Pergamon

Tetrahedron, Vol. 53, No. 33, pp. 11355-11368, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00717-5

Novel Synthesis of 4(5)-Monosubstituted Imidazoles via Cycloaddition of Tosylmethyl Isocyanide to Aldimines[1]

Ronald ten Have,[a] Marco Huisman,[a] Auke Meetsma,[b] and Albert M. van Leusen[a]*

[a]Department of Organic and Molecular Inorganic Chemistry, Groningen University, Nijenborgh 4, NL-9747 AG Groningen, The Netherlands

[b]Crystal Structure Centre, Department of Chemical Physics, Materials Science Centre, Groningen University, Nijenborgh, NL-9747 AG Groningen, The Netherlands

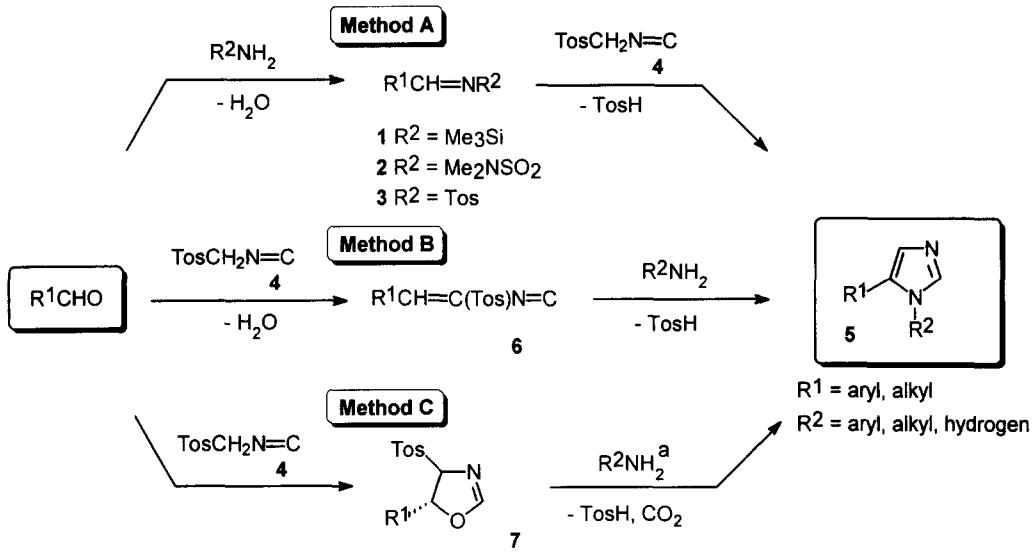
Abstract : 4(5)-Monosubstituted imidazoles (**9**) have been prepared via base-induced cycloaddition of tosylmethyl isocyanide (TosMIC) to *N*-(dimethylsulfamoyl)aldimines (**2**) or *N*-tosylaldimines (**3**). In the first case, *N*-(dimethylsulfamoyl)imidazoles **8** are the initial reaction products, from which the dimethylsulfamoyl group is readily removed with aqueous HBr. In the second case, the tosyl group of 1-tosylimidazoles **10** is lost spontaneously to give 4(5)-monosubstituted imidazoles **9** in one operation. © 1997 Elsevier Science Ltd.

INTRODUCTION

Imidazole rings are incorporated in a great variety of molecules, many of which are of biological interest. Imidazole units not only are present in well known compounds such as histidine and histamines, adenine and guanine, and vitamin B12, they also occur in various pharmaceuticals, fungicides, and herbicides.[2] As a matter of fact four of the top twenty ethical pharmaceuticals prescribed in the US in 1994 contain either a simple imidazole ring (Tagamet) or the fused rings of benzimidazole (Losec, Prilosec) and purine (Zovirax).[3] The two nitrogen atoms of imidazoles proper are equivalent due to a rapid 1,3-hydrogen shift, and the aromatic structure has an extremely high thermal stability (up to 590 °C).[4] It is remarkable how many different synthetic approaches have been developed for imidazoles since the parent compound was prepared nearly 140 years ago from glyoxal and ammonia.[5] Clearly, there is not a single general synthetic method that fulfills all the needs in the preparation of functionalized imidazoles.[6]

Beginning in 1972,[7] we have contributed to the synthesis of the imidazole ring system with a novel approach in which the N1-C2 and C4-C5 bonds are formed by reaction of tosylmethyl isocyanides [TosMIC (**4**), and derivatives thereof] with various imino compounds.[8] Basically, this approach leads to 1,5-disubstituted imidazoles (Scheme 1, Methods A and B) or to 1,4,5-trisubstituted imidazoles when monosubstituted TosMIC derivatives are used.[9] Recently, Horne *et al.*[10] have extended this approach by the introduction of Method C (Scheme 1). Currently, there is a growing interest in the development of reliable methods for the synthesis of 4(5)-monosubstituted imidazoles, especially in relation to the search for new histamine receptor agonists and antagonists.[11]

Scheme 1 : Three Methods for Conversion of Aldehydes to 1,5-Disubstituted[a] or 4(5)-Monosubstituted Imidazoles **5** using TosMIC (**4**)



a) For R^2 = alkyl, Method C leads to 1,4-disubstituted imidazoles (instead of 1,5-disubstituted isomers)[10]

Each of the three Methods of Scheme 1 can be, and has been, adapted to prepare 4(5)-monosubstituted imidazoles. First, in 1979, we have shown that Method B leads to 4(5)-phenylimidazole (**5**, R^1 = Ph, R^2 = H, 65 % yield) when the reaction is carried out with ammonia instead of primary aliphatic amines. The reaction with ammonia, however, was not persued beyond this one example.[12] Recently, Shih has shown that Method A also leads to 4(5)-monosubstituted imidazoles **5** (R^2 = H, 5 examples, 24-55 % yield) when the reaction is carried out with *N*-(trimethylsilyl)aldimines (**1**).[13] Finally, Horne *et al.* have made a series of the same type of monosubstituted imidazoles **5** (R^2 = H) by reaction of oxazolines **7** with ammonia (Method C, 10 examples, 52-80 % yield).[10]

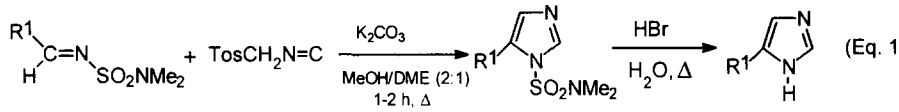
The intermediates of Methods B and C in the conversion aldehydes to 4(5)-monosubstituted imidazoles **5** (R^2 = H) are isolable compounds (**6** and **7**, respectively) which can be stored. The *N*-(trimethylsilyl)aldimines **1** of Method A, however, have been used only as *in situ* prepared transient intermediates.[13] In the present paper we describe two methods for the conversion of aldehydes to 4(5)-monosubstituted imidazoles by Method A that rely on the use of isolable and storable intermediates : *N*-(dimethylsulfamoyl)aldimines (**2**) and *N*-tosylaldimines (**3**).

RESULTS AND DISCUSSION

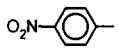
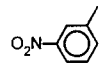
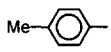
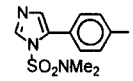
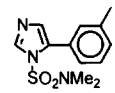
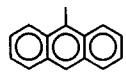
N-(Dimethylsulfamoyl)aldimines (**2**) constitute a new type of *N*-protected aldimines, which are readily prepared from aldehydes and *N*-(dimethylsulfamoyl)amide (obtained from commercially available Me_2NSO_2Cl and aqueous ammonia) in refluxing toluene. We have described the synthesis of these sulfamoylaldimines **2** elsewhere.[14] The reaction of sulfamoylaldimines **2** with TosMIC (**4**) proceeds smoothly using K_2CO_3 in MeOH/DME (2:1, reflux, 1.5 h) to give 1-(dimethylsulfamoyl) substituted

imidazoles **8** (Eq. 1, Table 1). The dimethylsulfamoyl group is readily removed from compounds **8** under acid conditions, in refluxing 30 % HBr, to give the 4(5)-monosubstituted imidazoles **9**, which are isolated as HBr salts, in moderate to good yields (Table 1).[15] Compounds **8** are readily obtained in analytically pure state by crystallization from isopropanol.

Table 1. 1-(Dimethylsulfamoyl)imidazoles **8** and Corresponding 4(5)-Monosubstituted Imidazoles[a] **9** from *N*-(Dimethylsulfamoyl)aldimines (**2**) and TosMIC (**4**)



2 **4** **8** **9**

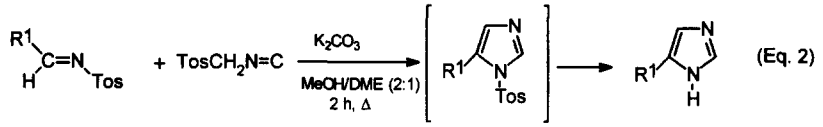
Entry	Compounds **8** R^1 =		Yield (%)	Mp (°C)	Compounds **9**. **n HBr**	Yield (%)	n =	Mp (°C)
1		**8a**	65	117-118	**9a**	55	1	> 300
2		**8b**	68	192-193	**9b**	49	1	226-227
3		**8c**	67	95-96	**9c**	93	1	274-276
4		**8d**	55	113-114	**9d**	75	1	192-194
5		**8e**	69	156-157	**9e**[b]	94	2	> 300
6		**8f**	65	141-142	**9f**[b]	91	2	> 300
7		**15g**	57[c]	167-168				
8	(*E*)-PhCH=CH–	**8h**	72	105-106				
9	Me_2N-N=CH–	**8i**	70	oil				
10	(*E,E*)-$CH_3(CH=CH)_2$-	**8j**	50[d]	oil				

a) Isolated as HBr salts. b) The dimethylsulfamoyl group of substituent R 1 is removed simultaneously. c) Under the conditions given in Eq. 1, only 5-(9-anthranyl)-1-(dimethylsulfamoyl)-4-methoxy-4 *H*,5*H*-imidazoline (**15g**) is obtained, instead of the corresponding imidazole **8g**. d) Yield estimated by ^{1}H NMR.

