A New Class of Fused Imidazoles by Intramolecular Nucleophilic *ipso*-Substitution in 2-Alkylsulfonylimidazoles: Synthesis of 2,3-Dihydroimidazo[2,1-*b*][1,3]oxazoles

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Abstract: Starting from readily available thiouronium salts **1** and α-halocarbonyl compounds **2**, a simple and efficient synthesis of 2-alkylthioimidazoles **3** was accomplished. Reduction of the carbonyl group, followed by oxidation of the 2-alkylthioether moiety, afforded sulfones **8**. Intramolecular nucleophilic *ipso*-substitution in 2-alkylsulfonylimidazoles **8** efficiently furnished a novel class of fused imidazoxazoles. This finding was extended towards the generation in solution of a small library of 2,3-dihydroimidazo[2,1-*b*][1,3]oxazoles.

Key words: synthesis, 2-alkylthioimidazoles, alkylsulfonyl groups, leaving groups, intramolecular nucleophilic *ipso*-substitution, imidazoles, 2,3-dihydroimidazo[2,1-*b*][1,3]oxazoles

Heteroaromatic nucleophilic addition-elimination reactions are commonly recognized in many electron-deficient heterocycles.[2] However, analogous reactions with electron-rich heterocycles,[3–5] and more accurately, with electron-rich imidazoles and condensed imidazoles, are rather uncommon.[6–8] On the other hand, alkyl- or arylsulfinyl or -sulfonyl substituents as leaving groups in electron-deficient heteroaromatic systems have been reported to have reactivity equivalent to, or greater than, that of a chloro group, and many examples concerning the reactivity of electron deficient azines bearing alkylsulfinyl- and -sulfonyl groups, with simple nucleophiles have been reported.[9,10] To the best of our knowledge, however, there is only one recent literature precedent for the use of sulfinyl or sulfonyl substituents as leaving groups on imidazoles.[11] However, only strongly activated imidazoles bearing electron-withdrawing groups were reported to undergo efficient *ipso*-substitution reactions with a variety of different nucleophiles.

During the course of our studies on the development of efficient methodologies that could be readily adapted for the combinatorial and/or parallel synthesis in solution or on solid supports of relevant core structures,[12-16] we focused our attention on the imidazole nucleus. Imidazoles are important pharmacophores, and many biologically active compounds incorporate this moiety into their structures. Particularly interesting, are fused [1,2-*a*]imidazoles, which have been reported to have antiulcer, antidepressant, antibacterial and T_xA_2 synthase inhibitory activities.[17-20] Recently, innovative protocols for the synthesis of [1,2-*a*]-fused imidazoles using intramolecular radical *ipso*-substitution at the C-2 position have been reported,[21,22] and although many efforts have been devoted to the synthesis of, for instance, imidazo[1,2-*a*]pyridines,[23] there are no literature reports on the synthesis of imidazo[2,1-*b*][1,3]oxazoles.

Herein, we wish to report our findings on the use for the first time of alkylsulfonyl substituents in electron-rich imidazoles, as effective leaving groups in intramolecular nucleophilic *ipso*-substitution reactions, and their application toward the preparation of a novel class of fused imidazoles. Thus, when thiouronium salts **1**, readily available from the corresponding alkyl halide and thiourea in refluxing ethanol, were allowed to react in MeCN

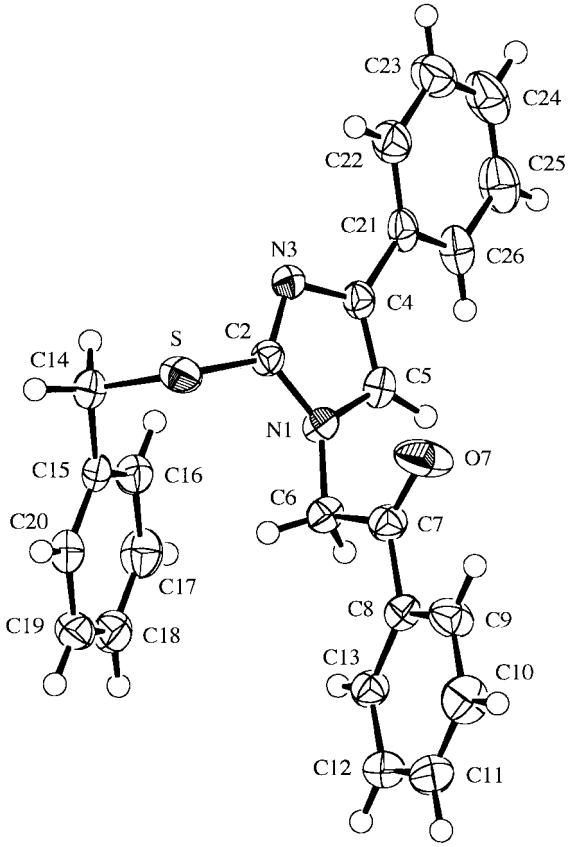
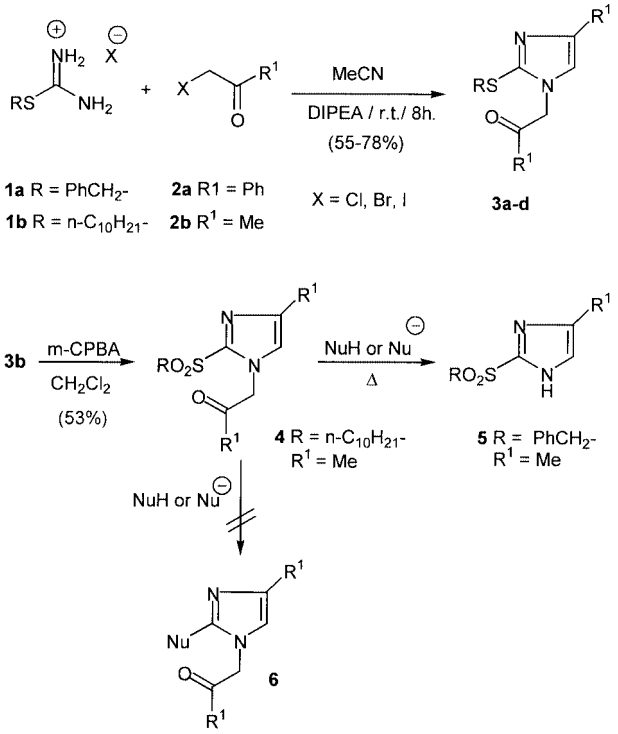


Figure ORTEP plot[27] of the molecular structure of **3a** with 50% probability ellipsoids



Scheme 1

with 2 equivalents of the corresponding α-halocarbonyl compound **2** in the presence of a suitable base such as diisopropylethylamine (DIPEA), the corresponding 2-alkylthioimidazoles **3** were isolated in good yields. The structural elucidation of compounds **3** was accomplished by the usual spectroscopic methods, and in addition, **3a** was subjected to an X-ray crystal-structure analysis that unambiguously confirmed the structure (Figure, Table 1). Next, as in the model case **3b**, we found that oxidation of the thioether moiety with *m*-CPBA in CH_2Cl_2, led to the corresponding sulfone **4** in 53% yield. When 2-alkylsulfonylimidazole **4** was prompted to react with a wide range of different nucleophiles (*N*-, *O*-, *S*-, and C-nucleophiles), even under very forcing conditions, no substitution products **6** were observed. These results confirmed the known

Table 1 Selected Bond Lengths (Å) and Angles (°) for **3a**

S–C(2)	1.751(3)		
S–C(14)	1.841(3)	C(2)–S–C(14)	99.3(1)
N(1)–C(2)	1.372(3)	C(2)–N(1)–C(5)	106.5(2)
N(1)–C(5)	1.364(3)	C(2)–N(3)–C(4)	105.5(2)
N(1)–C(6)	1.453(3)	N(1)–C(2)–N(3)	111.8(2)
N(3)–C(2)	1.313(3)	N(3)–C(4)–C(5)	109.7(2)
N(3)–C(4)	1.381(3)	N(1)–C(5)–C(4)	106.6(2)
C(4)–C(5)	1.368(4)		

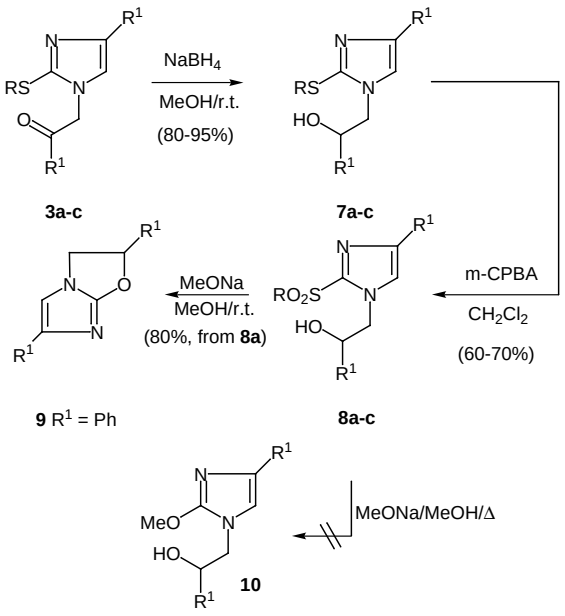
Table 2 Prepared 2-Alkylthio- and 2-Alkylsulfonylimidazoles **3a–d**, **4** and **5**

Product[a]	R	R^1	Yield (%)	mp (ºC)
3a	$PhCH_2$	Ph	78	142–143
3b	$C_{10}H_{21}$	Me	57	colourless oil
3c	$C_{10}H_{21}$	Ph	65	67.5–68
3d	$PhCH_2$	Me	55	74–75
4	$C_{10}H_{21}$	Me	53	colourless oil
5	$PhCH_2$	Me	50	207–208

[a] Satisfactory microanalyses obtained: C ± 0.28, H ± 0.30, N ± 0.27.

poor reactivity of this type of electron rich imidazoles towards nucleophilic *ipso*-substitution reactions. In most cases, together with unreacted starting material, only degradation products were obtained from which dealkylated imidazole, as exemplified by **5**, could be isolated and identified as the main product (Scheme 1 and Tables 2 and 3).

