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A New Approach to the Synthesis of *N*,*N*-Dialkyladenine Derivatives

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N,*N*-Dialkyladenine derivatives were prepared by two different reaction sequences starting from 5-amino-4-cyanoformimidoylimidazoles. When these imidazoles were treated with dimethylformamide diethyl acetal, a 5-aminomethyleneamino-4-cyanoformimidoylimidazole was isolated and evolved to the *N*,*N*-dialkyladenine in the presence of a secondary alkylamine. The same purine structure was isolated when the 5-amino-4-cyanoformimidoylimidazole was first treated with a secondary amine to give a stable 4-amidino-5-aminoimidazole. The desired product was generated when the 4-amidino-5-aminoimidazole was combined with dimethylformamide diethyl acetal, at room temperature.

Introduction

Purines are an important class of biologically active compounds, and their potency and selectivity depends on the nature of the substituents on the ring.[1] Among the adenine derivatives, puromycin is a *N*,*N*-dimethylated nucleoside, long known as an antibiotic produced by *Streptomyces alboniger*.[2] However, the lack of selectivity towards prokaryotic cells and the metabolism, which leads to the formation of toxic byproducts, makes it undesirable for medical purposes for humans.

The structure of this purine derivative has been an inspiration to find new analogs with biological activity, namely benzodiazepine receptor binding activity[3] and antirhinovirus activity,[4] as an anticonvulsant[5] or an antipsychotic,[6] and broad-band antibiotic agents.[7] Some of these compounds were also identified as potent selective antagonists at the A1 adenosine receptor.[8]

A wide range of biologically relevant adenines derived from carbocyclic nucleosides has been reported.[9] A number of C6-dialkylamino and cycloalkylamino purine derivatives were patented as anti-inflammatory, analgesic, antipyretic, and antiallergic agents and as inhibitors of platelet aggregation.[10] Similar compounds were also used as oral hypoglycemic agents in the treatment of type II diabetes and/or obesity with associated insulin resistance.[11] More recently, selective phosphodiesterase IV inhibition activity was reported, and some *N*,*N*-disubstituted adenine derivatives were active in treating disease states associated with abnormally high physiological levels of inflammatory cytokines and also with asthma, allergies, depression, dementia, including Alzheimer's disease, vascular dementia, and multifarct dementia, a disease caused by HIV.[12]

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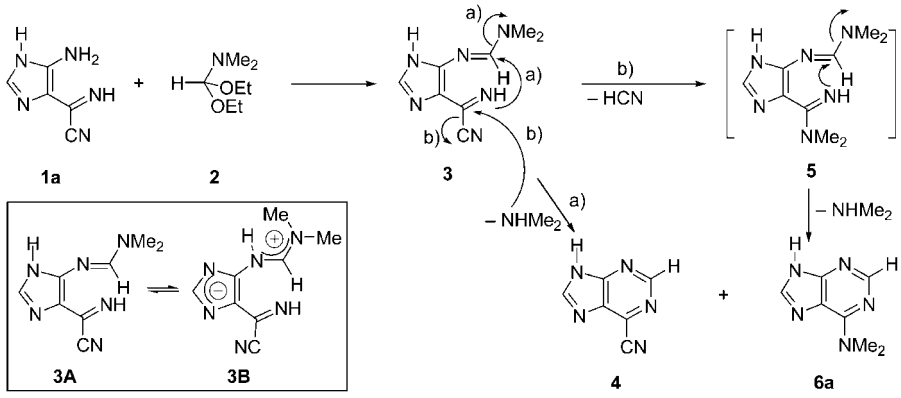
The adenine ring system is usually prepared from a substituted pyrimidine, ultimately leading to a 6-halopurine after a variable number of reaction steps. The amino group is incorporated by S_NAr of the halogen atom.[13]

In our research group, we have been studying the reactivity of 5-amino-4-cyanoformimidoyl imidazoles **1**, which proved to be versatile precursors to 6-substituted purines[14–22] and other fused nitrogen heterocycles.[23] The cyanoformimidoyl unit plays a fundamental role in the reactivity of these compounds.

Results and Discussion

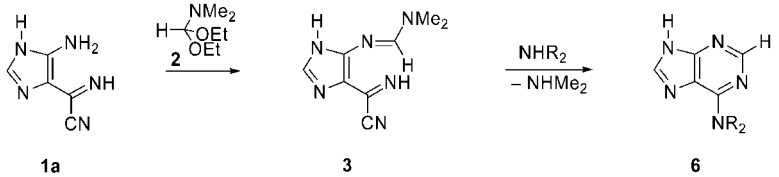
The reaction of 5-amino-4-cyanoformimidoylimidazole **1a** and *N*,*N*-dimethylformamide diethyl acetal (**2**) led to the formation of 6-cyanopurine **4** as the major product, but *N*,*N*-dimethyladenine (**6a**) was always present as a contaminant in the reaction mixture (Scheme 1). Attempts to follow the evolution of imidazole **1** by ^{1}H NMR spectroscopy when this compound was combined with *N*,*N*-dimethylformamide diethyl acetal (1.1 equiv.) at room temperature in deuterated acetonitrile were unsuccessful, as imidazole **3** precipitates from the reaction mixture even when a very dilute solution is used. The formation of adenine derivative **6a** was associated with the elimination of dimethylamine during the cyclization of imidazole **3** to generate the 6-cyanopurine (Scheme 1). Traces of this amine, present in solution, can be responsible for the formation of imidazole **5** by nucleophilic attack on the cyanoformimidoyl group in imidazole **3** and substitution of the cyano function.

When a large excess of dimethylamine or another secondary alkylamine was treated with imidazole **3** at room temperature, adenine derivatives **6** were isolated in good yield after 10 min to 6 d (Table 1).



Scheme 1.

Table 1. Reagents and reaction conditions for the synthesis of compounds **3** and **6a**–**e**.