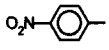
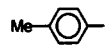
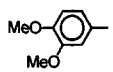
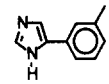
The corresponding reaction of TosMIC with *N*-tosylaldimines **3** (Eq 2, Table 2) takes a somewhat different course, in that the tosyl group is spontaneously removed from the initially formed 1-tosylimidazoles **10** under the same conditions [K_2CO_3 in MeOH/DME (2:1), reflux, 2 h] where the dimethylsulfamoyl

group of compounds **8** (Eq. 1) stays put. Apparently, the electrondonating Me_2N unit in compounds **8** reduces the aptitude of the Me_2NSO_2 group for solvolytic removal. Thus, 4(5)-phenylimidazole (**9a**) was obtained in one operation in 75 % yield of purified compound, based on *N*-tosylbenzaldimine (Table 2, entry 1). A singlet at δ 3.70 in the ^1H NMR spectrum of crude **9a** was assigned to 1-methyl-4-phenyl-

Table 2. 4(5)-Monosubstituted Imidazoles **9** from *N*-Tosylaldimines (**3**) and TosMIC (**4**)



3 **4** **10** **9**

Entry	R^1 =		Yield (%)	mp (°C)/Lit.	Entry	R^1 =		Yield (%)	mp (°C)/Lit.
1		**9a**	75	131-132/(128-129)	5	(*E*)-PhCH=CH–	**9h**	49	174-178/(181.5)
2		**9b**	62	210-212/(225)	6		**9k**	55	140-143/(147)
3		**9d**	53	112-114/(116-117)	7		**9l**	51	166-168
4		**9f**	a		8		**9m**	6	115-116

a) Complex reaction mixture; **9f** not isolated.

imidazole (**17a**, R^1 = Ph, Scheme 2), which was present in small amounts (< 5 %). Corresponding *N*-methylated side products were present more prominently in the products of entries 2, 3, 5, 6, and 8 (6-14 % yield). In these cases the side products were isolated with the use of column chromatography. For entry 6, the structure of the side product was identified by X-ray analysis as 4-(*p*-chlorophenyl)-1-methylimidazole (**17k**; Figure 1). The structures of the other side products **17** were correlated by NOESY

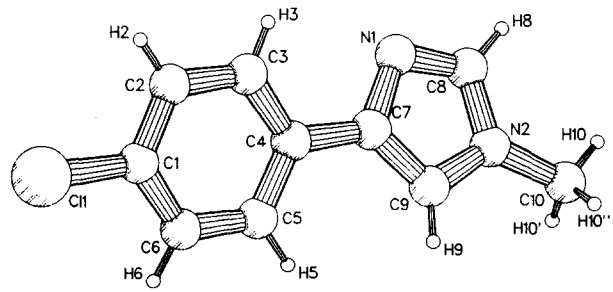
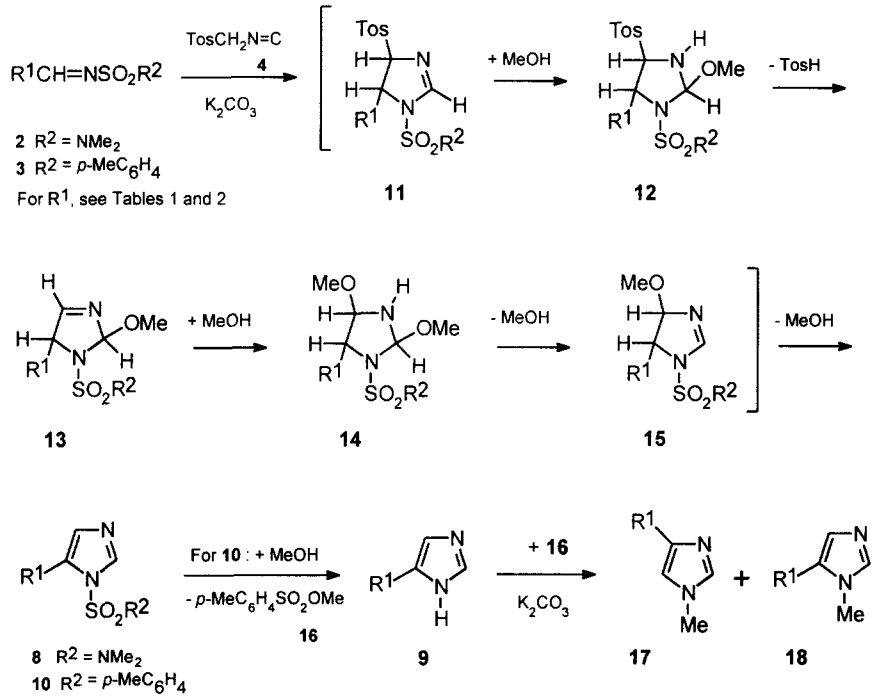


Figure 1. Pluto Representation of the Crystal Structure of 4-(*p*-Chlorophenyl)-1-methylimidazole (**17k**)

and the coupling constant of the aromatic protons of the 1,4-disubstituted imidazoles (J = 1.1-1.5 Hz for H-2,H-5).[16] Methylation of 4(5)-phenylimidazole (using dimethyl sulfate) has been reported to give a mixture of **17a** and 1-methyl-5-phenylimidazole (**18a**) in a ratio 5:1.[17]

When the reaction of Eq. 2 (for entry 2) was repeated with EtOH, instead of MeOH, 1-ethyl-4-(*p*-nitrophenyl)imidazole was formed, under otherwise similar conditions, as the side product (25 % yield). Evidently, the cosolvent (MeOH or EtOH) is responsible for the formation of the *N*-alkylated side products, such as **17b**, **17d**, **17h**, **17k**, and **17m**. However, it is unlikely that these side products are formed in a direct reaction between 4(5)-arylimidazoles **9** and the cosolvent. We propose that methyl *p*-toluenesulfonate (**16**), which is generated *in situ* during the formation of the imidazole ring, is the actual methylating agent (Scheme 2; with EtOH as cosolvent, *p*-$MeC_6H_4SO_2Et$ acts similarly as *N*-ethylating agent). This proposition is supported by the methylation of (*E*)-4-(2-phenylethenyl)-imidazole (**9h**), in a separate experiment, to (*E*)-1-methyl-4-(2-phenylethenyl)-imidazole (**17h**, R^1 = (*E*)-PhCH=CH, 69 % yield) with the use of **16**.

Scheme 2 : A Rationale of the formation of the 4(5)-Monosubstituted Imidazoles **9** and their *N*-Methyl Derivatives **17**



Most of the results discussed sofar are rationalized in Scheme 2. This scheme is modelled after a similar scheme that explains the various results of the reaction of TosMIC with aldehydes, described elsewhere.[8b] At first glance, Scheme 2 appears to ignore the virtues of Occam's razor, since the formation of compounds **8** and **10** can be explained more directly by assuming a base-induced elimination of *p*-toluenesulfinic acid (TosH) from **11**. Although we can not really exclude such an elimination of TosH in the synthesis of imidazoles (**11** → **8**, **10**), in the corresponding synthesis of

oxazoles from TosMIC and aldehydes the roundabout way analogous to Scheme 2 seems more likely. In the latter case several oxazolines comparable to **13** and **15** (read O for R^2SO_2N) have been isolated and characterized.[8b]

In the present study, imidazolines of type **11** and **15** have been identified in two cases. The first case was encountered when the reaction of Eq. 1 was carried out with *N*-(dimethylsulfamoyl)-9-anthraldimine (**2g**, Table 1, entry 7). Instead of the expected imidazole **8g**, 5-(9-anthranyl)-1-(dimethylsulfamoyl)-4-methoxy-4*H*,5*H*-imidazoline (**15g**) was obtained under the usual conditions. Apparently, the elimination of MeOH from **15g** to give **8g** does not take place in this particular case. Attempts to effect the elimination of MeOH in a separate experiment (using isolated **15g** and *t*-BuOK in THF)[8b] were inconclusive. It is tempting to ascribe this one anomalous result of Table 1 to the size of the 9-anthranyl substitutent. Possibly, deprotonation of **15g** at C5 is hampered by insufficient resonance stabilization of the corresponding anion. To maximize the overlap between the lone pair at C5 and the aromatic substituent, a planar carbanion conformation must be realized in which the anthranyl moiety and the imidazolinyl ring be in the same plane. This seems next to impossible.

As was mentioned above, Scheme 2 also accounts for the formation of the side products **17** (and possibly **18**) in the reactions of Eq. 2. According to Scheme 2, 1-tosylimidazoles **10** may react intermolecularly with the cosolvent MeOH to give 4(5)-monosubstituted imidazoles **9** together with methyl *p*-toluenesulfonate (**16**).[18] Alternatively, **16** could form intramolecularly from **13** (to give the 5*H* tautomer of **9** initially). Furthermore, the intramolecular elimination of **16** could precede aromatization in case of the intermediates **12** or **14** (always R^2 = *p*-MeC_6H_4).