The generation of **5** as the main product in these reactions suggested that the presence of the carbonyl group in **4** could negatively interfere in a possible nucleophilic substitution to afford **6**. Therefore, we proceeded further by reducing **3a–c** with $NaBH_4$ in MeOH to the corresponding alcohols **7a–c**. Subsequent oxidation with *m*-CPBA in CH_2Cl_2 led to the corresponding sulfones **8a–c** in good yields. When these sulfones **8** (as exemplified by **8a**, R^1 = Ph) were treated with MeONa in MeOH at room temperature, a smooth reaction leading to 2,3-dihydroimid-



Scheme 2

Table 3 MS, IR and NMR Data of Imidazoles **3**, **4** and **5**

Product	MS *m/z* (%)	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
3a	386 ([M+2]$^+$, 28), 385 ([M+1]$^+$, 100), 384 ([M]$^+$, 23), 291 (19), 264 (17), 263 (82), 262 (12), 145 (18), 121 (26), 105 (10), 93 (26), 92 (16), 91 (19)	3058, 3052, 2955, 2927, 1697, 1596, 1580, 1490, 1451, 1406, 1391, 1347, 1229, 1204, 1178, 1154, 1120, 1073, 982, 774, 752, 689	4.2 (s, 2 H), 5.0 (s, 2 H), 7.15–7.9 (m, 16 H)	40.95, 52 (t, CH_2), 118.4, 124.88, 126.89, 127.4, 127.9, 128.5, 128.6, 128.8, 128.9, (d, CH_{arom}), 133.7 (s, C_{arom}), 134.2, 137.9, 140.8, 142.7 (s, C_{arom}), 191.4 (s, CO)
3b	312 ([M+2]$^+$, 20), 311 ([M+1]$^+$, 100), 310 ([M]$^+$, 6), 255 (14), 171 (32), 170 (19)	2955, 2925, 2854, 1739, 1560, 1457, 1429, 1377, 1359, 1287, 1168, 1168, 1118, 1044, 998, 978, 800, 716	0.89 (t, 3 H, *J* = 6.4), 1.25–1.35 (m, 14 H), 1.55–1.65 (m, 2 H), 2.2 (s, 3 H), 2.25 (d, 3 H, *J* = 0.8), 3.0 (t, 2 H, *J* = 7.4), 4.7 (s, 2 H), 6.65 (d, 1 H, *J* = 0.8)	13.8, 14.02 (q, CH_3), 22.6 (t, CH_2), 26.9 (q, CH_3), 28.56, 29.02, 29.21, 29.41, 29.44, 29.6, 31.8, 35.35, 55.50 (t, CH_2), 118.2 (d, CH_{arom}), 139.17, 140.8, (s, C_{arom}), 201.5 (s, CO)
3c	436 ([M+2]$^+$, 23), 435 ([M+1]$^+$, 100), 434 ([M]$^+$, 10), 295 (37), 294 (18), 261 (12), 190 (11), 189 (31)	2954, 2925, 2853, 1702, 1598, 1455, 1430, 1348, 1226, 1208, 1182, 1226, 1208, 1182, 753, 690	0.91 (t, 3 H, *J* = 6.4), 1.25–1.4 (m, 14 H), 1.6–1.7 (m, 2 H), 3.05 (t, 2 H, *J* = 7.3), 5.42 (s, 2 H), 7.2–8.0 (m, 11 H)	14.05 (q, CH_3), 22.6, 28.6, 29.0, 29.25, 29.45, 29.5, 29.65, 31.8, 35.8, 55.45 (t, CH_2), 118.0, 124.85, 126.8, 128.0, 128.45, 129.0 (d, CHarom.), 133.85 (s, Carom.), 134.2 (d, CHarom.), 134.35, 142.4 (s, Carom.), 191.7 (s, CO)
3d	262 ([M+2]$^+$, 17), 261 ([M+1]$^+$, 100), 260 ([M]$^+$, 15), 171 (11)	3125, 3083, 3025, 2947, 2921, 2852, 1718, 1561, 1493, 1428, 1357, 1288, 1170, 1123, 1066, 806, 769, 704	2.0 (s, 3 H), 2.28 (s, 3 H), 4.12 (s, 2 H), 4.32 (s, 2 H), 6.61 (s, 1 H), 7.1–7.3 (m, 5 H)	13.8 (q, CH_3), 26.72 (q, CH_3), 40.65, 55.10 (t, CH_2), 118.70, 127.4, 128.65, 128.8 (d, CH), 137.65, 139.2, 139.5 (s, C_{arom}), 201.2 (s, CO)
4	344 ([M+2]$^+$, 18), 343 ([M+1]$^+$, 91), 341 ([M]$^+$, 8), 139 (44), 137 (36), 133 (35), 131 (30), 123 (49), 121 (42), 119 (58), 117 (30), 111 (48), 109 (100), 107 (69), 105 (76)	3150, 2953, 2921, 2850, 1727, 1465, 1406, 1362, 1324, 1303, 1290, 1224, 1175, 1154, 1114, 678	0.93 (t, 3 H), 1.3–1.45 (m, 14 H), 1.65–1.85 (m, 2 H), 2.3 (s, 6 H, CH_3CO, CH_3), 3.3–3.4 (m, 2 H), 5.13 (s, 2 H), 6.65 (s, 1 H)	13.5 (q, CH_3), 14.0 (q, CH_3), 21.5, 22.6 (t, CH_2), 26.9 (q, CH_3), 28.15, 28.9, 29.2, 29.4, 29.6, 31.8, 55.2, 56.8 (t, CH_2), 122.2 (d, CH_{arom}), 139.2, 140.1 (s, C_{arom}), 200.1 (s, CO)
5	238 ([M+2]$^+$, 14), 237 ([M+1]$^+$, 100), 236 ([M]$^+$, 6), 173 (11)	3043, 2966, 2918, 2853, 2810, 2723, 1653, 1577, 1495, 1439, 1323, 1282, 1254, 1200, 1147, 1121, 1007, 929, 875, 787, 700	2.16 (s, 3 H), 4.68 (s, 2 H), 6.99 (s, 1 H_{arom}), 7.1–7.35 (m, 5 H_{arom})	13.5 (q, CH_3), 60.3 (t, CH_2), 128.0 (s, C_{arom}), 129.2 (d, CH_{arom}), 128.95 (s, C_{arom}), 129.2, 129.7 (d, CH_{arom}), 140.3, 140.4 (s, C_{arom})

azo[2,1-*b*][1,3]oxazole **9** took place in a very clean and efficient manner. Although the 2-alkylsulfonyl groups in **8** were readily displaced in these reactions, not even traces of the corresponding 2-methoxyimidazole derivatives of type **10** were detected (Scheme 2, Tables 4 and 5).

This transformation presumably took place through initial formation of the corresponding alkoxy derivative **11**, followed by intramolecular nucleophilic *ipso*-substitution to afford **9**. These results were confirmed independently simply by treating a solution of **8a** in THF with 1.2 equivalents of NaH at room temperature to give **9** in good isolated yields. However, protection of the hydroxy group as the methyl ether derivative **12** (from **7a**) followed by oxidation to sulfone **13** and subsequent treatment with NaOMe in MeOH or with other nucleophiles even at high temperatures resulted in no reaction, and unreacted start-

Table 4 Prepared Imidazoles **7** and **8** and 2,3-Dihydroimidazo[2,1-*b*][1,3]oxazole **9**

Product[a]	R	R^1	Yield (%)	mp (ºC)
7a	$PhCH_2$	Ph	95	116–117
7b	$C_{10}H_{21}$	Me	82	colourless oil
7c	$C_{10}H_{21}$	Ph	82	70.5–72
8a	$PhCH_2$	Ph	65	134–135
8b	$C_{10}H_{21}$	Me	60	colourless oil
8c	$C_{10}H_{21}$	Ph	61	80–81
9	–	Ph	81	192–193 (dec)

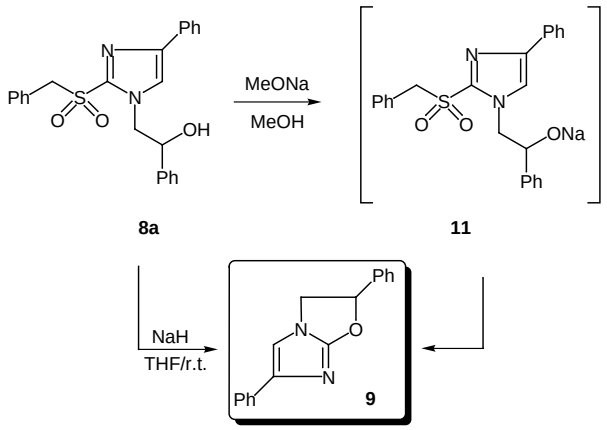
[a] Satisfactory microanalyses obtained: C ± 0.27, H ± 0.22, N ± 0.30.