Compound	NHR_2	Reaction Conditions	Yield [%]
3	-	acetonitrile; **2** (1.5 equiv.); 15 min; r.t.	66
6a	$NHMe_2$	acetonitrile; amine (aq., 8 equiv.); 30 min; r.t. chloroform; amine (gas, large excess); 2.5 h; 0 °C	74 62[a]
6b	piperidine	ethanol; amine (5 equiv.); 1.5 h; r.t.	45
6c	thiomorpholine	neat; 6 d; r.t.	84
6d	morpholine	neat; 1.5 h; r.t.	65
6e	pyrrolidine	acetonitrile; amine (5 equiv.); 10 min; r.t.	88

[a] Isolated as the cyanide salt.

Imidazole **3**, a useful intermediate for a diversity of *N*,*N*-disubstituted adenine derivatives, must be freshly prepared prior to use, as it progressively darkens and evolves mainly to a mixture of 6-cyanopurine and *N*,*N*-dimethyladenine, even in the solid state. The presence of an acidic imidazole proton and an amidine function in the same molecule may result in the formation of a zwitterionic structure **3B** (Scheme 1), facilitating the intramolecular cyclization reaction. Attempts to obtain the ^{1}H NMR spectrum of imidazole **3** always led to a mixture where the signals for the 6-cyanopurine were present from the beginning. Table 2 summarizes the conditions that were used to record the ^{1}H NMR spectrum (deuterated DMSO, methanol, or acetonitrile at 20 or 5 °C).

Table 2. Evolution of imidazole **3** by ^{1}H NMR spectroscopy.

Solvent	Temperature [°C]	Time [min]	Imidazole **3** [%]	Purine **4** [%]
[D_6]DMSO	20	2	25	75
		5	19	81
[D_4]Methanol	20	2	86	14
		10	57	43
[D_4]Methanol	5	2	89	11
		10	83	17
[D_3]Acetonitrile	20	5	44	56
		10	traces	ca. 100

The sample was prepared at room temperature, and the first spectrum was obtained after 2–5 min. The results indicate that a slower evolution of imidazole **3** to 6-cyanopurine **4** occurs when methanol is used as the solvent. Lowering the temperature to 5 °C further contributes to stabilize the imidazole. Compound **3** could only be characterized by infrared spectroscopy, where the stretching vibration of the cyano group was visible as a medium intensity band at 2200 cm^{-1}. The ^{1}H NMR spectroscopic data confirms the presence of the imidazole ring (δH = 7.39 ppm in [D_6]-DMSO) and of the amidine function (δH = 7.86 ppm in [D_6]DMSO).

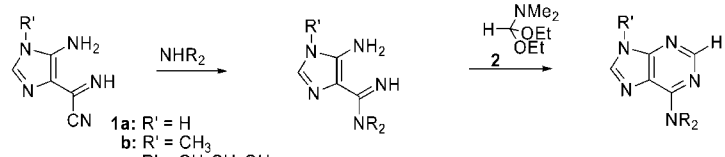
The use of a different approach for the synthesis of *N*,*N*-disubstituted adenines proved to be equally versatile and

much more convenient, considering the stability of the intermediate used in this new pathway. The addition of a secondary amine to imidazole **1** led to 4-amidinoimidazole **7**, which was usually isolated in a very good yield. The evolution occurs at room temperature or in an ice bath during 30 min. to 10 d (Table 3).

Imidazoles **7d** and **7i** were isolated as the cyanide salts. This was confirmed by elemental analysis and infrared spectroscopy, where the stretching vibration of the cyano group is present as a medium intensity band around 2070 cm^{-1}. The isolation of these cyanide salts was associated with the workup procedure. A large excess of dimethylamine gas was used in both cases, and when the reaction was complete, the solvent and the unreacted dimethylamine were removed in vacuo to afford an oily material. To remove completely the dimethylamine from this viscous oil, more solvent was added, followed by its removal in vacuo, and this procedure was repeated until all the volatile base was removed. When dichloromethane was used as solvent, HCN eliminated in the reaction remains in the mixture, probably associated to the amidine function, and the solid is isolated as the cyanide salt. When diethyl ether was used, HCN could be removed, probably through protonation of the ether functionality, and the solid was isolated as the neutral species. Imidazoles **7** are stable compounds and their ^1H NMR spectra shows the signal for the C-H proton in the δ = 7.0–7.5 ppm region, typical of a substituted imidazole. The NH and NH_2 signals are either absent (in the N1-H imidazoles) or can be seen as very broad singlets in the δ = 5.2–7.2 ppm region. In the ^{13}C NMR spectrum, the signal for C-2 in the δ = 130–140 ppm region confirms the presence of the imidazole ring.

N,*N*-Disubstituted adenine derivatives **6** were prepared by the addition of dimethylformamide diethyl acetal (1.2–2 equiv.) to the appropriate imidazole **7**. The purine was isolated in yields usually above 70% after 3 h to 2 d at room temperature by using acetonitrile as the solvent. In the ^1H NMR spectra of these compounds, the protons at C-2 and C-8 can be seen in the δ = 8.0–8.6 ppm region, which confirms the presence of a conjugated aromatic system. In the

Table 3. Reagents and reaction conditions for the synthesis of compounds **6a**–**m** and **7a**–**j**.



1a: R' = H
b: R' = CH_3
c: R' = CH_2CH_2OH
d: R' = 4-ClC_6H_4
e: R' = 4-$MeOC_6H_5$
f: R' = 4-MeC_6H_5