Two unsuccessful attempts have been made to prevent, or to minimize, the formation of *N*-alkylated side products **17** (and possibly **18**) in the reaction of Eq. 2. First of all, the reaction of entry 6 (Tabel 2) was carried out with *t*-BuOH as cosolvent, instead of MeOH. It was hoped that *t*-butyl *p*-toluenesulfonate, if formed at all, would be a less effective *N*-alkylating agent. Under otherwise the same reaction conditions (*t*-BuOH/DME 2 : 1, reflux, 2 h) 5-(*p*-chlorophenyl)-1,4-ditosyl-4*H*,5*H*-imidazoline (**11k**, R^1 = *p*-ClC_6H_4, R^2 = *p*-MeC_6H_4) was obtained in 82 % yield. This experiment shows : (1) that no direct elimination of TosH (**11k** → **10k**) is taking place, and (2) that no *p*-$MeC_6H_4SO_2Ot$-Bu is formed (apparently none of the four possible routes discussed above for the formation of **16** with MeOH is working for *t*-BuOH). This result is consistent with the rationale given in Scheme 2. Under more drastic conditions (*t*-BuOH/DME 2 : 1, reflux, 20 h), 5-(*p*-chlorophenyl)-1-tosylimidazole (**10k**) was formed in a yield of 10 %. When the reaction of entry 5 (Table 2) was repeated with water instead of *t*-BuOH (reflux, 2 h) imidazoline **11k** was isolated again, although in lower yield (37 %).[19]

In principle, aldimines derived from benzylamine[20] and *N*-tosylhydrazine[21] could serve the same purpose as aldimines **2** and **3** in Eq. 1 and 2, respectively. Potentially, the *N*-benzyl group and the *N*-tosylamine group can be removed from the 1,5-disubstituted imidazoles expected from reaction with TosMIC. It turned out, however, that neither PhCH=NCH_2Ph nor PhCH=NNHTos gave the desired imidazole in this reaction.

CONCLUSIONS

The overall yields of 4(5)-monosubstituted imidazoles **9** by the methods of Table 1 (Eq. 1) and Table 2 (Eq. 2) are comparable. The approach of Eq. 2 takes two steps, one to convert the aldehyde with (cheap) *p*-toluenesulfonamide to *N*-tosylaldimines (**3**) and a second for the reaction with TosMIC to form

9. A disadvantage of this method is the occasional formation of *N*-methylated side products **17** (in yields ranging from 5-14 %). In our hands, column chromatography was needed to remove the higher-yield side products. The approach of Eq. 1 is not hampered by the formation of side products **17**. However, the removal of the dimethylsulfamoyl protection from **8** takes an additional step. Furthermore, *N*-(dimethylsulfamoyl)amide, the reagent for the syntheses of aldimines **2** needs to be prepared from commercially available Me_2NSO_2Cl and ammonia.

EXPERIMENTAL

All experiments were performed in a dry nitrogen atmosphere. *N*-(Dimethylsulfamoyl)aldimines **2** were prepared as published.[14] *N*-Tosylaldimines **3** have been reported previously: compounds **3a, 3b, 3f, 3g, and 3k** were easily prepared by condensation of an aldehyde with $TosNH_2$ in refluxing toluene without the use of a catalyst. In case of aldimines **3d**, **3l**, and **3m** the procedure of Love *et al.* was followed.[22] Aldehydes and $TosNH_2$ are commercial products, which have been used as received. Tosylmethyl isocyanide (TosMIC) was purchased from Ofichem (Ter Apel, The Netherlands). Column chromatography was performed on alumina (Brockmann 90, II/III, 0.063-0.200 mm) using CH_2Cl_2 as eluent. CH_2Cl_2 was distilled over P_2O_5 before use. 1, 2-Dimethoxyethane (DME) was distilled from Na wire; EtOH (p.a.) and MeOH (p.a.) were dried over 3Å sieves. Melting points were measured on a Reichert melting point apparatus, equipped with a Reichert microscope and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Unity Plus spectrometer (500 MHz), on a Varian VXR-300 spectrometer (300 MHz), or on a Varian Gemini spectrometer (200 MHz). ^{1}H NMR chemical shifts were determined relative to the solvent and converted to the TMS scale using δ ($CHCl_3$) = 7.26 and δ (DMSO) = 2.49. ^{13}C NMR spectra were recorded on a Varian Unity Plus spectrometer (125.7 MHz), on a Varian VXR-300 spectrometer (75.4 MHz), or on a Varian Gemini spectrometer (50.3 MHz). ^{13}C NMR chemical shifts were determined relative to the solvent and converted to the TMS scale using δ ($CDCl_3$) = 76.91 and δ (DMSO) = 39.7. Mass spectra were recorded on a AEI-MS-902 mass spectrometer (DI system; e.v. 70 eV; acc.v. 8 kV; multiplier 2.1 kV; I.S. temp. 120 °C; D.I. temp. 110-120 °C). Elemental microanalyses were carried out in the Analytical Department of this laboratory.

1-(Dimethylsulfamoyl)-5-phenylimidazole (8a) (Typical Procedure) :
A mixture of TosMIC (0.20 g, 1.0 mmol), *N*-(dimethylsulfamoyl)benzaldimine (**2a**, 0.21 g, 1.0 mmol), and K_2CO_3 (0.15 g, 1.1 mmol) in MeOH/DME 2:1 (30 mL) was refluxed for 90 min. After cooling, the reaction mixture was quenched with water (10 mL) and stirred for 5 min at room temperature. The mixture was poured in 50 mL of water and extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. One crystallisation from isopropanol gave analytically pure **8a** as a white solid (0.16 g, 65 %): mp 117-118 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 6H), 7.03 (br s, 1H), 7.41-7.52 (m, 5H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 37.19 (q), 128.04 (d), 128.07 (s), 129.15 (d), 130.63 (d), 130.76 (d), 131.76 (s), 139.93 (d); MS (relative intensity, %): *m/z* = 28 (54.3), 42 (19.7), 57 (18.7), 89 (63.0), 108 (57.8), 116 (25.5), 143 (100), 251 (M^+, 80.1); HRMS: *m/z* calc. for $C_{11}H_{13}N_3O_2S$: 251.073; found 251.073; Anal calc. for $C_{11}H_{13}N_3O_2S$: C, 52.57; N, 16.72; H, 5.21; S, 12.75; found C, 51.94; N, 16.50; H, 5.21; S, 12.56.

1-(Dimethylsulfamoyl)-5-(*p*-nitrophenyl)imidazole (8b) :
Following the procedure described for **8a**, *N*-(dimethylsulfamoyl)-*p*-nitrobenzaldimine (**2b**, 0.26 g, 1.0 mmol) gave, after crystallisation from isopropanol, analytically pure **8b** as a yellow solid (0.20 g, 68%): mp 192-193 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.56 (s, 6H), 7.17 (br s, 1H), 7.73 (d, *J* = 8.79 Hz, 2H), 8.10 (br s, 1H), 8.30 (d, *J* = 8.79 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz): δ = 37.69 (q), 123.35 (d), 130.12 (s), 131.23 (d), 132.50 (d), 134.89 (s), 141.04 (d), 148.05 (s); MS (relative intensity, %): *m/z* 28 (9.70), 42 (9.44), 44 (19.64), 88 (12.80), 108 (100), 296 (M^+, 35.24); HRMS: *m/z* calc. for $C_{11}H_{12}N_4O_4S$: 296.058; found 296.058; Anal. calc. for $C_{11}H_{12}N_4O_4S$: C, 44.59; N, 18.91; H, 4.08; S, 10.82; found C, 44.68; N, 18.24; H, 4.30; S, 10.41.

1-(Dimethylsulfamoyl)-5-(*m*-nitrophenyl)imidazole (8c) :
Following the procedure described for **8a**, *N*-(dimethylsulfamoyl)-*m*-nitrobenzaldimine (**2c**, 0.26 g, 1.0 mmol) gave, after crystallisation from isopropanol, analytically pure **8c** as an off-white solid (0.20 g, 67 %): mp 95-96 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.58 (s, 6H), 7.16 (br s, 1H), 7.63 (dd, *J* = 7.57 Hz, *J* = 7.81 Hz, 1H), 7.89 (d, *J* = 7.81 Hz, 1H), 8.09 (br s, 1H), 8.30 (d, *J* = 8.06 Hz, 1H), 8.37 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75.4 MHz): δ = 37.87 (q), 124.09 (d), 125.29 (d), 129.41 (d), 130.01 (s),

130.32 (s), 132.41 (d), 136.83 (d), 140.81 (d), 148.11 (s); MS (relative intensity, %): *m/z* = 28 (34.91), 42 (11.34), 44(22.61), 88 (10.18), 108 (100), 296 (M^+, 18.91); HRMS: *m/z* calc. for $C_{11}H_{12}N_4O_4S$: 296.058; found 296.058; Anal. calc. for $C_{11}H_{12}N_4O_4S$: C, 44.59; N, 18.91; H, 4.08; S, 10.82; found C, 44.23; N, 18.75; H, 4.11; S, 10.61.