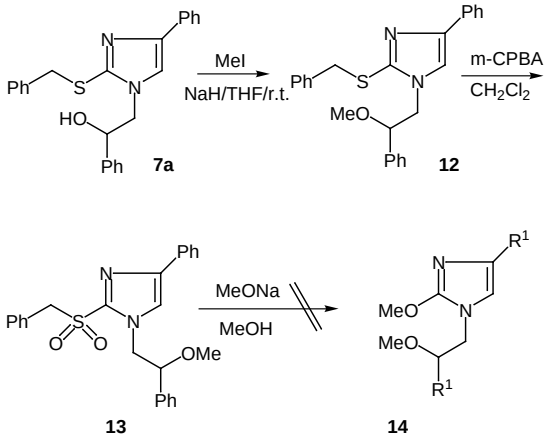
Table 5 MS, IR and NMR Data of Imidazoles **7**, **8** and Dihydroimidazoxazole **9**

Product	MS *m/z* (%)	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
7a	388 ($[M+2]^+$, 6), 387 ($[M+1]^+$, 24), 386 ($[M]^+$, 8), 293 (24), 279 (10), 266 (21), 265 (100), 264 (23), 247 (16), 145 (18), 121 (12), 105 (13), 93 (46), 92 (25), 91 (31), 79 (15), 63 (11), 55 (17)	3438, 3063, 1600, 1492, 1454, 1412, 1190, 1061, 751, 696	3.74 (dd, 1 H, *J* = 14.0, 8.8), 3.9 (dd, 1 H, *J* = 14.0, 3.3), 4.15(s, 2 H), 4.8 (s, 1 H, OH), 4.96 (dd, 1 H, *J* = 8.8, 3.3), 7.1–7.65 (m, 16 H)	40.85 (t, CH_2), 54.5 (t, CH_2), 73.0 (d, CH), 118.6, 124.6, 125.85, 126.6, 127.3, 127.9, 128.4, 128.45, 128.5, 128.75, (d, CH_{arom}), 133.45, 137.7, 140.2, 141.05, 141.6 (s, C_{arom})
7b	312 ($[M+2]^+$, 20), 311 ($[M+1]^+$, 100), 310 ($[M]^+$, 6), 255 (14), 171 (32), 170 (19)	3205, 2959, 2924, 2853, 1567, 1468, 1412	0.9 (t, 3 H, *J* = 6.4), 1.25–1.35 (m, 17 H), 1.5–1.6 (m, 2 H), 2.2 (s, 3 H), 2.9–3.0 (m, 2 H), 3.79 (dd, 1 H, *J* = 14, 8.4), 4.01 (dd, 1 H, *J* = 14, 3.4), 4.1–4.15 (m, 1 H), 6.75 (s, 1 H)	13.55 (q, CH_3), 14.0 (q, CH_3), 20.5(q, CH_3), 22.6, 28.6, 29.0, 29.25, 29.45, 29.5, 29.6, 31.85, 35.5, 53.9 (t, CH_2), 66.9 (d, CH), 118.6 (d, CH_{arom}), 137.9, 140.1 (s, C_{arom})
7c	438 ($[M+2]^+$, 24), 437 ($[M+1]^+$, 86), 436 ($[M]^+$, 9), 279 (25), 203 (10), 191 (17), 190 (27), 189 (21), 179 (11), 178 (18), 177 (74), 176 (100), 175 (20), 173 (10)	3150, 3063, 3030, 2954, 2925, 2853, 1602, 1489, 1455, 1415, 1191, 1063, 747, 698	0.91 (t, 3 H, *J* = 6.4), 1.25–1.45 (m, 14 H), 1.55–1.60 (m, 2 H), 3.0–3.05 (m, 2 H), 4.05 (dd, 1 H, *J* = 14, 9), 4.23 (dd, 1 H, *J* = 14,0, 5.0 (s, 1 H, OH), 5.19 (dd, *J* = 9, 3), 7.2–7.6 (m, 11 H)	14.05 (q, CH_3), 22.6, 28.55, 29.05, 29.25, 29.4, 29.5, 29.65, 31.85, 35.65, 54.8 (t, CH_2), 73.15 (d, CH), 118.25, 124.55, 125.9, 126.5, 127.95, 128.35, 128.6, (d, CH_{arom}), 133.5, 141.2, 141.25, 141.7 (s, C_{arom})
8a	420 ($[M+2]^+$, 28), 419 ($[M+1]^+$, 100), 401 (10), 293 (11), 265 (45), 264 (10), 93 (16), 91 (16), 65 (22)	3448, 3149, 3070, 3050, 3030, 2924, 1596, 1496, 1455, 1412, 1376, 1329, 1256, 1236, 1152, 1113, 1089, 1061, 962, 906, 786, 762, 696	2.5 (s, 1 H, OH), 3.73 (dd, 1 H, *J* = 14, 8.8), 4.2 (dd, 1 H, *J* = 14.0, 3), 4.57 (dd, 1 H, *J* = 8.8, 3), 4.67, 4.70 (2d, 2 H, *J* = 14), 7.15–7.85 (m, 16 H)	54.85 (t, CH_2), 62.1 (t, CH_2), 73.25 (d, CH), 121.75, 125.3, 125.6 (d, CH_{arom}), 127.25 (s, C_{arom}), 127.8, 128.2, 128.6, 128.65, 128.7, 129.05, 131.2 (d, CH_{arom}), 132.4, 138.8, 140.3, 141.75 (s, C_{arom})
8b	346($[M+2]^+$, 18), 345 ($[M+1]^+$, 100), 344 ($[M]^+$, 8), 141 (58), 140 (12), 139 (68)	3371, 2954, 2925, 2855, 1559, 1463, 1422, 1344, 1322, 1217, 1154, 1118, 1012, 937, 841, 780, 711	0.93 (t, 3 H, *J* = 6.6), 1.25–1.4 (m, 17 H), 1.75–1.9 (m, 2 H), 2.2 (s, 3 H), 2.4 (s, 1 H, OH), 3.4–3.45 (m, 2 H), 4.0–4.15 (m, 2H), 4.4–4.45 (m, 1 H), 6.9 (s, 1 H)	13.45 (q, CH_3), 14.0 (q, CH_3), 20.7 (q, CH_3), 21.8, 22.6, 28.1, 28.9, 29.2, 29.4, 29.6, 31.8, 54.45, 55.4 (t, CH_2), 67.65, 122.3 (d, CH), 138.5, 140.3 (s, C_{arom})
8c	470 ($[M+2]^+$, 31), 469 ($[M+1]^+$, 100), 468 ($[M]^+$, 4), 279 (12), 277 (11), 266 (15), 265 (68), 264 (17), 263 (52), 261 (11), 245 (24), 193 (20), 191 (49)	3415, 3143, 3063, 3030, 2953, 2925, 2854, 1715, 1602, 1489, 1463, 1404, 1377, 1321, 1224, 1150, 1115, 1091, 1062, 760, 701	0.92 (t, 3 H, *J* = 6.4), 1.2–1.5 (m, 14 H), 1.8–2.0 (m, 2 H), 2.85 (s, 1 H, OH), 3.5–3.55 (m, 2 H), 4.38 (dd, 1 H, *J* = 14, 8.6), 4.78 (dd, 1 H, *J* = 14, 3.2), 5.2 (dd, 2 H, *J* = 8.6, 3.2), 7.3–7.8 (m, 11 H)	14.05 (q, CH_3), 21.85, 22.6, 28.15, 28.9, 29.2, 29.4, 31.8, 55.1, 55.2 (t, CH_2), 73.65, (d, CH), 121.2, 125.2, 125.8, 127.7, 128.35, 128.6, 128.7 (d, CH_{arom}), 132.5, 140.35, 141.35, 141.55 (s, C_{arom})
9	263 ($[M+1]^+$, 13), 262 ($[M]^+$, 65), 171 (29), 128 (12), 116 (23), 105 (11), 104 (100), 103 (23), 78 (16), 77 (18)	3029, 2882, 1604, 1585, 1571, 1494, 1480, 1381, 1286, 976, 930, 765, 709, 695	4.21 (dd, 1 H, *J* = 10, 8), 4.73 (dd, 1 H, *J* = 10, 8), 6.41 (t, 1 H, *J* = 8), 7.25–7.8 (m, 11 H)	50.25 (d, CH), 86.7 (t, CH_2), 107.9, 123.8, 126.05, 126.55, 128.5, 128.9, 129.2, (d, CH_{arom}), 135.0, 137.9, 141.0, 159.1 (s, C_{arom})

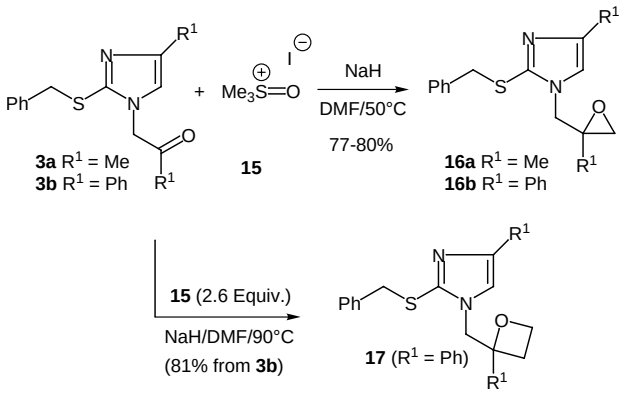
ing material was recovered almost quantitatively (Scheme 3).

Obviously, the entropy factor seems to be the driving force for the formation of fused imidazoxazoles **9**, favouring intramolecular versus intermolecular nucleophilic addition-elimination reactions in electron rich imidazoles. Therefore, due to the exceptionally mild reaction conditions used to efficiently achieve the transformations to these novel fused imidazoxazoles of type **9**, we decided to explore further the synthetic applicability of these findings. With the aim of adapting the methodology to the solid support[12] in such a way that could afford libraries of fused imidazoxazoles with increased molecular diversity, we initially explored in solution an epoxidation reaction on the carbonyl group in imidazoles of type **3**. Epoxide