Compound	R'	NHR_2	Reaction Conditions	Yield [%]
7a	H	$NHMe_2$	acetonitrile; **1a** + amine (aq., 8 equiv.); 30 min; r.t.	75
7a	H	$NHMe_2$	chloroform; **1a** + amine (gas, excess); 2.5 h; 0 °C	62
7b	H	piperidine	acetonitrile; **1a** + amine (5 equiv.); 24 h; r.t.	91
7c	H	thiomorpholine	acetonitrile; **1a** + amine (1.1 equiv.); 10 d; r.t.	94
7d	CH_3	$NHMe_2$	chloroform; **1b** + amine (gas, excess); 4 h; 0 °C	81[a]
7e	CH_2CH_2OH	piperidine	acetonitrile; **1c** + amine (1.2 equiv.); 24 h; r.t.	81
7f	4-ClC_6H_4	$NHMe_2$	chloroform; **1d** + amine (gas, excess); 5.5 h; 0 °C	57[b]
7g	4-ClC_6H_4	piperidine	acetonitrile; **1d** + amine (5 equiv.); 18 h; r.t.	89
7h	4-$MeOC_6H_4$	$NHMe_2$	chloroform; **1e** + amine (gas, excess); 19 h; 0 °C	79
7i	4-MeC_6H_4	$NHMe_2$	chloroform; **1f** + amine (gas, excess); 2 h; 0 °C	87[a]
7j	4-MeC_6H_4	piperidine	acetonitrile; **1f** + amine (2.5 equiv.); 19 h, r.t.; 3 d, 8 °C	67
6a	H	$NHMe_2$	1. chloroform; **1a** + amine (gas, excess); 20 h; 5 °C 2. chloroform; **2** (1.2 equiv.); 7 h; r.t.	75
6b	H	piperidine	acetonitrile; **7b** + **2** (2 equiv.); 3.5 h; r.t.	91
6c	H	thiomorpholine	acetonitrile; **7c** + **2** (1.2 equiv.); 17 h; r.t.	86
6f	CH_3	$NHMe_2$	acetonitrile; **7d** + **2** (2 equiv.); 3 h, 0 °C; 2 h, r.t.	80
6g	CH_2CH_2OH	$NHMe_2$	1. chloroform; **1c** + amine (gas, excess); 20 h; –18 °C 2. dichloromethane, **2** (1 equiv.); 3 h; r.t.	38
6h	CH_2CH_2OH	piperidine	acetonitrile; **7e** + **2** (2.2 equiv.); 18 h; r.t.	51
6i	4-ClC_6H_4	$NHMe_2$	acetonitrile; **7f** + **2** (1.2 equiv.); 2 d; r.t.	77
6j	4-ClC_6H_4	piperidine	acetonitrile; **7g** + **2** (1.2 equiv.); 7 h; r.t.	78
6k	4-$MeOC_6H_4$	$NHMe_2$	acetonitrile; **7h** + **2** (2 equiv.); 2 h; r.t.	74
6l	4-MeC_6H_4	$NHMe_2$	acetonitrile; **7i** + **2** (2 equiv.); 3 h, r.t.	84
6m	4-MeC_6H_4	piperidine	1. dichloromethane; **1f** + amine (2.5 equiv.); 21 h; r.t. 2. acetonitrile; **2** (1.2 equiv.); 14 h, 8 °C; 5 h, r.t.	51

[a] Isolated as the cyanide salt. [b] Purine **6i** was also isolated (8%).

^{13}C NMR spectrum, the signal at δ = 151–152 ppm is typical of the C-2 in the pyrimidine ring, whereas the signal at δ = 138–140 ppm can be assigned to the imidazole C-8.

Conclusion

A mild and efficient synthesis of *N*,*N*-dialkyladenine derivatives was developed. These compounds are well known for their diverse and interesting biological activities, and the development of simple and versatile methods for their synthesis is a very important tool for the scientific community and in particular for the drug industry.

Experimental Section

The 5-amino-4-(cyanoformimidoyl)imidazole and the corresponding *N*1-substituted derivatives used in this work were prepared according to previously described procedures.[14,15,21,24] NMR spectra were recorded with a Varian Unity Plus, including the ^{1}H-^{13}C correlation spectra (HMQC and HMBC). IR spectra were recorded with a FT-IR Bomem MB 104 by using nujol mulls and NaCl cells. The reactions were monitored by thin-layer chromatography (TLC) with the use of silica gel 60 F_{254} (Merck). The melting points were determined with a Gallenkamp melting point apparatus and are uncorrected. Elemental analyses were performed with a LECO CHNS-932 instrument.

Imidazole 1b: An aqueous solution of methylamine (0.25 g, 8.04 mmol, 1.2 equiv.) was added to a suspension of ethyl (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)formimidate (0.51 g, 3.09 mmol) in ethanol (4 mL), and the mixture was kept under magnetic stirring at r.t. Five minutes later, an off-white solid precipitated out of the homogeneous solution. The solid was filtered and washed with chloroform. This solid was suspended in ethanol (4 mL), followed by the addition of DBU (20 μL, 0.12 mmol). The reaction mixture was maintained at r.t. under magnetic stirring until TLC indicated that the starting material was no longer present. The light green solid was filtered, washed with diethyl ether, and identified as the title compound (0.31 g, 2.10 mmol, 68%). M.p. 138.0–142.4 °C. ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 10.82 (br. s, 1 H), 7.17 (s, 1 H), 6.63 (br. s, 2 H), 3.41 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 144.90, 143.10, 132.81, 116.31, 113.70, 29.7 ppm. IR (nujol mull): $\tilde{\nu}$ = 2223, 1637, 1588, 1544, 1503 cm^{-1}. HRMS: calcd. for $C_6H_7N_5$ $[M + H]^+$ 150.07796; found 150.0774.

Imidazole 3: *N*,*N*-Dimethylformamide diethyl acetal (0.46 g, 3.17 mmol) was added to a suspension of 5-amino-4-cyanoformimidoylimidazole[14] (**1a**; 0.29 g, 2.12 mmol) in acetonitrile (5 mL). The red solution was stirred at r.t., and after 15 min, the solvent was removed in vacuo. The solid residue was suspended in acetonitrile (2 mL) and filtered to afford a yellow-orange solid identified as the title compound (0.27 g, 1.41 mmol, 66%). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.86 (s, 1 H), 7.39 (s, 1 H), 3.09 (s, 3 H), 2.97 (s, 3 H) ppm. ^{1}H NMR (300 MHz, [D_3]acetonitrile): δ = 8.16 (s, 1 H), 7.49 (s, 1 H), 3.22 (s, 3 H), 3.07 (s, 3 H) ppm. ^{1}H NMR (300 MHz, [D_4]methanol): δ = 8.32 (s, 1 H), 7.59 (s, 1 H), 3.19 (s, 6 H) ppm. IR (nujol mull): $\tilde{\nu}$ = 3387, 3287, 2200, 1650, 1587 cm^{-1}.