1-(Dimethylsulfamoyl)-5-*p*-tolylimidazole (8d) :

Following the procedure described for **8a**, *N*-(dimethylsulfamoyl)-*p*-tolualdimine (**2d**, 0.22 g, 1.0 mmol) gave, after crystallisation from isopropanol, analytically pure **8d** as a white solid (0.15 g, 55%): mp 113-114 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.40 (s, 3H), 2.46 (s, 6H), 7.01 (br s, 1H), 7.23 (d, *J* = 8.06 Hz, 2H), 7.40 (*d*, J = 7.82 Hz, 2H), 8.04 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 21.22 (q), 37.26 (q), 125.11 (s), 128.72 (d), 130.53 (d), 130.66 (d), 131.88 (d), 139.20 (s), 139.80 (s); MS (relative intensity, %): *m/z* = 28 (9.35), 42 (9.60), 44 (11.05), 57 (10.94), 77 (14.41), 103 (41.08), 108 (13.03), 130 (15.16), 157 (100), 158 (21.03), 265 (M^+, 41.15); HRMS: *m/z* calc. for $C_{12}H_{15}N_3O_2S$: 265.088; found 265.088; Anal. calc. for $C_{11}H_{12}N_4O_4S$: C, 54.32; N,15.85; H, 5.70; S, 12.06; found C, 54.28; N, 15.70; H, 5.97; S, 12.10.

1,4-Di-[1-(dimethylsulfamoyl)-5-imidazolyl]benzene (8e) :

A solution TosMIC (0.39 g, 2.0 mmol), *N,N* -bis-(dimethylsulfamoyl)terephthaldialdimine (**2e**, 0.35 g, 1.0 mmol), and K_2CO_3 (0.29 g, 2.1 mmol) in MeOH/DME 2:1 (30 mL) was refluxed for 90 min. The reaction mixture was quenched with water (10 mL) and stirred for 5 min at room temperature. The precipated solid was collected and washed several times with portions of hexane (20 mL) to give analytically pure **8e** as a white solid (0.29 g, 69%): mp 156-157 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.56 (s, 12H), 7.09 (d, *J* = 0.97 Hz, 2H), 7.76 (s, 4H), 8.05 (d, *J* = 0.97 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 37.54 (q), 129.12 (d), 130.26 (d), 131.24 (s), 131.28 (d), 140.06 (s); MS (relative intensity, %): *m/z* = 28 (13.33), 42 (14.35), 44 (24.52), 64 (11.21), 108 (61.86), 127 (14.17), 154 (11.21), 181 (10.62), 209 (19.33), 316 (100), 424 (M^+, 56.31); HRMS: *m/z* calc. for $C_{16}H_{20}N_6O_4S_2$: 424.099; found 424.099; Anal. calc. for $C_{16}H_{20}N_6O_4S_2$: C, 45.27; N, 19.81; H, 4.75; S, 15.08; found C, 45.14; N, 19.73; H, 4.75; S, 15.08.

1,3-Di-[1-(dimethylsulfamoyl)-5-imidazolyl]benzene (8f) :

Following the procedure described for **8e**, *N,N* -bis-(dimethylsulfamoyl)isophthaldialdimine (**2f**, 0.35 g, 1.0 mmol) gave analytically pure **8f** as an off-white solid (0.27 g, 65%): mp 141-142 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.56 (s, 12H), 7.09 (br s, 2H), 7.45-7.65 (m, 4H), 8.05 (br s, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 37.53 (q), 127.82 (d), 128.29 (s), 131.11 (d), 131.34 (d), 132.54 (d), 132.57 (d), 139.97 (s); MS (relative intensity, %): *m/z* = 28 (15.10), 42 (16.1), 44 (22.90), 64 (11.30), 108 (59.60), 127 (14.20), 154 (13.60), 209 (21.10), 316 (53.50), 424 (M^+, 100); HRMS: *m/z* calc. for $C_{16}H_{20}N_6O_4S_2$: 424.099, found 424.099; Anal. calc. for $C_{16}H_{20}N_6O_4S_2$: C, 45.27; N, 19.81; H, 4.75; S, 15.08; found C, 45.20; N, 19.57; H, 4.78; S, 14.83.

5-(9-Anthranyl)-1-(dimethylsulfamoyl)-4-methoxy-4*H*,5*H*-imidazoline (15g) :

TosMIC (0.70 g, 3.6 mmol), *N*-(dimethylsulfamoyl)-9-anthraldimine (**2g**, 0.94 g, 3.0 mmol), and K_2CO_3 (0.99 g, 7.2 mmol) were refluxed in a mixture of MeOH/DME 2 :1 (30 mL) for 2 h. After cooling, the reaction mixture was quenched with water (50 mL) and the mixture was stirred for 10 min at room temperature. The mixture was extracted with CH_2Cl_2 (2 X 50 mL) and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was crystallized from EtOH (96 %) to give **15g** as orange crystals (1.70 g, 57 %). Recrystallization of **15g** from the same solvent gave pale yellow crystals : mp. 167-168 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.68 (s, 6H), 3.60 (s, 3H), 5.76 (d, *J* = 6.59 Hz, 1H), 6.25 (d, *J* = 6.59 Hz, 1H), 7.47-7.79 (m, 6H), 8.00-8.11 (m, 2H), 8.51-8.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 36.20 (q), 56.37 (d), 62.32 (d), 106.82 (d), 123.00 (d), 123.47 (d), 125.06 (d), 125.29 (d), 126.43 (d), 127.12 (s), 127.47 (d), 129.07 (d), 129.20 (s), 129.38 (d), 129.88 (d), 131.21 (s), 131.36 (s), 131.56 (s), 152.51 (d); MS (relative intensity, %): *m/z* = 28 (60.81), 32 (13.69), 45 (33.46), 204 (10.81), 275 (100), 216 (86.89), 351 (6.66), 383 (M^+, 5.34); HRMS: *m/z* calc. for $C_{20}H_{21}N_3O_3S$: 383.130, found 383.130; Anal calc. for $C_{20}H_{21}N_3O_3S$: C, 62.64; N, 10.96; H, 5.52; S, 8.34; found C, 62.88; N, 10.81; H, 5.49; S, 7.93.

Attempts to prepare the corresponding imidazole **8g** by elimination of MeOH from **15g** using *t*-BuOK in THF remained inconclusive.

(*E*)-1-(Dimethylsulfamoyl)-5-(2-phenylethenyl)imidazole (8h) :

Following the procedure described for **8a**, *N*-(dimethylsulfamoyl)cinnamaldimine (**2h**, 0.48 g, 2.0 mmol) gave, after crystallization from isopropanol, analytically pure **8h** as white crystals (0.40 g, 72 %): mp 105-106 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.99 (s, 6H), 7.14 (d, *J* = 16.5 Hz, 1H), 7.43-7.63 (m, 7H), 8.08 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 38.05 (q), 114.03 (d), 126.44 (d), 128.03 (d), 128.29 (d), 128.71 (d), 131.12 (s), 131.83 (d), 136.04 (s), 138.74 (d); MS (relative intensity, %): *m/z* = 28 (42.32), 32 (9.47), 115 (5.98), 143 (19.49), 170 (5.67), 277 (M^+, 100); HRMS: *m/z* calc. for $C_{13}H_{15}N_3O_2S$: 277.088,

found 277.088; Anal. calc. for $C_{13}H_{15}N_3O_2S$: C, 56.30; N, 15.16; H, 5.46; S, 11.54; found C, 56.24; N, 15.00; H, 5.30; S, 11.74.

1-(Dimethylsulfamoyl)imidazole-2-carboxaldehyde dimethylhydrazone (8i) :
Following the procedure described for **8a**, *N*-(dimethylamino)-*N'*-(dimethylsulfamoyl)-1,4-diaza-1,3-butadiene (**2i**, 0.21 g, 1.0 mmol) gave, after workup, **8i** in almost pure form as a red brown oil (1.71 g, 70 %): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.83 (s, 6H), 2.98 (s, 6H), 7.32 (m, 2H), 7.85 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 37.95 (q), 42.19 (q), 119.56 (d), 126.98 (d), 130.25 (s), 137.47 (d); MS (relative intensity, %): *m/z* = 28 (50.35), 42 (60.10), 44 (99.40), 52 (11.14), 67 (26.17), 94 (57.77), 110 (42.06), 137 (47.84), 245 (M^+, 100); HRMS calc.$C_8H_{15}N_5O_2S$: 245.095, found 245.095.

(*E, E*)-1-(Dimethylsulfamoyl)-5--(1,3-pentadienyl)imidazole (8j) :
Following the procedure described for **8a**, (*E, E*)-N-(dimethylsulfamoyl)-2,4-hexadienaldimine (**2j**, 0.20g, 1.0 mmol) gave, after column chromatography (silicagel, Et_2O), **8j** as a crude brown oil (0.12 g, ca. 50 %). Further attempts of purification by crystallisation and distillation were unsuccessful; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.83 (d, *J* = 6.84 Hz, 3H), 2.85 (s, 6H), 5.82-5.93 (m, 1H), 6.14-6.30 (m, 1H), 6.61-6.64 (m, 2H), 7.20 (br s, 1H), 7.88 (br s, 1H).

4(5)-Phenylimidazole hydrobromide (9a.HBr) (Typical Procedure) :
Following the conditions of Vollinga *et al.*,[11g] **8a** (0.76 g, 3.03 mmol) was dissolved in 30% aqueous HBr and heated under reflux for 90 min. The mixture was cooled and concentrated under vacuum. The residue was dissolved in absolute EtOH (50 mL, heated under reflux for 30 min, and concentrated under reduced pressure. The remaining yellow solid was washed with acetone to give almost pure **9a.HBr** as an off-white solid (0.37 g, 55%): mp > 300 °C; ^{1}H NMR (DMSO.d_6, 200 MHz): δ 7.53-8.31 (m, 5H), 9.16 (m, 2H);^{13}C NMR (DMSO.d_6, 75.4 MHz): δ =116.38 (d), 122.93 (d), 125.69 (d), 128.09 (s), 130.35 (d), 132.15 (s), 135.65 (d); MS (relative intensity, %): *m/z* = 80 (6.9), 89 (15.3), 90 (17.1), 117 (16.5), 144 (M^+, 100); Anal. calc. for $C_9H_9N_2Br$: C, 48.03; N, 12.45; H, 4.03; Br, 35.50; found C, 47.16; N, 12.11; H, 3.84; Br, 34.86 (the sample of **9a.HBr** used for elemental analysis was not subjected to further purification).