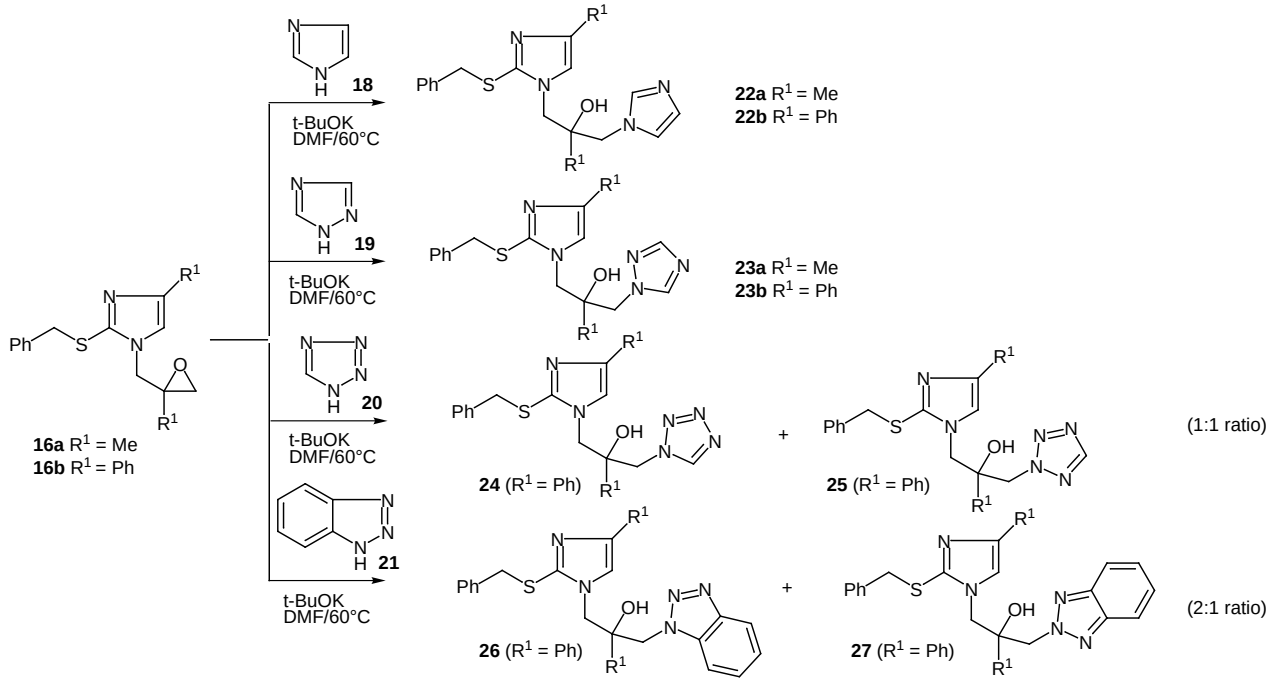
Scheme 3



Scheme 4

opening with different nucleophiles should lead to the corresponding tertiary alcohols, which, by subsequent oxidation to the corresponding sulfone followed by intramolecular *ipso*-substitution reactions with concomitant release of the 2-alkylsulfonyl group, under the above described conditions, should afford different 2,3-dihydroimidazo[2,1-*b*][1,3]oxazoles.

Thus, when imidazoles **3a,b**, were allowed to react under optimized conditions of 1.1 equivalents of trimethylsulfonium iodide **15** in the presence of 1 equivalent of NaH in DMF at 50ºC, the epoxides **16a,b** were formed exclusively and isolated in good yields. Other reaction conditions, such as varying the amount of base, the amount of sulfonium reagent **15**, solvents and temperatures, resulted in the formation of oxetane derivatives **17**, together with the epoxide **16**, in different proportions. When the reaction



Scheme 5

Table 6 Prepared Epoxides **16** and Oxetane **17**

Product[a]	R^1	Yield (%)	mp (ºC).
16a	Me	68	yellowish oil
16b	Ph	80	90.1–91.7
17	Ph	81	82.4–84.9

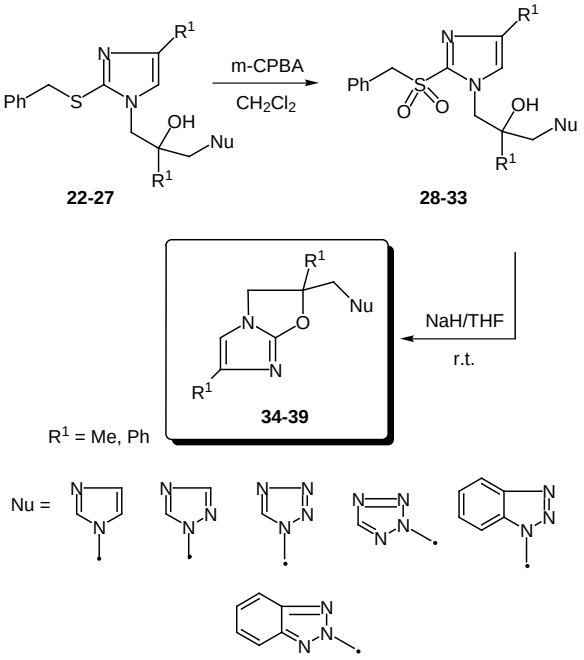
[a] Satisfactory microanalyses obtained: C ± 0.28, H ± 0.26, N ± 0.18.

was carried out with 2.5 equivalents of base and 2.6 equivalents of **15** in DMF at 90 ºC, the oxetane derivative **17** was the sole isolated product in 81% yield (from **3b**, Scheme 4 and Tables 6 and 7).

With a good procedure in our hands to selectively form epoxides **16**, or oxetanes **17** if desired, we proceeded further by studying the epoxide opening reaction with different azoles. Thus, when epoxides **16a,b** were treated with 2.5 equivalents of 1*H*-imidazole **(18)**, 1*H*-1,2,4-triazole **(19)**,1*H*-tetrazole **(20)** or benzotriazole (**21)**, in the presence of *t*-BuOK in DMF at 60–100 ºC for 5–7 hours, the corresponding azolyl derivatives **22–27** were obtained in 94–98% yield. When the potassium salts of 1*H*-imidazole

Table 7 MS, IR and NMR Data of Epoxides **16** and Oxetane **17**

Product	MS *m/z* (%)	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
16a	276 ([M+2]$^+$, 19), 275 ([M+1]$^+$, 100), 274 ([M]$^+$, 7), 219 (13), 205 (12), 185 (18), 171 (11), 167 (16), 165 (12)	3056, 3029, 2966, 2927, 2853, 1564, 1492, 1446, 1429, 1358, 1285, 1170, 1113, 1071, 895, 791, 768, 703	1.13 (s, 3 H), 2.27 (d, 3 H, *J* = 0.8), 2.52 (dd, 2 H, *J* = 14.4), 3.56 (d, 1 H, *J* = 14.6), 3.85 (d, 1 H, *J* = 14.6), 4.2 (s, 2 H), 6.75 (d, 1 H, *J* = 0.8), 7.15–7.3 (m, 5 H)	13.84, 18.4 (q, CH_3), 40.45, 50.6, 51.65 (t, CH_2), 55.8 (s, C), 118.4 (s, C_{arom}), 127.3, 128.45, 128.75 (d, CH_{arom}), 137.7, 139.25 (s, C_{arom})
16b	400 ([M+2]$^+$, 29), 399 ([M+1]$^+$, 100), 398 ([M]$^+$, 13), 177 (18), 176 (35), 123 (30), 121 (32), 119 (41), 109 (61), 107 (47), 105 (82)	3142, 3064, 3029, 2924, 1728, 1602, 1494, 1455, 1433, 1194, 756, 697	2.71 (dd, 2 H, *J* = 5), 4.05 (d, 1 H, *J* = 15), 4.25, 4.30 (2d, 2 H, *J* = 12.8), 4.43 (d, 1 H, *J* = 15), 7.2–7.45 (m, 14 H), 7.8-7.85 (m, 2 H)	40.3, 49.75, 52.8 (t, CH_2), 59.44 (s, C), 117.7, 124.75, 126.0, 126.85, 127.5, 128.35, 128.5, 128.5, 128.85 (d, CH_{arom}), 133.75, 136.4, 137.8, 141.1, 142.45 (s, C_{arom})
17	414 ([M+2]$^+$, 19), 413 ([M+1]$^+$, 64), 412 ([M]$^+$, 13), 133 (93), 105 (100)	3056, 3031, 2938, 2967, 2873, 1602, 1488, 1451, 1422, 1357, 1342, 1233, 1189, 1114, 1069, 1027, 979, 958, 868, 776, 747, 694	2.6–2.7 (m, 2 H), 3.85 (d, 1 H, *J* = 14.8), 4.2 (d, 1 H, *J* = 14.8), 4.2–4.45 (m, 4 H), 7.2–7.55 (m, 14 H), 7.85–7.9 (m, 2 H)	30.55, 40.1, 55.3, 65.3 (t, CH_2), 87.5 (s, C), 118.4, 124.0, 124.7, 126.75, 127.35, 127.55, 128.4, 128.45, 128.5, 128.8 (d, CH_{arom}), 134.0, 137.75, 141.6, 142.2, 143.5 (s, C_{arom})



Scheme 6

Table 8 Prepared Epoxide Ring Opening Products **22–27**

Product	R^1	Reaction Time (h)	Reaction Temperature (ºC)	Yield (%)	mp (ºC)
22a	Me	6	60	92	colourless oil
22b	Ph	6	60	95	176–177
23a	Me	5	60	93	colourless oil
23b	Ph	5	100	88	164–165
24	Ph	7	60	45	77–78
25	Ph	7	60	53	158–159
26	Ph	6	60	56	128–130 (dec.)
27	Ph	6	60	38	183–184 (dec.)

[a] Satisfactory microanalyses obtained: C ± 0.27, H ± 0.26, N ± 0.28.