6-Cyanopurine 4: A solution of imidazole **3** (0.23 g, 1.18 mmol) in ethanol (200 mL) was stirred at r.t. in the presence of silica gel (1 g). After 1.5 h, the solvent was removed in vacuo, and the solid residue was extracted with acetonitrile (5 × 10 mL). The acetonitrile solution was concentrated in vacuo to afford a white solid that was filtered, washed with diethyl ether, and identified as the title compound (0.13 g, 0.56 mmol, 48%), by comparison of the ^{1}H and ^{13}C NMR spectra with the data reported in the literature.[25] ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 14.2 (br. s, 1 H), 9.06 (s, 1 H), 8.90 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 155.22, 152.03, 149.09, 133.66, 127.55, 114.312 ppm.

General Procedure for the Synthesis of 5-Amino-4-amidinoimidazoles (7b, 7c, 7e, 7g, 7j): The secondary amine (1.2–5.0 equiv.) was added to a suspension of 5-amino-4-cyanoformimidoylimidazole **1a**,[14] **1c**,[15] **1d**,[24] or **1f**[24] in acetonitrile. The mixture was stirred at r.t. until the starting material was consumed (evidence by TLC). The off-white solid that precipitated from the reaction mixture was filtered and washed with acetonitrile and diethyl ether.

General Procedure for the Synthesis of 5-Amino-4-*N*,*N*-dimethylamidinoimidazoles (7a, 7d, 7f, 7h, 7i): A suspension of 5-amino-4-cyanoformimidoylimidazole **1a**,[14] **1b**, **1d**,[24] **1e**,[24] or **1f**[24] in chloroform was kept in a round-bottom flask equipped with a serum cap and a magnetic bar and stirred in an ice-salt bath. Dimethylamine was bubbled through the reaction mixture for 20 min. and stirring at 0–8 °C was continued until the starting material was no longer present (evidence by TLC). The solvent was removed in vacuo, and the oily product was washed several times with dichloromethane or diethyl ether, followed by removal of the solvent in vacuo (until dimethylamine was no longer present and a solid product was formed). The solid was filtered and washed with diethyl ether.

5-Amino-4-(*N*,*N*-dimethylamidino)imidazole (7a): Yield: 0.78 mmol, 75%; m.p. 148 °C (dec.). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 6.96 (s, 1 H), 4.98 (br. s, 2 H), 3.05 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 159.7, 151.8, 140.7, 108.7, 39.8 ppm. IR (nujol mull): $\tilde{\nu}$ = 1662, 1632, 1581, 1534 cm^{-1}. HRMS (FAB): calcd. for $C_6H_{12}N_5$ 154.109317; found 154.109271.

5-Amino-4-(piperidinylamidino)imidazole (7b): Yield: 2.77 mmol, 91%; m.p. 178 °C (dec.). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 6.92 (s, 1 H), 4.77 (br. s, 2 H), 3.44 (s, 4 H), 1.57 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 159.5, 151.0, 140.2, 108.9, 48.6, 25.7, 24.1 ppm. IR (nujol mull): $\tilde{\nu}$ = 3422, 3380, 3031, 1655 cm^{-1}. $C_9H_{15}N_5$ (193.25): calcd. C 55.94, H 7.82, N 36.24; found C 55.75, H 7.81, N 36.47.

5-Amino-4-(thiomorpholinylamidino)imidazole (7c): Yield: 1.49 mmol, 94%; m.p. 197–198 °C. ^{1}H NMR (300 MHz, [D_6]-DMSO): δ = 7.05 (s, 1 H), 4.90 (br. s, 2 H), 3.65 (m, 4 H), 2.65 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 160.5, 147.9, 136.6, 108.6, 49.8, 26.5 ppm. IR (nujol mull): $\tilde{\nu}$ = 2239, 1706, 1602, 1528 cm^{-1}. $C_8H_{13}N_5S{\cdot}0.25H_2O$ (215.79): calcd. C 44.53, H 6.31, N 32.45, S 14.85; found C 44.57, H 5.99, N 32.33, S 14.73.

Cyanide Salt of 5-Amino-4-(*N*,*N*-dimethylamidino)-1-methylimidazole (7d): Yield: 1.09 mmol, 81%; m.p. 150 °C (dec.). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.22 (s, 1 H), 7.0–4.0 (br. s, 3 H), 3.40 (s, 3 H), 3.00 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 161.2, 141.7, 131.7, 115.0, 39.3, 29.9 ppm. IR (nujol mull): $\tilde{\nu}$ = 2072, 1660, 1614, 1576, 1537 cm^{-1}. $C_8H_{14}N_6{\cdot}H_2O$ (212.26): calcd. C 45.27, H 7.60, N 39.59; found C 45.56, H 7.29, N 39.19.

5-Amino-1-(2-hydroxyethyl)-4-(piperidinylamidino)imidazole (7e): Yield: 2.80 mmol, 81%; m.p. 160 °C (dec.). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.10 (s, 1 H), 6.82 (br. s, 1 H), 5.22 (br. s, 2 H), 3.82 (t, J = 5.4 Hz, 2 H), 3.60 (t, J = 5.4 Hz, 2 H), 3.21 (s, 4 H), 1.52 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 164.1, 138.7, 130.6, 114.8, 60.0, 47.6, 45.4, 25.4, 24.5 ppm. IR (nujol

mull): $\tilde{\nu}$ = 1637, 1590, 1557, 1528 cm^{-1}. $C_{11}H_{19}N_5O$ (237.30): calcd. C 55.67, H 8.07, N 29.51; found C 55.62, H 8.23, N 29.42.