4(5)-(*p*-Nitrophenyl)imidazole hydrobromide (9b.HBr) :
From **8b** (0.20 g, 0.7 mmol) by 16 h of reflux with 30 % HBr. After workup the remaining yellow solid was washed with acetone to give pure **9b.HBr** as a white solid (95 mg, 49%): mp 226-227 °C. ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 8.07 (d, *J* = 8.79 Hz, 2H), 8.35 (d, *J* = 8.79 Hz, 2H), 8.34 (br s, 1H), 9.06 (br s, 1H); ^{13}C NMR (DMSO.d_6, 75.4 MHz): δ = 118.04 (d), 124.46 (d), 126.02 (d), 131.67 (s), 134.39 (s), 136.54 (d), 146.93 (s); MS (relative intensity, %): *m/z* = 28 (11.86), 50 (3.21), 62 (5.90), 63 (9.87), 80 (18.47), 82 (19.23), 89 (34.86), 116 (42.75), 143 (36.37), 189 (M^+, 100); HRMS: *m/z* calc. for $C_9H_7N_3O_2$:189.054, found 189.054.[23]

4(5)-(*m*-Nitrophenyl)imidazole hydrobromide (9c.HBr) :
From **8c** (0.29 g, 1.0 mmol) by 2 h of reflux with 30% HBr. After workup the remaining yellow solid was washed with acetone to give pure **9c.HBr** as a white solid (0.25 g, 93%): mp 274-276 °C. ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 7.67-7.72 (dd, *J* = 8.05 Hz, *J* = 8.06, 1H), 8.16 (d, *J* = 7.0 Hz, 2H), 8.30 (br s, 1H), 8.60 (br s, 1H), 9.17 (br s, 1H); ^{13}C NMR (DMSO.d_6, 75.4 MHz): δ = 117.43 (d), 120.01 (d), 123.72 (d), 129.08 (s), 131.06 (d), 131.75 (d), 132.21 (s), 136.15 (d), 148.58 (s); MS (relative intensity, %): *m/z* = 28 (57.83), 32 (12.59), 63 (8.25), 80 (20.90), 82 (19.79), 89 (29.13), 116 (36.95), 143 (32.94), 189 (M^+, 100), 191 (10.96); HRMS: *m/z* calc. for $C_9H_7N_3O_2$:189.054, found 189.054[23].

4(5)-(*p*-Tolyl)imidazole hydrobromide (9d.HBr) :
From **8d** (0.25 g, 1.0 mmol) by 16 h of reflux with 30 % HBr. After workup the remaining yellow solid was washed with acetone to give pure **9d.HBr** as a white solid (0.17 g, 75%): mp 192-194 °C. ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 2.33 (s, 3H), 7.32 (d, *J* = 7.81, 2H), 7.69 (d, *J* = 8.30 Hz, 2H), 8.10 (s, 1H), 9.17 (s, 1H); ^{13}C NMR (DMSO.d_6, 75.4 MHz): δ = 20.85 (q), 124.03 (s), 114.89 (d), 125.22 (s), 129.73 (s), 132.64 (d), 134.93 (d), 138.86 (s); MS (relative intensity, %): *m/z* = 28 (5.02), 41 (4.59), 51 (6.12), 63 (4.90), 65 (3.31), 77 (10.81), 79 (6.18), 80 (13.38), 82 (12.92), 103 (14.70), 130 (23.58), 157 (28.66), 158 (M^+, 100); HRMS: *m/z* calc. for $C_{10}H_{10}N_2$: 158.084, found 158.084.[23]

1,4-Di[(4(5)-imidazolyl)benzene dihydrobromide (9e.2HBr) :
From **8e** (0.54 g, 2.0 mmol) by 16 h of reflux with 30 % HBr. After workup the remaining yellow solid was washed with acetone to give almost pure **9e.HBr** as a white solid (0.33 g, 94 %): mp > 300 °C. ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 7.99 (s, 4 H), 8.30 (d, *J* = 1.22 Hz, 2H), 9.28 (d, *J* = 1.47 Hz, 2H); MS (relative intensity, %): *m/z* = 28 (72.71), 32 (15.97), 79 (13.69), 80 (40.42),

82 (38.98), 155(8.73), 171 (17.08), 211 (M^+, 100), 212 (14.66); HRMS: *m/z* calc. for $C_{12}H_{10}N_4$: 210.091, found 210.091.[23]

1,3-Di[4(5)-imidazolyl]benzene dihydrobromide (9f.2HBr) :

From **9f** (0.42 g, 1.0 mmol) by 16 h of reflux with 30 % HBr. After workup the remaining yellow solid was washed with acetone to give pure **9f.HBr** as a white solid (0.35 g, 91%): mp > 300 °C. ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 7.70 (dd, *J* = 7.80 Hz, *J* = 8.30 Hz, 1H), 7.87 (d, *J* = 7.0 Hz, 2H), 8.30 (br s, 2H), 8.44 (br s, 1H), 9.31 (d, *J* = 0.98 Hz, 2H); ^{13}C NMR (DMSO.d_6, 75.4 MHz): δ = 116.41 (d), 123.01 (d), 125.75 (d), 128.11 (s), 130.41 (d), 132.18 (s), 135.69 (d); MS (relative intensity, %): *m/z* = 28 (50.61), 32 (12.62), 79 (20.02), 80 (46.60), 81 (18.45), 82 (49.17), 155 (10.19), 210 (M^+, 100.00), 211 (16.50); HRMS: *m/z* calc. for $C_{12}H_{10}N_4$: 210.091, found 210.091.[23]

4(5)-(Phenyl)imidazole (9a) (Typical Procedure) :

A mixture of TosMIC (0.64 g, 3.3 mmol), *N*-tosylbenzaldimine (**3a**, 0.78 g, 3.0 mmol), and K_2CO_3 (1.24 g, 9.0 mmol) in MeOH/DME 2:1 (30 mL) was refluxed for 90 min. After cooling, the reaction mixture was quenched with water (10 mL) and stirred for 15 min at room temperature. The mixture was poured in 50 mL of water and extracted once with Et_2O (50 mL) and then with CH_2Cl_2 (50 mL). The combined organic layers were concentrated and the crude product was dissolved in Et_2O (50 mL) and extracted with 3 N HCl (50 mL). The acidic layer was made slighly alkaline with 50 % NaOH and the resulting layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The brown oil was treated with pentane to give **9a** as a white solid. The ^{1}H NMR spectrum of this material showed *i.a.* a singlet at δ 3.70 which was assigned to a small amount (< 5 %) of 1-methyl-4-phenylimidazole (**17b**, see text). This impurity was removed by crystallization from CH_2Cl_2/pentane to give **9a** as white crystals (0.32g, 75 %): mp. 131-132 °C (Lit.[17a] 128-129 °C); ^{1}H NMR (DMSO.d_6, 200 MHz): δ = 7.26-7.42 (m, 4H), 7.70-7.75 (m, 3H), 9.81 (br, 1H).

4(5)-(*p*-Nitrophenyl)imidazole (9b) and 1-methyl 4-(*p*-nitrophenyl)imidazole (17b) :

p-Nitrophenyl-*N*-tosylaldimine (**3b**, 0.91 mg, 3.0 mmol) was reacted with TosMIC (0.64 g, 3.3 mmol) and K_2CO_3 (1.24 g, 9.0 mmol) in EtOH/DME 2:1 (30 mL) for 2 h, analogously to the procedure described for **9a** The mixture obtained upon acid/base extraction was chromatographed (Al_2O_3, CH_2Cl_2) to give two fractions. The second fraction gave **9b** as a orange solid (0.35 g, 62 %), pure according to ^{1}H-NMR. Yellow crystals were obtained by crystallization from EtOH (96 %): mp. 195-196 °C (Lit.[17a] 225 °C); ^{1}H NMR (DMSO.d_6, 300 MHz): δ = 7.71 (s, 1H), 7.81 (s, 1H), 7.90 (d, *J* = 8.78 Hz, 2H), 8.09 (d, *J* = 8.79 Hz, 2H), 12.20-12.60 (br, 1H); ^{13}C NMR (DMSO.d_6, 75.4 MHz): δ = 117.18 (s), 124.14 (d), 124.56 (s), 124.71 (d), 137.20 (d), 141.31 (s), 145.20 (d); MS (relative intensity, %): *m/z* = 28 (100), 32 (52.43), 63 (14.51), 89 (50.87), 116 (58.02), 131 (9.77), 143 (25.93), 159 (12.65), 189 (M^+, 100); HRMS: *m/z* calc. for $C_9H_7N_3O_2$: 189.054, found 189.054.