Table 9 MS, IR and NMR Data of Epoxide Ring Opening Products **22–27**

Product	MS *m*/*z* (%)	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
22a	344 ([M+2]$^+$, 21), 343 ([M+1]$^+$, 100), 342 ([M]$^+$, 9), 219 (11), 185 (57), 171 (13), 167 (13), 165 (12)	3147, 3113, 3030, 2978, 2933, 2856, 1566, 1509, 1447, 1412, 1378, 1289, 1237, 1140, 1107, 1078, 1035, 913, 818, 740, 701, 663	0.97 (s, 3 H), 2.23 (s, 3 H), 3.57, 3.60 (2 d, 2 H, *J* = 14.2), 3.68 (s, 2 H), 4.14, 4.18 (2 d, 2 H, *J* = 12.6), 5.68 (s, 1 H, OH), 6.81 (s, 1 H), 6.9–7.6 (m, 8 H)	13.8, 22.4 (q, CH_3), 40.75, 53.55, 55.0 (t, CH_2), 71.5 (s, C), 119.55, 120.60, 127.4, 127.85, 128.45, 128.65 (d, CH_{arom}), 137.65 (s, C_{arom}), 138.1 (d, CH_{arom}), 138.7, 139.45 (s, C_{arom})
22b	468 ([M+2]$^+$, 32), 467 ([M+1]$^+$, 100), 466 ([M]$^+$, 9), 189 (17), 187 (53), 109 (41), 107 (42), 105 (61)	3280, 3108, 3060, 3028, 2937, 2878, 1649, 1603, 1509, 1494, 1454, 1415, 1288, 1194, 1132, 1107, 1080, 787, 756, 698	3.76 (d, 1 H, *J* =14), 4.0, 4.2 (2 d, 2 H, *J* = 14.4), 4.12 (d, 1 H, *J* = 14), 4.26, 4.30 (2 d, 2 H, *J* = 12), 6.19 (s, 1 H), 6.36 (s, 1 H), 6.91 (s, 1 H), 7.15–7.45 (m, 14 H), 7.75–7.8 (m, 2 H)	40.5, 54.2, 54.4 (t, CH_2), 76.4 (s, C), 118.65, 119.7166, 124.75, 125.7, 126.85, 127.45, 128.0, 128.15, 128.5, 128.6, 128.75 (d, CH_{arom}), 133.85 (s, C_{arom}), 137.9 (d, CH_{arom}), 138.15, 140.4, 141.25, 142.15 (s, C_{arom})
23a	345 ([M+2]$^+$, 21), 344 ([M+1]$^+$, 100), 343 ([M]$^+$, 18), 185 (21)	3219, 3149, 3030, 2977, 2936, 1657, 1566, 1507, 1445, 1412, 1382, 1276, 1245, 1207, 1168, 1137, 1016, 767, 702, 678	0.95 (s, 3 H), 2.23 (s, 3 H), 3.64, 3.70 (2 d, 2 H, *J* = 14.4), 3.96, 4.0 (2 d, 2 H, *J* = 14), 4.15, 4.25 (2 d, 2 H, *J* = 12.6), 4.65 (s, 1 H, OH), 6.92 (s, 1 H), 7.1–7.3 (m, 5 H), 7.88 (s,1 H), 8.0 (s, 1 H)	13.75, 22.9 (q, CH_3), 40.6, 52.95, 56.35 (t, CH_2), 71.8 (s, C), 119.4, 127.4, 128.45, 128.7 (d, CH_{arom}), 137.6, 138.8, 139.65 (s, C_{arom}), 144.45, 151.45 (d, CH_{arom})
23b	469 ([M+2]$^+$, 31), 468 ([M+1]$^+$, 100), 467 ([M]$^+$, 25), 190 (23), 189 (17), 188 (16), 154 (22), 149 (22), 137 (18), 136 (28), 121 (16), 109 (17), 107 (23), 105 (38)	3425, 3192, 3125, 3058, 3027, 2923, 1657, 1601, 1497, 1445, 1413, 1347, 1272, 1192, 1129, 1069, 1014, 753	3.91 (d, 1 H, *J* = 14.6), 3.95 (d, 1 H, *J* = 14), 4.17 (d, 1 H, *J* = 14.6), 4.27 (d, 1 H, *J* = 14), 4.39, 4.42 (2 d, 2 H, *J* = 12.8), 4.82 (s, 1 H, OH), 7.2–7.6 (m, 14 H), 7.81 (s, 1 H), 7.8–7.85 (m, 3 H)	40.3, 53.85, 55.3 (t, CH_2), 76.65 (s, C), 118.65, 124.75, 124.95, 126.95, 127.55, 128.25, 128.55, 128.6, 128.7, 128.75, 128.8 (d, CH_{arom}), 133.7, 138.1, 139.75, 141.1, 142.35 (s, C_{arom}), 144.2, 151.8 (d, CH_{arom})
24	470 ([M+2]$^+$, 21), 469 ([M+1]$^+$, 65), 468 ([M]$^+$, 14), 191 (19), 190 (37), 189 (40), 149 (89), 107 (61), 105 (100)	3291, 3104, 3059, 3029, 2925, 2853, 1651, 1603, 1485, 1450, 1424, 1241, 1171, 1102, 1069, 1028, 952, 911, 756, 696, 658	4.04, 4.10 (2 d, 2 H, *J* = 14.8), 4.19, 4.22 (2 d, 2 H, *J* = 12.8), 4.44, 4.52 (2 d, 2 H, *J* = 14.4), 7.2–7.45 (m, 14 H), 7.7–7.75 (m, 2 H), 8.34 (s, 1 H)	40.5, 53.15, 54.95 (t, CH_2), 75.75 (s, C), 118.3, 124.85, 125.0, 127.15, 127.55, 128.6, 128.65, 128.75, 128.95 (d, CH_{arom}), 133.35, 137.75, 138.65, 141.5, 142.45 (s, C_{arom}), 143.6 (d, CH_{arom})
25	470 ([M+2]$^+$, 32), 469 ([M+1]$^+$, 100), 468 ([M]$^+$, 33), 189 (22), 154 (44), 149 (68), 107 (58), 105 (75)	3489, 3059, 3030, 2922, 2852, 1603, 1489, 1455, 1362, 1329, 1277, 1195, 1152, 1126, 1073, 1023, 888, 749, 699	3.94 (d, 1 H, *J* = 14.6), 4.18 (d, 1 H, *J* = 14.6), 4.27 (s, 1 H, OH), 4.32, 4.40 (2 , 2 H, *J* = 12.8), 4.48 (d, 1 H, *J* = 14), 5.21 (d, 1 H, *J* = 14), 7.15–7.45 (m, 14 H), 7.8–7.85 (m, 2 H), 8.37 (s, 1 H)	40.4, 53.95, 58.65 (t, CH_2), 76.95 (s, C), 118.5, 124.8, 125.1, 126.95, 127.5, 128.45, 128.55, 128.60, 128.65, 128.75 (d, CH_{arom}), 133.65, 137.75, 138.6, 141.35, 142.35 (s, C_{arom}), 152.5 (d, CH_{arom})
26	519 ([M+2]$^+$, 35), 518 ([M+1]$^+$, 100), 517 ([M]$^+$, 25), 154 (47), 137 (29), 136 (45), 120 (21), 105 (36)	3178, 3136, 3021, 2968, 2940, 1596, 1486, 1447, 1421, 1381, 1172, 1141, 1106, 1068, 747, 691	4.07 (d, 1 H, *J* = 14.6), 4.15–4.4 (m, 4 H), 4.59 (d, 1 H, *J* = 14.2), 4.88 (d, 1 H, *J* = 14.2), 7.1–7.4 (m, 17 H), 7.45–7.95 (m, 3 H)	40.45, 53.55, 54.6 (t, CH_2), 76.9 (s, C), 109.5, 118.6, 119.8, 124.05, 124.8, 125.1, 126.9, 127.45, 127.65, 128.25, 128.55, 128.6, 128.7, (d, CH_{arom}), 133.75, 137.75, 139.7, 141.25, 142.4, 145.1 (s, C_{arom})
27	519 ([M+2]$^+$, 36), 518 ([M+1]$^+$, 100), 517 ([M]$^+$, 30), 190 (23), 154 (74), 137 (29), 136 (66), 120 (20), 107 (23), 105 (29)	3485, 3061, 3029, 2985, 2947, 1604, 1562, 1492, 1456, 1427, 1412, 1359, 1276, 1200, 1167, 886, 749, 725, 690	3.93, 4.0 (2 d, 2 H, *J* = 14.4), 4.22 (s, 2 H), 4.76 (d, 1 H, *J* = 14), 5.22 (d, 1 H, *J* = 14), 5.49 (s, 1 H, OH), 7.15–7.45 (m, 16 H), 7.8–7.85 (m, 4 H)	40.5, 54.05, 61.7 (t, CH_2), 76.35 (s, C), 117.85, 118.5, 124.75, 125.35, 126.8, 126.85, 127.35, 128.1, 128.5, 128.75 (d, CH_{arom}), 133.9, 137.7, 139.45, 141.4, 142.15,143.75 (s, C_{arom})

Table 10 Prepared Sulfone Derivatives **28–33**

Product[a]	R^1	Yield (%)	mp (ºC)
28a	Me	62	86–87
28b	Ph	81	197–198
29a	Me	65	72–74
29b	Ph	81	109–110
30	Ph	57	92–94
31	Ph	78	165–166
32	Ph	67	147–148
33	Ph	62	222–223

[a] Satisfactory microanalyses obtained: C ± 0.28, H ± 0.26, N ± 0.30.

(**18**) or 1*H*-1,2,4-triazole (**19**) were employed, only one type of isomers **22a,b** and **23a,b** were obtained in near quantitative yields; however, under identical conditions, the use of the potassium salts of 1*H*-tetrazole (**20**) or benzotriazole (**21**) afforded two types of isomers **24/25** and **26/27**, in 1:1 and 2:1 ratios, respectively, as a result of epoxide ring opening through the *N*-2 atom in the azole moiety. These isomers, **24/25** and **26/27** could easily be separated by flash-chromatography (Scheme 5, Tables 8 and 9).

Oxidation of **22–27** to the corresponding alcohol sulfones **29–33** with 2.1 equivalents of *m*-CPBA followed by intramolecular *ipso*-substitution by treatment with NaH in THF at room temperature, efficiently furnished 2-azolyl imidazoxazoles **34–39** in good overall yields (Scheme 6, Tables 10,11, 12 and 13).

In summary, we have shown that the reaction between thiouronium salts of type **1** and α-halocarbonyl compounds **2** under the described conditions efficiently leads to 2-alkylthioimidazoles **3** in good yields. These compounds are useful precursors in the preparation of novel 2,3-dihydroimidazo[2,1-*b*][1,3] oxazoles **9** by intramolecular nucleophilic displacement of the 2-sulfonyl derivatives **8**. This is the first time that such intramolecular nucleophilic *ipso*-substitution reactions using alkylsulfonyl groups as leaving groups in electron rich imidazoles have been described. Their synthetic applicability in the preparation of a series of imidazoxazoles **34–39** has been demonstrated. Further developments of this strategy, including the use of polymer-bound thiouronium salts that may have widespread synthetic utility, are now in progress in our laboratory and will be published in due course.

All commercially available chemicals were used without prior purification, except that THF was dried over Na/benzophenone prior to use. Melting points (capillary tube) were determined using a Gallenkamp apparatus and are uncorrected. NMR (^{1}H and ^{13}C) spectra were recorded on Bruker DPX200 Advance at 200 and 50 MHz respectively using TMS as internal standard. IR spectra were recorded on a Nicolet 205FT-IR. MS spectra were recorded on a VG Quattro instrument in the positive ionization FAB mode, using 3-NBA or 1-thioglycerol as matrix. Elemental analyses were performed on a Carlo Erba 1106 elemental analyser instrument. Analytical TLC was performed on precoated TLC plates, silica gel SIL G/UV_{254} from Macheray-Nagel. Flash chromatography purifications were performed SDS silica gel (230–400 mesh).