5-Amino-1-(4-chlorophenyl)-4-(*N*,*N*-dimethylamidino)imidazole (7f): Yield: 0.49 mmol, 57%; m.p. 184 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 7.61 (d, J = 8.4 Hz, 2 H), 7.53 (d, J = 8.4 Hz, 2 H), 7.38 (s, 1 H), 6.8–6.2 (br. s, 1 H), 6.2–5.4 (br. s, 2 H), 2.94 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 162.7, 140.1, 134.0, 132.3, 129.6, 128.9, 126.4, 115.3, 38.6 ppm. IR (nujol mull): $\tilde{\nu}$ = 1591, 1574, 1559, 1544 cm^{-1}. $C_{12}H_{14}ClN_5$ (263.73): calcd. C 54.65, H 5.35, N 26.56; found C 54.56, H 5.31, N 26.43.

5-Amino-1-(4-chlorophenyl)-4-(piperidinylamidino)imidazole (7g): Yield: 0.27 mmol, 89%; m.p. 161 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 7.61 (d, J = 8.7 Hz, 2 H), 7.52 (d, J = 8.7 Hz, 2 H), 7.41 (s, 1 H), 6.6–5.8 (br. s, 1 H), 5.8–5.0 (br. s, 2 H), 3.27 (s, 4 H), 1.54 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 163.2, 139.1, 133.9, 132.4, 129.8, 129.7, 126.5, 115.2, 47.6, 25.5, 24.4 ppm. IR (nujol mull): $\tilde{\nu}$ = 1666, 1626, 1592, 1574, 1548, 1517 cm^{-1}. $C_{15}H_{18}ClN_5$ (303.80): calcd. C 59.30, H 5.97, N 23.05; found C 58.94, H 6.25, N 23.44.

5-Amino-4-(*N*,*N*-dimethylamidino)-1-(4-methoxyphenyl)imidazole (7h): Yield: 0.66 mmol, 78%; m.p. 177 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 7.39 (d, J = 9.0 Hz, 2 H), 7.28 (s, 1 H), 7.08 (d, J = 9.0 Hz, 2 H), 6.2–5.5 (br. s, 3 H), 3.80 (s, 3 H), 2.94 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 162.6, 158.5, 140.5, 129.5, 128.0, 126.3, 115.0, 114.8, 55.5, 38.7 ppm. IR (nujol mull): $\tilde{\nu}$ = 1613, 1577, 1546, 1514 cm^{-1}. $C_{13}H_{17}N_5O$ (259.31): calcd. C 60.21, H 6.61, N 27.01; found C 60.33, H 6.53, N 26.99.

5-Amino-4-(*N*,*N*-dimethylamidino)-1-(4-tolyl)imidazole (7i): Yield: 1.56 mmol, 87%; m.p. 134–135 °C. ^1H NMR (300 MHz, [D_6]-DMSO): δ = 7.46 (s, 1 H), 7.37 (s, 4 H), 3.05 (s, 6 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 161.9, 142.1, 138.9, 132.9, 131.9, 131.2, 125.9, 112.3, 40.4, 21.6 ppm. IR (nujol mull): $\tilde{\nu}$ = 2070, 1681, 1634, 1608, 1584, 1522, 1500 cm^{-1}. $C_{14}H_{18}N_6$ (270.34): calcd. C 62.20, H 6.71, N 31.09; found C 61.90, H 6.80, N 30.60.

5-Amino-4-(piperidinylamidino)-1-(4-tolyl)imidazole (7j): Yield: 1.21 mmol, 67%; m.p. 181 °C (dec.). ^1H NMR (300 MHz, [D_6]-DMSO): δ = 7.34 (s, 1 H), 7.35 (s, 4 H), 7.20–6.40 (br. s, 1 H), 5.60–5.20 (br. s, 2 H), 3.27 (s, 4 H), 2.36 (s, 3 H), 1.55 (s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 163.7, 138.9, 137.4, 132.5, 130.1, 129.6, 124.5, 115.3, 47.5, 25.5, 24.5, 20.6 ppm. IR (nujol mull): $\tilde{\nu}$ = 1624, 1594, 1584 cm^{-1}. $C_{16}H_{21}N_5$ (283.38): calcd. C 67.78, H 7.47, N 24.71; found C 67.70, H 7.36, N 24.80.

General Procedure for the Synthesis of Adenine Derivatives (6) from Imidazole (3) and Secondary Amines: The secondary amine (5 equiv. for compounds **6b** and **e** or a large excess for compounds **6c** and **d**) was added to a suspension of freshly prepared imidazole **3** in acetonitrile (or ethanol for compound **6b**). The orange suspension was stirred at r.t., and the formed white solid was filtered and washed with diethyl ether. The product was identified as the corresponding adenine derivative **6**, contaminated with a small amount of *N*,*N*-dimethyladenine **6a**.

General Procedure for the Synthesis of Adenine Derivatives (6) from Imidazole (7) and *N*,*N*-Dimethylformamide Diethyl Acetal: *N*,*N*-Dimethylformamide diethyl acetal (1.2–2 equiv.) was added to a suspension of imidazole **7b**–**i** in acetonitrile. The suspension was stirred at r.t., and the formed white solid was filtered and washed with a small amount of acetonitrile and diethyl ether. The product was identified as the adenine derivative **6b**–**l**.

Synthesis of *N*,*N*-Dimethyladenine (6a) from 5-Amino-4-cyanoformimidoylimidazole (1a): A suspension of imidazole **1a** (0.20 g, 1.48 mmol) in chloroform (2 mL) was kept in a round-bottom flask equipped with a serum cap and a magnetic bar and stirred in an ice-salt bath. Dimethylamine was bubbled through the reaction mixture for 20 min by using a syringe needle. The reaction mixture was stirred at 5 °C for 20 h, at which point TLC indicated the absence of starting material. The excess of dimethylamine was removed in vacuo to afford an oil that was solubilized in chloroform (5 mL). *N*,*N*-Dimethylformamide diethyl acetal (0.31 mL, 1.78 mmol) was added, and the mixture was stirred at r.t. for 7 h. The solvent was removed in vacuo, and the addition of diethyl ether led to a solid that was filtered and washed with diethyl ether. The product was identified as imidazole **6a** (0.18 g, 1.09 mmol, 74%).