The first fraction gave a side product, *i.e.* the *N*-ethylation derivative of **9b**, as a yellow solid (160 mg, 25%), pure according to ^{1}H NMR. Yellow crystals were obtained by crystallization from CH_2Cl_2/hexane: mp 125-126 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.53 (t, *J* = 7.39 Hz, 3H), 4.06 (q, *J* = 7.37 Hz, 2H), 7.39 (d, *J* = 1.31 Hz, 1H), 7.57 (d, *J* = 1.26 Hz, 1H), 7.90 (d, *J* = 9.06 Hz, 2H), 8.23 (d, *J* = 9.06 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 16.16 (q), 42.13 (t), 116.68 (d), 124.01 (d), 124.66 (d), 137.52 (d), 139.90 (s), 140.55 (s), 145.98 (s); MS (relative intensity, %): *m/z* = 28 (75.6), 32 (16.3), 8.9 (11.0), 116 (17.6), 171 (27.2), 187 (10.5), 217 (M^+, 100); HRMS: *m/z* calc. for $C_{11}H_{11}N_3O_2$: 217.085, found 217.085.

When MeOH was used as cosolvent, 1-methyl-4-(*p*-nitrophenyl)imidazole (**17b**) was obtained as a yellow solid (0.08 g, 12 %). Yellow crystals were obtained by crystallization from CH_2Cl_2/hexane: mp 194-196 °C (Lit. [17b] 195 °C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.76 (s, 3H), 7.34 (d, *J* = 1.30 Hz, 1H), 7.52 (d, *J* = 1.00 Hz, 1H), 7.88 (d, *J* = 8.79 Hz, 2H), 8.22 (d, *J* = 8.79 Hz, 2H) ; ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 33.61 (q), 118.25 (d), 124.04 (d), 124.72 (d), 138.76 (d), 140.12 (s), 140.48 (s), 146.67 (s); MS (relative intensity, %): *m/z* = 28 (59.22), 32 (12.39), 89 (16.77), 116 (11.37), 142 (8.75), 157 (23.19), 173 (8.07), 203 (M^+, 100); HRMS: *m/z* calc. for $C_{10}H_9N_3O_2$: 203.068, found 203.068.

4(5)-(*p*-Tolyl)imidazole (9d) and 1-methyl-4-(*p*-tolyl)imidazole (17d) :

p-Tolyl-*N*-tosylaldimine (**3d**, 082 mg, 3.0 mmol) was reacted with TosMIC (0.64 g, 3.3 mmol), and K_2CO_3 (1.24 g, 9.0 mmol) in MeOH/DME 2:1 (33 mL) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction was chromatographed (Al_2O_3, CH_2Cl_2) to give two fractions. The second fraction gave **9d** as a pale orange solid (0.25 g, 53 %), pure according to ^{1}H-NMR: mp 112-114 °C (Lit.[20] 116-117 °C); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.35 (s, 3H), 7.18 (d, *J* = 7.81 Hz, 2H), 7.33 (br s, 1H), 7.62 (d, *J* = 8.05 Hz, 2H), 7.68 (br s, 1H), 11.73-11.80 (br, 1H); ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 21.04 (q), 115.76 (d), 124.78 (d), 129.32 (d), 129.82 (s), 135.51 (d), 136.55 (s), 137.94 (s); MS (relative intensity, %): *m/z* = 28 (80.94), 32 (18.14), 77 (6.60), 91 (10.70), 103 (9.37), 118 (7.29), 130 (16.62), 157 (23.73), 158 (M^+, 100); HRMS: *m/z* calc. for $C_{10}H_{10}N_2$: 158.084, found 158.084.

The first fraction gave a side product **17d**, *i.e.* the *N*-methylated derivative of **9d**, as a white solid (25 mg, 5 %), pure according to ^{1}H NMR. White crystals were obtained by crystallization from petroleum ether (bp 40-60 °C): mp 115-118 °C; H NMR ($CDCl_3$, 500 MHz): δ = 2.35 (s, 3H), 3.71 (s, 3H), 7.12 (d, *J* = 1.35 Hz, 1H), 7.17 (d, *J* = 7.85 Hz, 2H), 7.44 (d, *J* = 1.28 Hz, 1H), 7.65 (d, *J* = 8.06, 2H); ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 21.12 (q), 33.39 (q), 115.32 (d), 124.53 (d), 129.13 (d), 131.31 (s), 136.21 (s), 137.74 (d), 142.41 (s); MS (relative intensity, %): *m/z* = 77 (4.2), 103 (6.3), 130 (13.9), 172 (M^+, 100); HRMS: *m/z* calc. for $C_{11}H_{12}N_2$: 172.100, found 172.100.

1,3-Di[(4(5)-imidazolyl)benzene dihydrobromide (9f) :

N,N'-Ditosylisophthaldialdimine (**3f**, 0.88 g, 2.0 mmol) was reacted with TosMIC (0.43 g, 2.2 mmol) and K_2CO_3 (1.21 g, 8.8 mmol) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction contained **9f** and several methylated imidazoles. Attempts to isolate **9f** were not successful.

(*E*)-4(5)-(2-Phenylethenyl)imidazole (9h) and (*E*)-1-methyl-4-(2-phenylethenyl)imidazole (17h) :

N-Tosylcinnamaldimine (**3h**, 0.86 g, 3.0 mmol) was reacted with TosMIC (0. 64 g, 3.3 mmol) and K_2CO_3 (0.91 g, 6.6 mmol) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction was chromatographed (Al_2O_3, CH_2Cl_2) to give two fractions. The second fraction gave **9h** as a white solid (0.25 g, 49 %) pure according to ^{1}H NMR: mp 174-178 °C (Lit. [24] 181.5 °C); ^{1}H NMR (DMSO.d_6, 300 MHz): δ = 6.90-7.58 (m, 9H), 11.90-12.30 (br, 1H); ^{13}C NMR (DMSO .d_6, 125.7 MHz): δ = 119.80 (br s), 124.96 (d), 125.81 (d), 126.77 (d), 126.85 (d), 128.68 (d), 136.31 (d), 137.45 (d); MS (relative intensity, %): *m/z* = 28 (47.00), 39 (18.31), 51 (15.52), 63 (19.12), 77 (9.93), 89 (14.02), 102 (5.43), 115 (82.33), 142 (39.71), 143 (26.74), 169 (100), 170 (M^+, 83.83); HRMS: *m/z* calc. for $C_{11}H_{10}N_2$: 170.084, found 170.084.

The first fraction gave a side product **17h**, *i.e.* the *N*-methylated derivative of **9h**, as a pale orange solid (50 mg, 10 %), pure according to ^{1}H NMR. White crystals were obtained by crystallization from CH_2Cl_2/hexane: mp 125-127 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.68 (s, 3H), 6.91 (d, J = 1.50 Hz, 1H), 6.98 (d, J = 16.09 Hz, 1H), 7.19-7.37 (m, 4H), 7.42 (br s, 1H), 7.48 (d, J = 8.29 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ = 33.29 (q), 118.19 (d), 120.06 (d), 126.07 (d), 126.73 (d), 126.88 (d), 128.42 (d), 137.58 (s), 138.06 (d), 140.08 (s); MS (relative intensity, %): *m/z* = 28 (100), 32 (22.30), 42 (22.93), 115 (19.88), 143 (26.53), 183 (98.13), 184 (M^+, 53.03); HRMS: *m/z* calc. for $C_{12}H_{12}N_2$: 184.100, found 184.100.

In a separate experiment, (*E*)-4(5)-(2-phenylethenyl)imidazole (**9h**, 0.10 g, 0.59 mmol), methyl *p*-toluenesulfonate (0.22 g, 1.18 mmol), and K_2CO_3 (0.15 g, 1.10 mmol) were refluxed in MeOH/DME 2:1 (7.5 mL) for 135 min. After cooling, addition of H_2O (50 mL), extraction with Et_2O (2 x 50 mL), drying ($MgSO_4$), and removal of the solvent, the crude product was filtered through a short column of Al_2O_3 (CH_2Cl_2), to give, after washing with pentane, **17h** as a white solid (0.75 g, 69 %): mp 176-179 °C, which was identical with the above material according to ^{1}H NMR. 2D-NMR (NOESY) was consistent with the 1,4-disubstituted imidazole structure of **17h**.

4(5)-(*p*-Chlorophenyl)imidazole (9k) and 4-(*p*-chlorophenyl)-1-methylimidazole (17k) :

p-Chlorophenyl-*N*-tosylaldimine (**3k**, 0.88 g, 3.0 mmol) was reacted with TosMIC (0. 64 g, 3.3 mmol), and K_2CO_3 (0.91 g, 6.6 mmol) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction was chromatographed (Al_2O_3, CH_2Cl_2) to give two fractions. The second fraction gave **9k** as a white solid (0.30 g, 55 %), pure according to ^{1}H NMR: mp 140-143 °C (Lit.[25] 147 °C). 1H NMR (DMSO.d_6, 200 MHz): δ = 7.38 (d, *J* = 8.30 Hz, 2H), 7.65 (br s, 1H), 7.73 (d, *J* = 7.57 Hz, 2H), 7.80 (br s, 1H); ^{13}C NMR (DMSO.d_6, 125 MHz): δ = 113.05 (d), 125.85 (d), 128.40 (d), 130.22 (s), 133.85 (s), 136.08 (d), 138.85 (s); MS (relative intensity, %): *m/z* = 28 (70.58), 32 (16.52), 41 (23.42), 63 (17.04), 89 (47.35), 116 (19.28), 123 (16.03), 151 (16.48), 178 (M^+, 100); HRMS: *m/z* calc. for $C_9H_7ClN_2$: 178.030, found 178.030.