2-Alkylthioimidazoles 3a–d; General Procedure

To a mixture of thiouronium salt **1a–b** (20 mmol) and the appropriate α-haloketone **2a–b** (40mmol) in MeCN (100 mL), was added DIPEA (10.45 mL, 60 mmol) dropwise and the mixture was stirred at r.t. for 6–8 h. The solution was evaporated to dryness, and the residue was partitioned between EtOAc (150 mL) and H_2O (100 mL). The organic phase was separated, washed with brine (50 mL), dried ($MgSO_4$) and the solvent evaporated to give a crude material **3a–d** which was purified by flash chromatography using hexanes/EtOAc (4:1 to 1:1) as eluent (Tables 2 and 3).

Crystal Data for 3a[24]

$C_{24}H_{20}N_2OS$, M_r = 384.49, orthorhombic, space group $P2_12_12_1$, a = 12.630(2), b = 18.828(2), c = 8.406(3) Å, V = 1998.9(8) Å^3, Z = 4, D_c = 1.278 g cm^{-3}, crystal dimensions: 0.27 × 0.40 × 0.40 mm, T = –83 °C, Rigaku AFC5R diffractometer, Mo Kα radiation, λ = 0.71069 Å, μ = 0.178 mm^{-1}, ω-2θ scans, $2\theta_{max}$ = 55°, 5172 measured reflections of which 4176 were unique. Friedel opposites were recorded for all unique reflections with 2θ < 50°. The intensities were corrected for Lorentz and polarization effects, but not for absorption. The structure was solved by direct methods using SHELXS86[25] and refined on F by full-matrix least-squares methods using teXsan.[26] H-atoms were in calculated positions. The refinement of 254 parameters using 3026 observed reflections with $I > 2\sigma(I)$ gave R = 0.0427, wR = 0.0309, S = 1.308, $\Delta\rho_{max}$ = 0.25 eÅ^{-3} and absolute structure parameter = 0.04(10).

Alcohol Derivatives 7a–c; General Procedure

To a stirred and cooled (0 ºC) solution of 2-alkylthioimidazoles **3a–c** (12 mmol) in MeOH (60 mL) was added $NaBH_4$ (1.14 g, 30 mmol) in small portions while stirring (vigorous evolution of gas observed). Stirring was continued for 1 h at 0 ºC and at r.t. overnight. The solution was evaporated to dryness, and the crude residue was partitioned between EtOAc (100 mL) and aq satd NH_4Cl solution (200 mL). The organic layer was separated, washed with H_2O (50 mL), dried ($MgSO_4$), and evaporated to give a residue which was purified by flash chromatography using hexanes/EtOAc (9:1 to 4:1) as eluent (Tables 4 and 5).

2-(2-Benzylsulfanyl-1-(2-methoxy-2-phenylethyl)-4-phenyl-1*H*-imidazole (12)

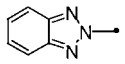
To a solution of **7a** (4.25 g, 11 mmol) in anhyd THF (35 mL) was added NaH (60% dispersion in mineral oil, 0.48 g, 12.1 mmol) in small portions at r.t. After the gas evolution had ceased, MeI (2.05 mL, 33 mmol) was added in one portion. The resulting mixture was stirred at r.t. under N_2, for 6 h. The solvent was evaporated and the resulting residue was partitioned between EtOAc (150 mL) and (50 mL). The organic phase was separated, washed with brine (50 mL), separated, dried ($MgSO_4$) and filtered. The solvent was evaporated and the resulting residue purified by flash chromatography (hexanes/EtOAc, 14:1) to afford pure **12** as a colourless oil; yield: 4.05 g (92%).

^{1}H NMR (DMSO-d_6): δ = 3.18 (s, 3 H, OCH_3), 3.93 (d, 2 H, J = 5 Hz), 4.1 (t, 1 H, J = 5 Hz), 4.29, 4.35 (2 d, 2 H, J = 12.8 Hz), 7.2–7.5 (m, 14 H_{arom}), 7.85–7.9 (m, 2 H_{arom}).

Table 11 MS, IR and NMR Data of Sulfone Derivatives **28–33**

Product	MS *m/z* (%)	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
28a	376 ($[M+2]^+$, 17), 375 ($[M+1]^+$, 100), 221 (19), 219 (23)	3366, 3143, 2923, 2853, 1653, 1601, 1510, 1456, 1417, 1322, 1253, 1151, 1120, 1079, 915, 879, 782, 747, 699	0.95 (s, 3H), 2.34 (s, 3 H), 3.51 (d, 1 H, *J* = 14.2), 3.6 (s, 1 H, OH), 3.67 (dd, 2 H, *J* = 14.2), 3.77 (d, 1 H, *J* = 14.2), 4.65, 4.70 (2 d, 2 H, *J*= 13.8), 6.75 (s, 1 H), 6.81 (s, 1H), 7.0 (s, 1 H), 7.0–7.15 (m, 2 H), 7.3–7.35 (m, 4 H)	13.7, 22.23 (q, CH_3), 53.65, 54.7, 62.3 (t, CH_2), 70.95 (s, C), 120.6, 123.2 (d, CH_{arom}), 127.15 (s, C_{arom}), 127.8, 128.65, 129.2, 131.1, 138.1 (d, CH_{arom}), 139.25, 139.3 (s, C_{arom})
28b	500 ($[M+2]^+$, 33), 499 ($[M+1]^+$, 100), 187 (40), 154 (44), 149 (33), 137 (33), 136 (49)	3453, 3141, 3063, 3033, 1713, 1604, 1512, 1451, 1403, 1378, 1321, 1291, 1251, 1238, 1154, 1110, 1081, 919, 766, 745, 697, 637	3.5 (d, 1 H, *J* = 14.2), 3.84 (d, 1 H, *J* = 14.4), 4.3 (d, *J* = 14.2), 4.56 (d, 1 H, *J* = 14.4), 4.9, 5.0, (2 d, 2H, *JJ* = 13.8), 6.12 (s, 1 H), 6.41 (s, 1 H), 6.88 (s, 1 H), 7.2–7.6 (m, 14 H), 7.8–7.85 (m, 2 H)	53.8, 54.95, 62.0, (t, CH_2), 75.7 (s, C), 119.7, 121.8, 125.3, 125.65, 126.9, 127.95, 128.35, 128.7, 129.25, 131.2, 132.35 (d, CH_{arom}), 138.1 (s, C_{arom}), 138.13 (d, CH), 140.2, 140.5, 142.1 (s, C_{arom})
29a	377 ($[M+2]^+$, 16), 376 ($[M+1]^+$, 100), 375 ($[M]^+$, 6), 222 (27), 221 (12), 220 (53)	3244, 3135, 3034, 2979, 2926, 1627, 1554, 1508, 1454, 1418, 1323, 1277, 1248, 1204, 1134, 1014, 912, 879, 783, 730, 699	0.91 (s, 3 H), 2.31 (s, 3 H), 3.64 (d, 1 H, *J* = 14.2), 3.72, 3.78 (2 d, 2 H, *J* = 14.4), 4.07 (d, 1 H, *J* = 14.2), 4.22 (s, 1 H, OH), 4.64, 4.70, (2 d, 2 H, *J* = 13.8), 7.04 (s, 1 H), 7.1–7.3 (m, 5 H), 7.91 (s, 1 H), 8.02 (s, 1 H).	13.6, 22.75 (q, CH_3), 53.05, 55.4, 65.75, (t, CH_2), 71.15 (s, C), 123.25 (d, CH_{arom}), 127.0 (s, C), 128.6, 129.15, 131.0 (d, CH_{arom}), 139.2, 139.3 (s, C_{arom}), 144.55, 151.8 (d, CH_{arom})
29b	501 ($[M+2]^+$, 24), 500 ($[M+1]^+$, 75), 154 (61), 149 (41), 137 (53), 136 (76), 123 (44), 121 (46), 109 (77), 105 (100)	3423, 3128, 3061, 2956, 2924, 2853, 1719, 1508, 1457, 1380, 1322, 1276, 1251, 1200, 1155, 1138, 1116, 1072, 1025, 944, 767, 696, 677	3.64 (d, 1 H, *J* = 14), 3.79 (d, 1 H, *J* = 14.6), 4.57 (d, 1 H, *J* = 14), 4.65, 4.7 (2 d, 2 H, *J* = 13.9), 4.72, 4.76 (2 d, 1 H, *J* = 14.6), 5.0 (d, 1 H, *J* = 13.9), 5.01 (s, 1 H, OH), 7.25–7.9 (m, 18 H)	54.25, 54.75, 61.95 (t, CH_2), 76.15 (s, C), 122.15, 124.9, 125.3, 127.0, 128.0, 128.3, 128.7, 128.75, 129.2 (d, CH_{arom}), 131.25, 132.3, 139.55, 140.45 (s, C_{arom}), 142.25, 151.85 (d, CH_{arom})
30	502 ($[M+2]^+$, 31), 501 ($[M+1]^+$, 100), 500 ($[M]^+$, 8), 154 (50), 149 (75)	3432, 3140, 3061, 3032, 2922, 2853, 1716, 1604, 1486, 1451, 1417, 1381, 1329, 1257, 1155, 1110, 1072, 945, 767, 729, 695	3.79 (d, 1 H, *J* = 14.8), 4.17 (d, 1 H, *J* = 14), 4.33 (s, 1 H, OH), 4.42 (d, 1 H, *J* = 14.8), 4.69, 4.72, (2 d, 2 H, *J* = 14.2), 4.85 (d, 1 H, *J* = 14), 7.5–7.1 (m, 14 H), 7.75–7.8 (m, 2 H), 8.23 (s, 1H)	53.95, 54.7, 62.0 (t, CH_2), 75.15(s, C), 121.6, 124.95, 125.3 (d, CH_{arom}), 125.5 (s, C_{arom}), 126.6, 128.15, 128.75, 128.9, 129.1, 129.4, 131.2 (d, CH_{arom}), 131.95, 138.3, 140.5, 142.45 (s, C_{arom}), 143.5 (d, CH)
31	502 ($[M+2]^+$, 4), 501 ($[M+1]^+$, 12), 500 ($[M]^+$, 8), 149 (77), 133 (100), 119 (57), 109 (77), 107 (72), 105 (96)	3468, 3138, 3031, 2922, 2853, 1491, 1452, 1381, 1321, 1287, 1246, 1197, 1150, 1113, 1025, 697	3.86 (d, 1 H, *J* = 14.8), 4.16 (d, 1 H, *J* = 14), 4.44 (s, 1 H, OH), 4.66 (d, 1 H, *J* = 14.8), 4.69 (d, 2 H, *J* = 13.8), 4.94 (d, 1 H, *J* = 13.8), 5.27 (d, 1 H, *J* = 14), 7.15–7.45 (m, 14 H), 7.8–7.85 (m, 2 H), 8.37 (s, 1H)	54.2, 58.3, 61.7 (t, CH_2), 75.6 (s, C), 121.75, 125.1, 125.3 (d, CH_{arom}), 126.85 (s, C_{arom}), 128.0, 128.55, 128.7, 128.85, 129.1, 131.2 (d, CH_{arom}), 132.2, 138.45, 140.6, 142.2 (s, C_{arom}), 152.5 (d, CH_{arom})
32	551 ($[M+2]^+$, 15), 550 ($[M+1]^+$, 42), 155 (30), 154 (100)	3168, 3128, 3063, 2952, 1496, 1449, 1386, 1317, 1259, 1206, 1159, 1115, 755, 694	4.65–4.75 (m, 3 H), 4.85 (d, 1 H, *J* = 13.2), 5.15, 5.25, (2 d, 2 H, *J* = 14.4), 6.19 (s, 1 H, OH), 7.2–8.0 (m, 20 H)	54.0, 55.45, 61.2 (t, CH_2), 76.05 (s, C), 111.7, 118.85, 121.95, 123.65, 124.75, 125.95, 126.95 (d, CH_{arom}), 127.25 (s, C_{arom}), 127.65, 127.85, 128.15, 128.35, 128.6, 128.85, 131.35 (d, CH_{arom}), 132.55, 134.2, 140.05, 140.45, 141.3, 144.9 (s, C_{arom})
33	551 ($[M+2]^+$, 2), 550 ($[M+1]^+$, 4), 307 (15), 155 (28), 154 (100), 136 (81)	3433, 3129, 3021, 2976, 2924, 1486, 1448, 1373, 1318, 1279, 1239, 1190, 1148, 1107, 786, 752, 692	4.17 (dd, 4 H, *J* = 13.8), 5.14, 5.20 (2 d, 2 H, *J* = 14), 6.31 (s, 1 H, OH), 7.1–7.95 (m, 20 H)	54.4, 61.6, 63.4 (t, CH_2), 75.85 (s, C), 118.3, 122.25, 125.05, 126.2 (d, CH_{arom}), 126.9 (s, C_{arom}), 127.6, 127.9, 128.15, 128.45, 128.7, 129.0, 129.15, 131.65 (d, CH_{arom}), 132.9, 140.25, 140.85, 141.75, 144.1 (s, C_{arom})