Synthesis of Adenine Derivative (6m) from 5-Amino-4-cyanoformimidoylimidazole (1f): A solution of piperidine (0.22 mL, 2.23 mmol) in dichloromethane (0.8 mL) was added to a suspension of imidazole **1f** (0.20 g, 0.89 mmol) in acetonitrile (4 mL). An orange solution was immediately formed, and the mixture was stirred at r.t. for 22 h. After this time, *N*,*N*-dimethylformamide diethyl acetal (0.18 mL, 1.07 mmol) was added, and the reaction mixture was stirred for 5 h at r.t. and 14 h at 8 °C. A solid suspension developed and was filtered and washed with acetonitrile and diethyl ether. The product was identified as imidazole **6m** (0.13 g, 0.45 mmol, 51%).

***N*,*N*-Dimethyladenine (6a):** Yield: 1.11 mmol, 75% from the reaction of imidazole **1a** and amine, followed by addition of acetal **2**. M.p. 259–260 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 12.90 (br. s, 1 H), 8.16 (s, 1 H), 8.07 (s, 1 H), 3.43 (br. s, 6 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 154.17, 151.76, 151.09, 137.78, 118.82, 37.85 ppm. IR (nujol mull): $\tilde{\nu}$ = 1677, 1591, 1530 cm^{-1}. $C_7H_9N_5 \cdot 0.1H_2O$ (164.99): calcd. C 50.96, H 5.62, N 42.45; found C 51.03, H 5.49, N 42.51.

6-(Piperidin-1-yl)-9*H*-purine (6b): Yield: 1.46 mmol, 91% from the reaction of imidazole **7b** and acetal **2**; Yield: 0.54 mmol, 45% from the reaction of imidazole **3** and amine. M.p. 277–278 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 13.00 (br. s, 1 H), 8.17 (s, 1 H), 8.08 (s, 1 H), 4.19 (br. s, 4 H), 1.66 (m, 2 H), 1.57 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 153.1, 151.8, 151.3, 137.7, 118.6, 45.5, 25.7, 24.3 ppm. IR (nujol mull): $\tilde{\nu}$ = 1603, 1578, 1514 cm^{-1}. $C_{10}H_{13}N_5$ (203.25): calcd. C 59.10, H 6.45, N 34.46; found C 59.00, H 6.36, N 34.32.

6-Thiomorpholino-9*H*-purine (6c): Yield: 0.53 mmol, 86% from the reaction of imidazole **7c** and acetal **2**; Yield: 1.02 mmol, 84% from the reaction of imidazole **3** and amine. M.p. 317 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 13.00 (br. s, 1 H), 8.22 (s, 1 H), 8.13 (s, 1 H), 4.90 (br. s, 4 H), 2.67 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 152.8, 151.6, 151.5, 138.1, 118.7, 40.2, 26.2 ppm. IR (nujol mull): $\tilde{\nu}$ = 1604, 1575, 1512, 1485 cm^{-1}. $C_9H_{11}N_5S$ (221.29): calcd. C 48.85, H 5.01, N 31.65, S 14.49; found C 48.65, H 5.05, N 31.43, S 14.48.

6-Morpholino-9*H*-purine (6d): Yield: 0.75 mmol, 65% from the reaction of imidazole **3** and amine. M.p. 319 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 12.50 (br. s, 1 H), 8.22 (s, 1 H), 8.13 (s, 1 H), 4.20 (br. s, 4 H), 3.71 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 153.2, 151.7, 151.5, 138.4, 118.8, 66.2, 45.2 ppm. IR (nujol mull): $\tilde{\nu}$ = 1607, 1585, 1513 1480 cm^{-1}. $C_9H_{11}N_5O$ (205.22): calcd. C 52.67, H 5.40, N 34.13; found C 52.75, H 5.49, N 34.02.

6-(Pyrrolidin-1-yl)-9*H*-purine (6e): Yield: 1.02 mmol, 88% from the reaction of imidazole **3** and amine. M.p. 225 °C (dec.). ^1H NMR (300 MHz, [D_6]DMSO): δ = 12.90 (br. s, 1 H), 8.15 (s, 1 H), 8.04 (s, 1 H), 4.02 (br. s, 2 H), 3.65 (br. s, 2 H), 1.94 (s, 4 H) ppm. ^{13}C

NMR (75 MHz, [D$_6$]DMSO): δ = 152.4, 152.0, 151.0, 138.3, 118.8, 47.5, 25.1 ppm. IR (nujol mull): $\tilde{\nu}$ = 1601, 1517 cm^{-1}. $C_9H_{11}N_5$ (189.22): calcd. C 57.13, H 5.86, N 37.01; found C 57.02, H 5.72, N 37.28.

***N*,*N*,9-Trimethyladenine (6f):** Yield: 0.93 mmol, 80% from the reaction of imidazole **7d** and acetal **2**. M.p. 124 °C (dec.). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.17 (s, 1 H), 8.05 (s, 1 H), 3.69 (s, 3 H), 3.41 (br. s, 6 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 154.2, 151.7, 150.6, 140.2, 119.1, 37.9, 29.4 ppm. IR (nujol mull): $\tilde{\nu}$ = 1593, 1561 cm^{-1}. $C_8H_{11}N_5$ (177.21): calcd. C 54.22, H 6.26, N 39.52; found C 54.07, H 6.18, N 39.20.

9-(2-Hydroxyethyl)-*N*,*N*-dimethyladenine (6g): Yield: 1.40 mmol, 38%; m.p. 135–136 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.19 (s, 1 H), 8.08 (s, 1 H), 4.99 (t, *J* = 5.7 Hz, 1 H), 4.18 (t, *J* = 5.7 Hz, 2 H), 3.71 (q, *J* = 5.7 Hz, 2 H), 3.44 (br. s, 6 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 154.3, 151.6, 150.3, 140.3, 119.2, 59.2, 45.7, 37.8 ppm. IR (nujol mull): $\tilde{\nu}$ = 1645, 1604, 1584, 1548, 1498 cm^{-1}. HRMS: calcd. for $C_9H_{14}N_5O$ [M + H]$^+$ 208.119835; found 208.120586.