The first fraction gave a side product **17k**, *i.e.* the *N*-methylated derivative of **9k**, as a white solid (80 mg, 14 %), pure according to ^{1}H NMR. White crystals were obtained by crystallization from CH_2Cl_2/hexane: mp 144-145 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.71 (s, 3H), 7.14 (d, *J* = 1.43 Hz, 1H), 7.32 (d, *J* = 8.33 Hz, 2H), 7.45 (d, *J* = 0.87 Hz, 1H), 7.67 (d, *J* = 8.61 Hz, 2H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 33.35 (q), 116.00 (d), 125.87 (d), 128.62 (d), 132.12 (s), 132.68 (s), 138.06 (d), 141.26 (s); MS (relative intensity, %): *m/z* = 28 (96.68), 32 (22.08) 150 (19.39) 192 (M^+, 100); HRMS: *m/z* calc. for $C_{10}H_9ClN_2$: 192.045, found 192.045; Anal. calc. for $C_{10}H_9ClN_2$: C, 62.35; N, 14.54; H, 4.71; Cl, 18.40, found C, 62.01; N, 14.42; H, 4.65; Cl, 18.39.

4(5)-(3,4-Dimethoxyphenyl)imidazole (9l) :

3,4-Dimethoxyphenyl-*N*-tosylaldimine (**3l**, 0.91 g, 3.0 mmol) was reacted with TosMIC (0. 64 g, 3.3 mmol) and K_2CO_3 (0.91 g, 6.6 mmol) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction was purified by washing with CH_2Cl_2 to give a pink solid (**9l**, 0.32g, 51 %), pure according to ^{1}H NMR: mp 166-168 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.74 (s, 3H), 3.79 (s, 3H), 6.92 (d, *J* = 8.05 Hz, 1H), 7.27 (d, *J* = 8.05 Hz, 1H), 7.35 (s, 1H), 7.47 (br

s, 1H), 7.67 (br s, 1H), 12.05-12.30 (br, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 55.64 (q), 55.72 (q), 108.63 (d), 112.32 (d), 114.69 (s), 116.75 (d), 127.31 (s), 135.84 (d), 147.72 (s), 149.18 (s); MS (relative intensity, %): *m/z* = 28 (59.14), 32 (11.24), 63 (15.41), 76 (6.97), 77 (6.16), 91 (12.97), 118 (14.81), 161 (38.32), 189 (30.92), 204 (M^+, 100); HRMS: *m/z* calc.for $C_{11}H_{12}N_2O_2$: 204.090, found 204.090. Some *N*-methylated derivative was observed in ^{1}H NMR, but this side product was not isolated.

4(5)-(2-Furyl)imidazole (9m) and 4-(2-fuyl)-1-methylimidazole (17m) :

2-Furyl-*N*-tosylaldimine (**3m**, 1.50 g, 6.0 mmol) was reacted with TosMIC (1.29 g, 6.6 mmol), and K_2CO_3 (1.82 g, 13.2 mmol) for 2 h, analogously to the procedure described for **9a**. The mixture obtained upon acid/base extraction was chromatographed (Al_2O_3, CH_2Cl_2) to give two fractions. The second fraction gave a brown oil, which contained a mixture of **9m**, **17m**, and **18m** (5:1:2.3, 370 mg). The brown oil was dissolved in Et_2O (25 mL) and stirred vigoursly with NaOH (50 % in water, 25 mL) for 3 h. After separation, the basic layer was acidified with H_2SO_4. The resulting acidic water layer was neutralized with saturated $NaHCO_3$ and extracted with Et_2O (2 x 25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the brown oil obtained was crystallized from CH_2Cl_2/hexane to give pale **9m** as brown crystals (50 mg, 6 %), pure according to ^{1}H NMR: mp 115-116 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.43 (dd, *J* = 1.89 Hz, *J* = 1.83 Hz, 1H), 6.56 (d, *J* = 3.39 Hz, 1H), 7.31 (br s, 1H), 7.39 (d, *J* = 1.1 Hz, 1H), 7.69 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 104.25 (d), 111.19 (d), 114.31 (d), 131.65 (s), 135.29 (d), 140.92 (d), 148.78 (s); MS (relative intensity, %): *m/z* = 51 (11.4), 52 (12.8), 79 (25.6), 105 (19.1), 134 (100); HRMS: *m/z* calc. for $C_7H_6N_2O$: 134.048, found 134.049.

The first fraction gave, after crystallization from CH_2Cl_2/hexane, a side product **17m** as a pale yellow solid (50 mg, 6 %), pure according to ^{1}H NMR: mp 101-103 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.66 (s, 3H), 6.41-6.42 (m, 1H), 6.58 (dd, *J* = 0.86 Hz, *J* = 0.86 Hz, 1H), 7.07 (d, *J* = 1.39 Hz, 1H), 7.34 (dd, *J* = 0.85 Hz, *J* = 0.85 Hz), 7.38 (d, *J* = 1.32 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 33.30 (q), 103.76 (d), 111.03 (d), 115.59 (d), 134.81 (s), 137.81 (d), 140.59 (d), 149.93 (s); MS (relative intensity, %): *m/z* = 57 (10.3), 69 (18.1), 81 (11.9), 105 (14.3), 119 (19.7), 148 (M^+, 100); HRMS: *m/z* calc. for $C_8H_8N_2O$:148.064, found 148.066.

5-(*p*-Chlorophenyl)-1-tosylimidazole (10k) :

A mixture of TosMIC (0.64 g, 3.3 mmol), p-chlorophenyl-*N*-tosylaldimine (0.88 g, 3.0 mmol), and K_2CO_3 (0.91, 6.6 mmol) in *t*-BuOH/DME 2:1 (33 mL) was refluxed for 20 h. After cooling, addition of H_2O (50 mL), extraction with Et_2O (2 x 50 mL), drying ($MgSO_4$), and removal of the solvent, the crude product was filtered through a short column of Al_2O_3 (CH_2Cl_2), to give, after washing with pentane, **10k** as white crystals (0.10 g, 10 %): mp 174-176 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.44 (s, 3H), 7.34 (d, J = 8.69 Hz, 2H), 7.36 (d, J = 8.14 Hz, 2H), 7.51 (d, J = 1.38 Hz, 1H), 7.66 (d, J = 8.55 Hz, 2H), 7.87 (d, J = 8.41 Hz, 2H), 8.04 (d, J = 1.38 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.66 (q), 112.08 (d), 126.46 (d), 127.30 (d), 128.78 (d), 130.40 (d), 130.55 (s), 133.69 (s), 134.64 (s) 136.68 (d), 143.07 (s), 146.38 (s); MS (relative intensity, %): m/z = 28 (72.3), 63 (10.4), 91 (100), 92 (13.2), 123 (36.7), 125 (12.3), 150 (11.0), 155 (84.2), 177 (42.8), 332 (M^+, 73.2); HRMS calcd $C_{16}H_{13}N_2O_2SCl$: 332.039, found 332.039.

5-(*p*-Chlorophenyl)-1,4-ditosyl-4*H*,5*H*-imidazoline (11k, R^1 = *p*-ClC_6H_4) :

A mixture of TosMIC (0.64 g, 3.3 mmol), *p*-chlorophenyl-*N*-tosylaldimine (**9m**, 0.88 g, 3.0 mmol), and K_2CO_3 (0.91, 6.6 mmol) in *t*-BuOH/DME 2:1 (33 mL) was refluxed for 2 h. After cooling, addition of water (50 mL), extraction with Et_2O (2 x 50 mL), drying ($MgSO_4$), and removal of the solvent, the crude product was filtered through a short column of Al_2O_3 (CH_2Cl_2), to give **11** as a white solid (1.20 g, 82 %), pure according to ^{1}H NMR: mp 145-148 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 6H), 4.96 (d, *J* = 5.62 Hz, 1H), 5.29 (d, *J* = 5.37 Hz, 1H), 7.12 (d, *J* = 7.56 Hz, 2H), 7.24-7.35 (m, 5H), 7.57 (d, *J* = 7.82 Hz, 2H), 7.71-7.74 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.65 (q), 60.05 (d), 95.70 (d), 127.45 (d), 127.76 (d), 129.16 (d), 129.39 (d), 129.73 (d), 129.99 (d), 132.70 (s), 133.56 (s), 134.75 (s), 136.10 (s), 145.46 (s), 145.70 (s); MS (relative intensity, %): m/z = 28 (36.45), 65 (14.58), 91 (100), 155 (64.27), 333 (M^+-Tos, 72.83).

X-Ray crystal structure of 4-(*p*-Chlorophenyl)-1-methylimidazole (17k)

Crystal data :

Formula: $C_{10}H_9N_2Cl$; M = 192.65, crystal color and habit: transparent colorless parallepiped, crystal size: 0.20 x 0.25 x 0.50 mm; orthorhombic; space group: $P2_12_12_1$; a = 5.464(1) Å, b = 8.429 (1) Å, c = 19.788 (2) Å; V = 911.4 (2) Å^3; Z = 4, ρ = 1.404 g/cm^3; μ = 3.7 cm^{-1}; F(000) = 400.

Data collection :

The data were collected on an Enraf-Nonius CAD-4F diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-Kα radiation

(λ = 0.71073 Å), $\Delta\omega$ = 1.10 + 0.34 tg θ), interfaced to a MS-DOS computer; T = 130 K; θ range 1.04-27.5°; reflections collected: 4565; independent reflections: 2065.

Solution and refinement [26]:

The structure was solved by Patterson methods (DIRDIF) and refined anisotropically by full-matrix least squares based on $F_o^2>0$ (SHELXL-93); data/parameters 2013/154; data-to-parameter ratio: 13.1:1; R_1 = 0.0291 [$F_o>4.0\ \sigma(F_o)$], wR_2 = 0.0867 [I>0]; absolute-stucture parameter: Flack's **x**: -0.01(5); maximal residual electron density: 0.26(5) e/Å^3.

