl (**1**; 1.35 M in THF, 40.7 mL, 55 mmol) at 25 °C, and the resulting mixture was stirred for 30 min. $Pd(dba)_2$ (565 mg, 2 mol %) and P(2-furyl)$_3$ (465 mg, 4 mol %) dissolved in THF (20 mL) and mixed with 4-iodoanisole (14.0 g, 60 mmol) were then transferred via cannula, and the resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (diethyl ether/pentane, 15:85) furnished the compound **5** (11.3 g, 85%) as a yellowish solid. **Mp**: 81.3−84.9 °C. **^{1}H NMR (600 MHz, $CDCl_3$)** δ: 10.0 (s, 1 H), 8.77 (d, J = 8.2 Hz, 1 H), 7.73 (d, J = 7.9 Hz, 1 H), 7.51−7.45 (m, 3 H), 7.42−7.36 (m, 1 H), 7.01−6.97 (m, 2 H), 3.84 (s, 3 H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ: 186.5, 161.0, 160.8, 137.5, 131.7, 126.0, 125.5, 124.8, 123.7, 121.4, 114.3, 55.3. **MS (70 eV, EI)** m/z: 268 (100) [M^+], 253 (12), 237 (19), 225 (12), 197 (10). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3295, 3028, 2918, 2848, 2767, 1651, 1620, 1602, 1526, 1493, 1458, 1431, 1397, 1351, 1298, 1254, 1222, 1181, 1176, 1097, 1038, 1019, 826, 817, 751, 729, 697. **HRMS (EI) Calcd for $C_{16}H_{12}O_2S$**, 268.0558; Found, 268.0552.

Preparation of Ethyl 4-(3,5-dichloropyrazin-2-yl)benzoate (7). To a solution of 2,6-dichloropyrazine (**6**; 7.45 g, 50 mmol) dissolved in THF (50 mL) was added tmpZnCl·LiCl (**1**) (1.35 M in THF, 40.7 mL, 55 mmol) at 25 °C and the resulting mixture was stirred at this temperature for 30 min. A solution of $Pd(dba)_2$ (565 mg, 2 mol %) and P(2-furyl)$_3$ (465 mg, 4 mol %) dissolved in THF (50 mL) and mixed with 4-iodoethyl benzoate (16.5 g, 60 mmol) was then transferred via cannula to the reaction mixture. The resulting mixture was stirred at 25 °C for 3 h and then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (diethyl ether/pentane, 1:9) furnished the compound **7** (11.7 g, 79%) as a colourless solid. **Mp**: 88.5−90.0 °C. **^{1}H NMR (300 MHz, $CDCl_3$)** δ: 8.59 (s, 1 H), 8.14 (d, J = 8.6 Hz, 2 H), 7.84 (d, J = 8.6 Hz, 2 H), 4.40 (q, J = 7.2 Hz, 2 H), 1.40 (t, J = 7.0 Hz, 3 H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ: 165.8, 150.1, 145.9, 142.0, 139.0, 131.6, 129.4, 61.2, 14.3. **MS (70 eV, EI)** m/z: 296 (32) [^{35}Cl − M^+], 270 (24), 268 (38), 251 (100), 223 (26). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3086, 3005, 2985, 2359, 1966, 1708, 1611, 1569, 1537, 1507, 1482, 1466, 1446, 1423, 1366, 1310, 1283, 1190, 1175, 1140, 1131, 1114, 1098, 1028, 1021, 1009, 915, 858, 843, 786, 758, 719, 698, 675, 634, 621, 616, 610, 602. **HRMS (EI) Calcd for $C_{13}H_{10}Cl_2N_2O_2$**, 296.0119; Found, 296.0119.

Synthesis of (2-Chloro-3-nitropyridin-4-yl)(4-chlorophenyl)methanone (9). 2-Chloro-3-nitropyridine (**8**; 7.91 g, 50.0 mmol) dissolved in THF (50 mL) was reacted with a solution of tmpZnCl·LiCl (**1**) (1.35 M in THF, 40.7 mL, 55.0 mmol) at 25 °C, and the resulting mixture was stirred at this temperature for 5 h. The reaction mixture was cooled to −30 °C, CuCN·2LiCl (1 M solution in THF, 55.0 mL, 55.0 mmol) was added dropwise, and the resulting mixture was stirred for 30 min at the same temperature. Then, 4-chlorobenzoyl chloride (9.63 g, 55.0 mmol) was added dropwise at −30 °C, and the reaction mixture was allowed to warm up slowly to 25 °C within 3 h. The resulting mixture was then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/CH_2Cl_2, 65:35) furnished the compound **9** (11.45 g, 77%) as a colorless solid. **Mp**: 116.5−117.8 °C. **^{1}H NMR ($CDCl_3$, 300 MHz) δ:** 8.68 (d, J = 4.9 Hz, 2 H), 7.72 (d, J = 8.5 Hz, 2 H), 7.49 (d, J = 8.3 Hz, 1 H), 7.38 (d, J = 4.9 Hz, 1 H). **^{13}C NMR ($CDCl_3$, 75 MHz)** δ: 188.5, 151.4, 143.8, 143.3, 143.0, 142.0, 132.3, 131.2, 129.6, 121.5. **MS (EI, 70 eV)** m/z (%): 296 (8) [^{35}Cl − M^+], 169 (14), 141 (28), 139 (100), 129 (23), 127 (77), 111 (24). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3090, 2186, 2162, 1676, 1583, 1568, 1534, 1502, 1486, 1442, 1402, 1382, 1366, 974, 858, 846, 830, 814, 800, 776, 748, 738, 716, 684, 676, 648, 634, 616. **HRMS (EI) Calcd for $C_{12}H_6Cl_2N_2O_3$**, 295.9755; Found, 295.9743.