9-(2-Hydroxyethyl)-6-(piperidin-1-yl)-9*H*-purine (6h): Yield: 1.10 mmol, 51% from the reaction of imidazole **7e** and acetal **2**. M.p. 170 °C (dec.). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.19 (s, 1 H), 8.07 (s, 1 H), 4.99 (s, 1 H), 4.18 (t, *J* = 5.4 Hz, 6 H), 3.72 (s, 2 H), 1.65 (m, 4 H), 1.56 (m, 2 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 153.1, 151.7, 150.5, 140.1, 118.9, 59.2, 45.7, 43.6, 25.7, 24.3 ppm. IR (nujol mull): $\tilde{\nu}$ = 1637, 1589, 1557, 1528 cm^{-1}. $C_{12}H_{17}N_5O$ (247.30): calcd. C 58.28, H 6.93, N 28.32; found C 58.45, H 6.90, N 28.19.

9-(4-Chlorophenyl)-*N*,*N*-dimethyladenine (6i): Yield: 0.15 mmol, 77% from the reaction of imidazole **7f** and acetal **2**. M.p. 208–209 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.60 (s, 1 H), 8.27 (s, 1 H), 7.93 (d, *J* = 8.7 Hz, 2 H), 7.66 (d, *J* = 8.7 Hz, 2 H), 3.50 (br. s, 6 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 154.5, 152.5, 149.9, 138.4, 133.9, 131.9, 129.5, 124.9, 119.7, 38.0 ppm. IR (nujol mull): $\tilde{\nu}$ = 1604, 1586, 1560 cm^{-1}. $C_{13}H_{12}N_5Cl{\cdot}0.1H_2O$ (275.53): calcd. C 56.67, H 4.46, N 25.42; found C 56.49, H 4.34, N 25.16.

9-(4-Chlorophenyl)-6-(piperidin-1-yl)-9*H*-purine (6j): Yield: 0.39 mmol, 78% from the reaction of imidazole **7g** and acetal **2**. M.p. 149–150 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.59 (s, 1 H), 8.27 (s, 1 H), 7.92 (d, *J* = 6.6 Hz, 2 H), 7.66 (d, *J* = 6.6 Hz, 4 H), 4.23 (br. s, 2 H), 1.68 (m, 2 H), 1.59 (m, 4 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 153.3, 152.6, 150.1, 138.3, 133.8, 131.8, 129.4, 124.9, 119.4, 45.8, 25.7, 24.3 ppm. IR (nujol mull): $\tilde{\nu}$ = 1660, 1578, 1550, 1520, 1500 cm^{-1}. $C_{16}H_{16}ClN_5$ (313.79): calcd. C 61.24, H 5.14, N 22.32; found C 61.12, H 5.19, N 22.29.

9-(4-Methoxyphenyl)-*N*,*N*-dimethyladenine (6k): Yield: 0.48 mmol, 74% from the reaction of imidazole **7h** and acetal **2**. M.p. 165 °C (dec.). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.45 (s, 1 H), 8.23 (s, 1 H), 7.71 (d, *J* = 8.7 Hz, 2 H), 7.11 (d, *J* = 8.7 Hz, 2 H), 3.82 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 158.6, 154.5, 152.3, 150.1, 138.7, 127.9, 125.1, 119.6, 114.6, 55.5, 38.0 ppm. IR (nujol mull): $\tilde{\nu}$ = 1597, 1556, 1520, 1484 cm^{-1}. $C_{14}H_{15}N_5O$ (269.31): calcd. C 62.44, H 5.61, N 26.00; found C 62.47, H 5.62, N 25.98.

9-(4-Tolyl)-*N*,*N*-dimethyladenine (6l): Yield: 0.85 mmol, 84% from the reaction of imidazole **7** and acetal **2**. M.p. 162–163 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.52 (s, 1 H), 8.25 (s, 1 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 3.50 (br. s, 6 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 154.4, 152.3, 149.9, 138.5, 137.0, 132.5, 129.8, 123.1, 119.7, 37.9, 20.6 ppm. IR (nujol mull): $\tilde{\nu}$ = 1600, 1556, 1520 cm^{-1}. $C_{14}H_{15}N_5$ (253.31): calcd. C 66.38, H 5.97, N 27.65; found C 66.42, H 6.19, N 27.71.

6-(Piperidin-1-yl)-9-(4-tolyl)-9*H*-purine (6m): Yield 0.45 mmol, 51% from the reaction of imidazole **1f** and amine, followed by addition of acetal **2**. M.p. 126–127 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.49 (s, 1 H), 8.24 (s, 1 H), 7.69 (d, *J* = 8.1 Hz, 2 H), 7.37 (d, *J* = 8.1 Hz, 2 H), 4.23 (br. s, 4 H) 2.37 (s, 3 H), 1.68 (m, 4 H), 1.60 (m, 2 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 153.3, 152.5, 150.2, 138.5, 137.2, 132.5, 129.8, 123.3, 119.4, 45.6, 25.7, 24.3, 20.6 ppm. IR (nujol mull): $\tilde{\nu}$ = 1592, 1579, 1554, 1524, 1507 cm^{-1}. HRMS: calcd. for $C_{17}H_{20}N_5$ [M + H]$^+$ 294.171871; found 294.171615.