The program PLUTO has been used for graphical representation of the crystal structure.

Table 3. Bond Lengths and Selected Bond Angles for Compound **17k** (Excluding H Atoms)

Interatomic Distances (Å)			
Cl(1)-C(1)	1.7407(17)	C(1)-C(6)	1.383(2)
N(1)-C(7)	1.380(2)	C(2)-C(3)	1.388(2)
N(1)-C(8)	1.319(2)	C(3)-C(4)	1.397(2)
N(2)-C(8)	1.344(2)	C(4)-C(5)	1.397(2)
N(2)-C(9)	1.362(2)	C(4)-C(7)	1.463(2)
N(2)-C(10)	1.459(2)	C(5)-C(6)	1.380(2)
C(1)-C(2)	1.387(2)	C(7)-C(9)	1.369(2)

Bond Angles (deg.)			
C(7)-N(1)-C(8)	105.14(14)	C(3)-C(4)-C(7)	120.90(14)
C(8)-N(2)-C(9)	107.39(14)	C(5)-C(4)-C(7)	120.70(14)
C(8)-N(2)-C(10)	125.96(15)	C(4)-C(5)-C(6)	121.55(15)
C(9)-N(2)-C(10)	126.59(15)	C(1)-C(6)-C(5)	118.70(15)
Cl(1)-C(1)-C(2)	119.32(12)	N(1)-C(7)-C(4)	121.89(14)
Cl(1)-C(1)-C(6)	119.10(12)	N(1)-C(7)-C(9)	109.48(14)
C(2)-C(1)-C(6)	121.58(15)	C(4)-C(7)-C(9)	128.54(14)
C(1)-C(2)-C(3)	118.98(15)	N(1)-C(8)-N(2)	111.91(14)
C(2)-C(3)-C(4)	120.80(15)	N(2)-C(9)-C(7)	106.08(14)
C(3)-C(4)-C(5)	118.37(15)		

REFERENCES AND NOTES

1. Chemistry of Sulfonylmethyl Isocyanides 43. For part 42, see : ten Have, R.; Leusink, R.; van Leusen, A.M. *Synthesis* **1996**, 871.
2. Some recent reviews on the chemistry of imidazoles are : (a) Ebel, K. in *Methoden der Organischen Chemie (Houben-Weyl)*, Band E8c, Hetarene III/Teil 3 (Schaumann, E., Ed.), Georg Thieme Verlag, Stuttgart 1994, p. 1-215. (b) Ebel, K.; Koehler, H.; Garner, A.O.; Jäckh, R. in *Ullmann's Encyclopedia of Industrial Chemistry*, VCH, Weinheim 1989, Vol. A13, p. 661-668. (c) Grimmett, M.R. in *Comprehensive Heterocyclic Chemistry* (Katrizky, A.R.; Rees, C.W., Eds), Pergamon Press, Oxford, 1984, Vol. 5, p. 457-498. (d) Grimmett, M.R. in *Advances in Heterocyclic Chemistry : Advances in Imidazole Chemistry* (Katrizky, A.R.; Boulton, A.J., Eds), Academic Press, New York 1980, Vol. 27, p. 241-326.
3. Czarnik, A.W. *Acc. Chem. Res.* **1996**, *29*, 113.
4. Gelus, M.; Bonnier, J.M. *J. Chim. Phys. Chim. Biol.* **1968**, *65*, 253.
5. Debus, H. *Liebigs Ann. Chem.* **1858**, *107*, 199.
6. For a recent comprehensive and systematic review with 1252 references, emphasizing synthetic approaches to imidazoles, see ref 2a.

7. van Leusen, A.M.; Oldenziel, O.H. *Tetrahedron Lett.* **1972**, 2373.
8. These reactions have been summarized briefly in ref. 2a (p. 65 ff), and by (a) van Leusen, A.M.; van Leusen, D. in *Encyclopedia of Reagents for Organic Synthesis* (Paquette, L.A., Ed) Wiley 1995, Vol. 7, p. 4973 and 4979, see also Vol 5, p. 3605. (b) An exhaustive review by van Leusen, D.; van Leusen, A.M. will appear in *Organic Reactions*.
9. van Leusen, A.M.; Wildeman, J.; Oldenziel, O.H. *J. Org. Chem.* **1977**, *42*, 1153. Possel, O.; van Leusen, A.M. *Heterocycles* **1977**, *7*, 77.
10. Horne, D.A.; Yakushijin, K.; Büchi, G. *Heterocycles* **1995**, *39*, 139.
11. (a) Lim, B.L.; Iddon, B. *J. Chem. Soc., Perkin Trans. I* **1983**, 279. (b) Ngochindo, R.I.; Chadwick, D.J. *J. Chem. Soc., Perkin Trans. I* **1984**, 481. (c) Iddon, B. *Heterocycles* **1985**, *23*, 417. (d) Carpenter, A.J.; Chadwick, D.J. *Tetrahedron* **1986**, *42*, 2351. (e) Ngochindo, R.I. *J. Chem. Soc., Perkin Trans. I* **1990**, 1645. (f) Turnball Jr, S.P.; Kudzma, L.V. *Synthesis* **1991**, 1021. (g) Vollinga, R.C.; Menge, W.M.P.B.; Timmerman, H. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 123. (h) Iddon, B.; Ngochindo, R.I. *Heterocycles* **1994**, *38*, 2487.
12. van Leusen, A.M.; Schaart, F.J.; van Leusen, D. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 258. One further example of this type of reaction was reported recently by Bergstrom, D.E.; Zhang, P.; Zhou, J. *J. Chem. Soc., Perkin Trans. I*, **1994**, 3029.
13. Shih, N.-Y. *Tetrahedron Lett.* **1993**, *34*, 595 (the isocyanides in this paper are consequently, but erroneously, named isocyanates).
14. Huisman, M.; ten Have, R.; van Leusen, A.M. *Synth. Commun.* **1997**, *27*, 945.
15. For the removal of the dimethylsulfamoyl group we have restricted ourselves to the conditions used by Vollinga *et al.* [11g] However, milder conditions, like 2 N HCl [11b, 11f] or 2 % KOH, [11d] have been used previously for the same purpose. Such conditions may become necessary when more sensitive substituents are present at C5.
16. Matthews, H.R.; Rapoport, H. *J. Am. Chem. Soc.* **1973**, *95*, 2297.
17. (a) Grand, R.L; Pyman, F.L. *J. Chem. Soc.* **1921**, *119*, 1893. (b) Hazeldine, C.E.; Pyman, F.L.; Winchester, J. *J. Chem. Soc.* **1924**, *125*, 1431.
18. For precedents of the facile *N*-detosylation of *N*-heteroaromats, see (a) van der Eijk, J.M.; Zwikker, J.W.; Nolte, R.J.M. *J. Org. Chem.* **1980**, *45*, 547. (b) Shimizu, M.; Ando, R.; Kuwajima, I. *J. Org. Chem.* **1981**, *46*, 5248. (c) Merrick, R.D.; Tolbert, L.M. *J. Org. Chem.* **1981**, *47*, 2810.
19. For the sake of completeness, it should be mentioned that in two related reactions of (isocyanotosylmethylidene)cyclohexane (instead of TosMIC) with *N*-tosylaldimines in non-protic solvents **tri**substituted imidazoles were obtained, in which the *N*-tosyl group was retained in the product. See, Moskal, J.; van Stralen, R.; Postma, D.; van Leusen, A.M. *Tetrahedron Lett.* **1986**, *27*, 2173, and Leusink, F.R., Ph. D. Thesis, Groningen University, **1993**, p. 85-97.
20. Bamford, W.R.; Stevens, T.S. *J. Org. Chem.* **1952**, *17*, 4735.
21. Juday, R.; Adkins, H. *J. Am. Chem. Soc.* **1955**, *77*, 4559.
22. Love, B.E.; Raje, P.S.; William II, T.C. *Synlett.* **1994**, 493.
23. Not unexpectidly, HBr was lost in the process of determining the high resolution mass spectra of compounds **9.HBr**. Thus, the calculated *m/z* values refer to the imidazoles **9**. However, the elemental analysis of **9a.HBr** is consistent with the HBr salt structure.
24. Weidenhagen, R.; Herrmann, R.; Wegner, H. *Chem. Ber.* **1937**, *70*, 570.
25. Lindgren, G.; Stensiö, K-E.; Wahlberg, K.J. *Heterocyclic. Chem.* **1980**, *17*, 679.
26. **Programs :** Beurskens, P.T.; Beurskens, G.; Bosman, W.P.; de Gelder, R.; García-Granda, S.; Coul, R.O.; Israël, R.; Smits, J.M.M. *DIRDIFF-96*, **1996**, Crystallography Laboratory, University of Nijmegen, The Netherlands; least-square refinements : Sheldrick, G.M. *SHELXL93, Program for the Refinement of Crystal Structures*, **1993**, University of Göttingen, Germany; calculation of geometric data : Spek, A.L. Platon, Program for the Automated Analysis of Molecular Geometry, **1996**, University of Utrecht, The Netherlands; preparation of illustrations : Meetsma, A. *PLUTO*, Program for Display and Analysis of Crystal and Molecular Structures, **1996**, University of Groningen, The Netherlands.

(*Received in UK* 8 *April* 1997; *revised* 13 *June* 1997; *accepted* 19 *June* 1997)