Table 12 Prepared 2,3-Dihydroimidazo[2,1-*b*][1,3]oxazole Derivatives **34–39**

Compound[a]	R^1	Nu	Yield (%)	mp (ºC)
34a	Me		88	colourless oil
34b	Ph		88	188–189
35a	Me		77	colourless oil
35b	Ph		87	149–150 (dec.)
36	Ph		63	124–126 (dec.)
37	Ph		62	160–161 (dec.)
38	Ph		55	170–171 (dec.)
39	Ph		53	252–254 (dec.)

[a] Satisfactory microanalyses obtained: C ± 0.23, H ± 0.27, N ± 0.30.

^{13}C NMR($CDCl_3$): δ = 40.25 (t, CH_2), 52.5 (t, CH_2), 56.95 (q, CH_3), 82.75 (d, CH), 118.3 (s, C), 124.75, 126.5, 126.65, 127.3, 128.35, 128.5, 128.65, 128.85 (d, CH_{arom}), 134.15, 138.0, 138.25, 140.7, 141.9 (6 s, C_{arom}).

IR (film): ν = 3061, 3029, 2932, 1605, 1493, 1455, 1434, 1416, 1399, 1371, 1195, 1181, 1106, 1075, 1027, 747, 698 cm^{-1}.

MS: *m/z* (%) = 402 ($[M+2]^+$, 24), 401 ($[M+1]^+$, 100), 400 (M^+, 9), 279 (20), 267 (11), 266 (19), 233 (25).

Anal. Calcd for $C_{25}H_{24}N_2OS$ (400.5): C, 74.97; H, 6.04; N, 6.99. Found: C, 75.08; H, 6.28; N, 7.26.

Oxidation of 2-Alkylthioimidazoles 3b, 7a–c and 12 to the Corresponding Sulfones 4, 8a-c, 13; General Procedure

To a cooled (0ºC) solution of the different 2-alkylthioimidazoles **3b**, **7a–c** and **12** (10 mmol) in CH_2Cl_2 (60 mL) was added *m*-CPBA (6.66 g, 22 mmol) in small portions**.** The mixture was then stirred at r.t. overnight, then diluted with EtOAc (200 mL) and washed with aq satd $NaHCO_3$ solution (2 × 50 mL) and brine (50 mL). The separated organic layer was dried ($MgSO_4$), filtered and evaporated to give a residue which was purified by flash chromatography using hexanes/EtOAc (from 9:1 to 1:1) as eluent (Tables 2–5).

2,3-Dihydro-2,6-diphenylimidazo[2,1-*b*][1,3]oxazole (9)

To a solution of **8a** (0.418g, 1 mmol) in anhyd THF (3 mL) was added NaH (60% dispersion in mineral oil, 0.06g, 1.5 mmol) in small portions. The mixture was stirred under N_2 at r.t. for 5 h. The solvent was evaporated, and the residue was partitioned between EtOAc (30 mL) and H_2O (30 mL). The organic layer was separated, washed with brine (15 mL) and dried ($MgSO_4$). Elimination of the solvent and purification of the resulting residue by flash-chromatography (hexanes/EtOAc, 2:1 as eluent) afforded pure **9** as colourless solid. 0.21g, (81%) (Tables 4 and 5).

2-Benzylsulfonyl-1-(2-methoxy-2-phenylethyl)-4-phenyl-1*H*-imidazole (13)

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.12 (s, 3 H, OCH_3), 3.85 (dd, 2 H, CH_2, *J* = 13.4 Hz, *J'* = 8.4Hz), 4.1–4.25 (m, 1 H), 4.71, 4.75, 4.78 (2 d, 2 H, *J* = 13.8 Hz), 7.25–7.85 (m, 14 H_{arom}), 7.85–7.9 (m, 2 H_{arom}).

^{13}C NMR(50 MHz, $CDCl_3$): δ = 53.8 (t, CH_2), 56.95 (q, CH_3), 61.9 (t, CH_2), 82.8 (d, CH), 121.75 (s, C), 125.25, 126.4 (d, CH_{arom}), 127.3, (s, C_{arom}), 127.7, 128.35, 128.65, 128.7, 129, 131.15 (d, CH_{arom}), 132.65, 137.85, 139.85, 141.55, (s, C_{arom}).

IR (KBr): ν = 3139, 3033, 2948, 2920, 1701, 1601, 1493, 1455, 1411, 1380, 1329, 1242, 1155, 1016, 786, 759, 737 cm^{-1}.

MS: *m/z* (%):434 ($[M+2]^+$, 8), 433 ($[M+1]^+$, 100), 432 (($[M]^+$, 10), 279 (13), 277 (10).

Anal. Calcd for $C_{25}H_{24}N_2O_3S$ (432.5): C, 69.42; H, 5.59; N, 6.48. Found: C, 69.76; H, 5.79; N, 6.79.

2-Benzylsulfanyl-4-methyl-1-(2-methyl-2-oxiranylmethyl)-1*H*-imidazole (16a)

A mixture containing trimethylsulfoxonium iodide **15** (2.32 g, 10.56 mmol), and NaH (60% dispersion in mineral oil, 0.38g, 9.6 mmol) in DMF (29 mL) was stirred under N_2 at r.t. for 1 h. Then, **3a** (2.5 g, 9.6 mmol) was added in one portion. The mixture was stirred at r.t. for 1 h. DMF was distilled off, and the resulting residue was partitioned between EtOAc (100 mL) and H_2O (20 mL). The organic layer was separated, washed with brine (20 mL), dried ($MgSO_4$), filtered, and the solvent evaporated to give crude **16a** which was purified by flash chromatography (hexanes/EtOAc, 4:1); yellowish oil (1.79 g, 68%) (Tables 6 and 7).

2-Benzylsulfanyl-4-phenyl-1-(2-phenyl-2-oxiranylmethyl)-1*H*-imidazole (16b)

A mixture containing trimethylsulfoxonium iodide **15** (2.9g, 13.2 mmol) and NaH (60% dispersion in mineral oil, 0.48 g, 12 mmol) in DMF (36 mL) was stirred under N_2 at r.t for 1 h. Then, the mixture was heated until 50ºC and **3b** (4.61 g, 12 mmol) was added in one portion and the mixture stirred at 50 ºC for 15 h. DMF was distilled off and the resulting residue was partitioned between EtOAc (100 mL) and H_2O (50 mL). The organic layer was separated, washed with brine (20 mL), dried ($MgSO_4$), filtered, and evaporated to give a residue that was purified by flash chromatography (hexanes/EtOAc,14:1) to afford **16b** as a colourless solid 3.82 g (80%) (Tables 6 and 7).

2-Benzylsulfanyl-4-phenyl-1-(2-phenyl-2-oxetanylmethyl)-1*H*-imidazole (17)

A mixture containing trimethylsulfoxonium iodide **15** (2.48g, 11.28 mmol), NaH (60% dispersion in mineral oil, 0.43 g, 10.85 mmol), and DMF (14 mL) was stirred under N_2 at r.t. for 1h. Then, the mixture was heated to 90 ºC and **3b** (1.67 g, 4.34 mmol) was added in one portion and stirred at 90ºC for 15 h. DMF was distilled off, and the resulting residue was partitioned between EtOAc (100 mL) and H_2O (80 mL). The organic layer was separated, washed with brine (10 mL), dried ($MgSO_4$), filtered and evaporated to give a residue that was purified by flash chromatography (hexanes/EtOAc, 14:1) to afford **17** as a colourless oil, 1.45 g (81%), which solidified on standing (Tables 6 and 7).