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[1] For a recent review, see: M. Legraverend, D. S. Grierson, *Bioorg. Med. Chem.* **2006**, *14*, 3987–4006.
[2] J. Vara, G.-J. Perez, *Biochemistry* **1985**, *24*, 8074–8081.
[3] a) J. L. Kelley, E. W. McLean, R. M. Ferris, J. L. Howard, *J. Med. Chem.* **1989**, *32*, 1020–1024; b) J. L. Kelley, E. W. McLean, R. M. Ferris, J. L. Howard, *J. Med. Chem.* **1990**, *33*, 1910–1914; c) J. L. Kelley, E. W. McLean, J. A. Linn, M. P. Krochmal, R. M. Ferris, J. L. Howard, *J. Med. Chem.* **1990**, *33*, 196–202.
[4] a) J. L. Kelley, J. A. Linn, J. W. T. Selway, *J. Med. Chem.* **1991**, *34*, 157–160; b) J. L. Kelley, J. A. Linn, J. W. T. Selway, *J. Med. Chem.* **1989**, *32*, 218–224.
[5] a) J. L. Kelley, M. P. Krochmal, J. A. Linn, E. W. McLean, F. E. Soroko, *J. Med. Chem.* **1988**, *31*, 606–612; b) J. L. Kelley, M. P. Krochmal, J. A. Linn, E. W. McLean, F. E. Soroko, *J. Med. Chem.* **1988**, *31*, 1005–1009.
[6] a) J. L. Kelley, R. M. Bullock, M. P. Krochmal, E. W. McLean, J. A. Linn, *J. Med. Chem.* **1997**, *40*, 3207–3216.
[7] H. Chapuis, P. Strazewski, *Tetrahedron* **2006**, *62*, 12108–12115.
[8] a) R. D. Thompson, S. Secunda, J. W. Daly, R. A. Olsson, *J. Med. Chem.* **1991**, *34*, 2877–2882; b) K. A. Jacobson, X.-D. Ji, A.-H. Li, N. Melman, M. A. Siddiqui, K.-J. Shin, V.-E. Marquez, R. G. Ravi, *J. Med. Chem.* **2000**, *43*, 2196–2203.
[9] a) M. S. Wolf, R. T. Borchardt, *J. Med. Chem.* **1991**, *34*, 1521–1530; b) S. W. Schneller, *Curr. Top. Med. Chem.* **2002**, *2*, 1087–1092.
[10] a) W.-G. Friebe, M. Thiel, W. Winter, A. Roesch, W. Schaumann (Boehringer Mannheim GmbH), USP 3996361, **1976**; b) H. Yuki, H. Sueoka, M. Yasumoto, M. Terasawa, T. Imayoshi (Yoshitomi Pharmaceutical Industries Ltd), USP 4728644, **1988**.
[11] a) D. B. R. Johnston, M. MacCross, S. Marburg, L. C. Meurer, R. L. Tolman (Merck & Co., Inc.), USP 5057517, **1991**; b) D. A. Griffith (Pfizer, Inc.), USP 7129239, **2006**.
[12] D. J. Cavalla, M. Chasin, P. Hofer, A. Gehriq, P. Winterqerst (Euro-Celtique S.A), USP 6294541, **2001**.
[13] For recent reviews, see: a) M. K. Lakshman, *J. Organomet. Chem.* **2002**, *653*, 234–251; b) M. Hocek, *Eur. J. Org. Chem.* **2003**, 245–254. For representative references, see: c) H. Zhang, R. F. Schinazi, C. K. Chu, *Bioorg. Med. Chem.* **2006**, *14*, 8314–8322; d) C. K. L. Gilbert, C. R. Lisek, R. L. White, G. Gumina, *Tetrahedron* **2005**, *61*, 8339–8350; e) Y. Choi, C. George, P. Strazewski, V. E. Marquez, *Org. Lett.* **2002**, *4*, 589–592; f) O. Botta, E. Moyround, C. Lobato, P. Strazewski, *Tetrahedron* **1998**, *54*, 13529–13546; g) J. Barends, J. B. Linden, F. L. Delft, G. J. Koomen, *Nucleosides Nucleotides* **1999**, *18*, 2121–2126.
[14] M. J. Alves, B. L. Booth, A. P. Freitas, M. F. Proença, *J. Chem. Soc. Perkin Trans. 1* **1992**, 913–917.

[15] B. L. Booth, A. M. Dias, M. F. Proença, *J. Chem. Soc. Perkin Trans. 1* **1992**, 2119–2126.
[16] M. J. Alves, B. L. Booth, M. F. Proença, *J. Heterocycl. Chem.* **1994**, *31*, 345–350.
[17] B. L. Booth, R. D. Coster, M. F. Proença, *Synthesis* **1988**, 389–391.
[18] M. J. Alves, B. L. Booth, M. A. Carvalho, R. G. Pritchard, M. F. Proença, *J. Heterocycl. Chem.* **1997**, *34*, 739–743.
[19] A. Al-Azmi, B. L. Booth, R. A. Carpenter, M. A. Carvalho, E. Marrelec, R. G. Pritchard, M. F. Proença, *J. Chem. Soc. Perkin Trans. 1* **2001**, 2532–2537.
[20] B. L. Booth, I. M. Cabral, A. M. Dias, A. P. Freitas, A. M. Matos-Beja, M. F. Proença, M. Ramos-Silva, *J. Chem. Soc. Perkin Trans. 1* **2001**, 1241–1251.
[21] M. A. Carvalho, T. M. Esteves, M. F. Proença, B. L. Booth, *Org. Biomol. Chem.* **2004**, *2*, 1019–1024.
[22] M. A. Carvalho, Y. Álvares, M. E. Zaki, M. F. Proença, B. L. Booth, *Org. Biomol. Chem.* **2004**, *2*, 2340–2345.
[23] a) A. M. Dias, I. M. Cabral, M. F. Proença, B. L. Booth, *J. Org. Chem.* **2002**, *67*, 5546–5552; b) M. E. Zaki, M. F. Proença, B. L. Booth, *J. Org. Chem.* **2003**, *68*, 276–282; c) M. E. A. Zaki, M. F. Proença, B. L. Booth, *Synlett* **2005**, *16*, 2429–2432.
[24] a) M. J. Alves, B. L. Booth, O. K. Al-Duaij, P. Eastwood, L. Nezhat, M. F. Proença, A. S. Ramos, *J. Chem. Res. (S)* **1993**, 402–403; M. J. Alves, B. L. Booth, O. K. Al-Duaij, P. Eastwood, L. Nezhat, M. F. Proença, A. S. Ramos, *J. Chem. Res. (M)* **1993**, 2701–2718.
[25] C. J. Pouchert, J. Behnke (Eds.), *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, 1st ed., Aldrich Chemical Company, Inc., USA, **1993**, vol. 3, p. 225A.

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