Synthesis of 4,6-Dichloro-5-(cyclohex-2-en-1-yl)pyrimidine (11). 4,6-Dichloropyrimidine (**10**; 7.45 g, 50.0 mmol) dissolved in THF (50 mL) was added to a solution of tmpZnCl·LiCl (**1**) (1.35 M in THF, 40.7 mL, 55.0 mmol) at 25 °C, and the resulting mixture was stirred at this temperature for 1 h. The reaction mixture was cooled to −30 °C, CuCN·2LiCl (1 M solution in THF, 5.0 mL, 5.0 mmol) was added and stirred at this temperature for 10 min. Then, 3-bromocyclohexene (9.7 g, 60.0 mmol) was added dropwise at −30 °C, and the reaction mixture was allowed to warm up slowly to 25 °C for 3 h. The resulting mixture was then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash chromatography (pentane/diethyl ether, 95:5) furnished the compound **11** (9.23 g, 81%) as a yellow oil. **^{1}H NMR ($CDCl_3$, 300 MHz)** δ: 8.59 (s, 1 H), 5.91−5.84 (m, 1 H), 5.54−5.49 (m, 1 H), 4.21−4.14 (m, 1 H), 2.14−2.08 (m, 2 H), 2.01−1.83 (m, 2 H), 1.79−1.64 (m, 2 H). **^{13}C NMR ($CDCl_3$, 75 MHz)** δ: 161.7, 155.4, 135.4, 128.6, 126.2, 38.4, 25.7, 24.2, 22.5. **MS (EI, 70 eV)** m/z (%): 228 (34) [^{35}Cl − M^+], 228 (100), 227 (28), 216 (18), 215 (32), 214 (18), 213 (53), 202 (19), 200 (33), 193 (23), 177 (32), 175 (51), 139 (25), 81 (80), 70 (16), 68 (16), 67 (47), 54 (96). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 3025, 2934, 2861, 2835, 1650, 1532, 1510, 1447, 1432, 1408, 1376, 1350, 1329, 1307, 1228, 1215, 1194, 1162, 1127, 1046, 980, 934, 899, 882, 848, 808, 779, 721, 616. **HRMS (EI) Calcd for $C_{10}H_{10}Cl_2N_2$**, 228.0221; Found, 228.0220.

Synthesis of 8-(4-Chlorophenyl)-1,3,7-trimethyl-1*H*-purine-2,6(3H,7H) (13). 1,3,7-Trimethyl-1*H*-purine-2,6(3H,7H)-dione (**12**; 9.71 g, 50.0 mmol) dissolved in THF (100 mL) was reacted with a solution of tmpZnCl·LiCl (**1**) (1.35 M in THF, 40.7 mL, 55.0 mmol) at 25 °C, and the resulting mixture was stirred at this temperature for a maximum 10 min. Solution of $Pd(dba)_2$ (850 mg, 3 mol %) and P(2-furyl)$_3$ (700 mg, 6 mol %) dissolved in THF (50 mL) and mixed with 1-chloro-4-

iodobenzene (13.11 g, 55.0 mmol, 1.1 equiv) was then transferred via cannula to the reaction mixture. The resulting mixture was stirred for 2 h at 40 °C. The reaction mixture was then quenched with a sat. aq NH_4Cl solution (300 mL), extracted with diethyl ether (3 × 250 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. Purification by flash-chromatography (CH_2Cl_2/diethyl ether, 1:1) furnished compound **13** (12.09 g, 79%) as a colourless solid. **Mp**: 198.7−199.5 °C. **^{1}H NMR ($CDCl_3$, 300 MHz)** δ: 7.63 (d, J = 8.5 Hz, 2 H), 7.47 (d, J = 8.5 Hz, 2 H), 4.02 (s, 3 H), 3.58 (s, 3 H), 3.39 (s, 3 H). **^{13}C NMR ($CDCl_3$, 75 MHz)** δ: 155.5, 151.6, 150.8, 148.2, 136.7, 130.4, 129.2, 126.8, 108.7, 33.9, 29.8, 28.0. **MS (EI, 70 eV)** *m*/*z* (%): 304 (100) [^{35}Cl-M^+], 303 (25), 82 (21). **IR (ATR)** $\tilde{\nu}$ (cm^{-1}): 2964, 1695, 1646, 1606, 1570, 1538, 1473, 1454, 1431, 1408, 1375, 1339, 1289, 1230, 1180, 1108, 1091, 1074, 1030, 1008, 978, 835, 803, 760, 749, 739, 730, 708, 685, 672, 650, 645, 639, 632, 625, 620, 614, 606. 601. **HRMS (EI) Calcd for $C_{14}H_{13}ClN_4O_2$**, 304.0727; Found, 304.0719.

Acknowledgment

We thank the Fonds der Chemischen Industrie, the European Research Council (ERC), and the Deutsche Forschungsgemeinschaft (DFG) for their financial support. We also thank Evonik AG (Hanau), BASF AG (Ludwigshafen), W. C. Heraeus GmbH (Hanau), and Chemetall GmbH (Frankfurt) for the generous gift of chemicals.

Supporting Information Available

Copies of ^{1}H- and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

Received for review July 12, 2010.

OP1001935