Table 13 MS, IR and NMR Data of 2,3-Dihydroimidazo[2,1-*b*][1,3]oxazole Derivatives **34–39**

Product	MS *m/z* (%)	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
34a	219 ([M+1]$^+$, 100), 218 ([M]$^+$, 17), 217 (26), 215 (25), 207 (43), 205 (32), 203 (34), 197 (26), 195 (28)	2922, 2853, 1572, 1510, 1449, 1386, 1313, 1284, 1232, 1161, 1081, 780, 749, 701, 664	1.55 (s, 3 H), 2.11 (s, 3 H), 3.83 (s, 2 H), 4.25 (s, 2 H), 6.21 (s, 1 H), 7.05 (s, 2H$_{arom}$), 7.53 (s, 1H$_{arom}$)	14.56, 23.44 (q, CH_3), 51.49, 53.66 (t, CH_2), 91.34 (s, C), 106.53 (s, C_{arom}), 120.25, 129.84, 137.94, 139.41 (d, CH_{arom}), 157.54 (s, C_{arom})
34b	343 ([M+1]$^+$, 100), 342 ([M]$^+$, 22), 183 (37), 154 (80), 137 (56), 136 (75)	3428, 3128, 3026, 2976, 1577, 1499, 1441, 1373, 1287, 1229, 1176, 1071, 1018, 743, 696	4.37 (s, 2 H), 4.52, 4.55 (2 d, 2 H, *J* = 15), 6.83 (s, 1H$_{arom}$.), 6.9 (s, 1H$_{arom}$), 6.95 (s, 1H$_{arom}$), 7.2-7.4 (m, 9 H), 7.65–7.70 (m, 2 H)	52.77, 55.3 (t, CH_2), 94.56 (s, C), 106.22, 120.31, 124.32, 124.43, 126.82, 128.49, 129.14, 129.21, 129.44 (d, CH_{arom}), 134.07 (s, C_{arom}), 137.91 (d, CH_{arom}), 138.41, 143.11, 157.99 (s, C_{arom})
35a	220 ([M+1]$^+$, 100), 219 ([M]$^+$, 20), 217 (11), 215 (12)	3117, 2922, 2854, 1654, 1572, 1509, 1446, 1387, 1356, 1307, 1275, 1209, 1138, 1016, 959, 904, 786, 750, 701	1.59 (s, 3 H), 2.08 (d, 3 H, *JJ* = 1.1), 3.82 (d, 1 H, *J* = 9.6), 4.25 (d, 1 H, *J* = 9.6), 4.51, 4.55 (2 d, 2 H, *J* = 14.6), 6.18 (d, 1 H, *J* = 1.1), 7.9 (s, 1H$_{arom}$), 8.22 (s, 1H$_{arom}$).	14.52, 23.64 (q, CH_3), 51.50, 55.72 (t, CH_2), 90.75 (s, C), 106.54, 139.26 (s, C_{arom}), 144.60, 151.92, 157.39 (d, CH_{arom})
35b	344 ([M+1]$^+$, 100), 343 ([M]$^+$, 32), 185 (21), 184 (47), 136 (30), 105 (38)	3405, 3123, 3061, 1604, 1577, 1505, 1445, 1374, 1328, 1274, 1137, 1024, 1001, 786, 678, 650	4.34 (d, 1 H, *J* = 9.8), 4.74 (s, 2 H), 4.9 (d, 1 H, *J* = 9.8), 6.7 (s, 1 H), 7.90–7.20 (m, 10H$_{arom}$), 7.91 (s, 1H$_{arom}$), 8.05 (s, 1H$_{arom}$)	52.36, 56.94 (t, CH_2), 93.74 (s, C), 106.2, 124.32, 124.41, 126.7, 129.06, 129.16, 129.27 (d, CH_{arom}), 134.05, 138.33, 142.86 (s, C_{arom}), 144.8, 151.99 (d, CH_{arom}), 157.79 (s, C_{arom})
36	345 ([M+1]$^+$, 12), 344 ([M]$^+$, 5), 154 (100), 138 (44), 137 (87), 136 (97), 107 (40), 105 (32)	3047, 2970, 2908, 1582, 1481, 1432, 1311, 1186, 1153, 1103, 996, 831, 748, 711, 693	4.46, 4.50 (2 d, 2 H, *J* = 10), 5.32, 5.40 (2 d, 2 H, *J* = 15), 6.82 (s, 1H$_{arom}$), 7.25–7.60 (m, 10H$_{arom}$), 8.74 (s, 1H$_{arom}$)	52.72, 55.44 (t, CH_2), 93.42 (s, C), 106.4, 124.29, 124.37, 126.98, 128.5, 129.46, 129.71 (d, CH_{arom}), 133.73, 137.21 (s, C_{arom}), 143.14 (d, CH_{arom}), 143.65, 157.42 (s, C_{arom})
37	345 ([M+1]$^+$, 100), 344 ([M]$^+$, 69), 275 (34), 155 (37), 154 (97), 137 (84), 136 (98)	3135, 3062, 3006, 2959, 1694, 1653, 1584, 1502, 1450, 1410, 1377, 1326, 1306, 1283, 1126, 1023, 885, 748, 702	4.45 (d, 1 H, *J* = 10), 5.02 (d, 1 H, *J* = 10), 5.25, 5.35 (2 d, 2 H, *J* = 15), 6.81 (s, 1H$_{arom}$), 7.25–7.65 (m, 10H$_{arom}$), 8.45 (s, 1H$_{arom}$)	50.90, 53.86 (t, CH_2), 93.11 (s, C), 106.05, 124.99, 125.81, 127.98, 128.43, 129.27, 129.49 (d, CH_{arom}), 134.06, 137.84, 143.02 (s, C_{arom}), 153.05 (d, CH_{arom}), 157.98 (s, C_{arom})
38	394 ([M+1]$^+$, 10), 393 ([M]$^+$, 5), 307 (15), 155 (30), 154 (100)	3063, 3029, 2978, 2931, 1682, 1586, 1497, 1448, 1374, 1274, 1173, 1103, 1020, 1003, 886, 738, 701	4.42 (d, 1 H, *J* = 9.8), 5.02 (d, 1 H, *J* = 9.8) 5.28, 5.37 (2 d, 2 H, *J* = 15.4) 6.7 (s, 1H$_{arom}$), 7.2–8.0 (m, 14H$_{arom}$)	52.32, 55.85 (t, CH_2), 94.96 (s, C), 106.17, 110.06, 119.64, 124.28, 124.53, 126.63, 128.34, 129.18, 129.28 (d, CH_{arom}), 133.76, 134.05, 138.63, 142.66, 145.57, 157.7 (s, C_{arom}).
39	394 ([M+1]$^+$, 6), 275 (20), 149 (100), 133 (30), 132 (20)	3073, 3030, 2959,, 1692, 1580, 1502, 1454, 1378, 1330, 1280, 1173, 1123, 1020, 1013, 896, 758, 701, 693	5.75 (s, 2 H), 5.83 (s, 2 H), 7.208.0 (m, 15H$_{arom}$)	61.60, 64.95 (t, CH_2), 93.48 (s, C), 104.24 (d, CH_{arom}), 107.15 (s, C_{arom}), 119.64 (d, CH $_{arom}$), 119.98 (s, C_{arom}), 122.64, 126.34, 128.88, 129.10, 129.23, 129.28 (d, CH_{arom}), 135.11, 137.36, 143.66, 152.80 (s, C_{arom})

Epoxide Ring Opening Reaction; Azolyl Derivatives 22–27; General Procedure

To a mixture of the appropriate epoxide **16a**,**b** (1.13 mmol) and the different azoles **18–21** (4.52 mmol) in DMF (5.6 mL) was added KOBu-*t* (0.32 g, 2.82 mmol) at r.t. The resulting mixture was stirred under N_2 at the temperature and time specified in Table 8. DMF was distilled off and the residue was partitioned between EtOAc (50 mL) and H_2O (50 mL). The organic phase was separated, washed with brine (15 mL), dried ($MgSO_4$), filtered and concentrated. The resulting residue was purified by flash chromatography (hexanes/EtOAc, 9:1 to 100% EtOAc as eluent) (Tables 8 and 9).

Oxidation of 22–27 to Sulfones 28–33; General Procedure

To a cooled, (0 ºC) solution of the corresponding alcohols **22–27** (0.6 mmol) in CH_2Cl_2 (6 mL) was added *m*-CPBA (3.99 g, 1.32 mmol) in small portions. The mixture was stirred overnight as the temperature was increased from 0 ºC to r.t. and then diluted with EtOAc (50 mL), washed with aq satd $NaHCO_3$ solution (2 × 10

mL) and brine (10 mL). The separated organic layer was dried ($MgSO_4$), filtered and concentrated. The resulting crude material was purified by flash chromatography (hexanes/EtOAc, 4:1 to 100% EtOAc as eluent) (Tables 10 and 11).

Intramolecular *ipso*-Substitution; 2-Azolyl-2,3-dihydroimidazo[2,1*b*][1,3]oxazole Derivatives 34–39; General Procedure

To a solution of the appropriate alcohol sulfones **28–33** (0.4 mmol) in anhyd THF (1.5 mL) was added NaH (60% dispersion in mineral oil, 17.6 mg, 0.44 mmol) in one portion at r.t. H_2 gas evolution began immediately. The mixture was stirred at r.t. under N_2 for the time specified in Table 12. The solvent was removed in vacuo and the residue was partitioned between EtOAc (50 mL) and H_2O (20 mL). The organic phase was separated, washed with brine (15 mL), dried ($MgSO_4$), filtered, and the filtrate was concentrated. The resulting residue was purified by flash chromatography (hexanes/EtOAc, 9:1 to 100% EtOAc as eluent) (Tables 12 and 13).

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