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N-Trihalomethyl derivatives of benzimidazole, benzotriazole and indazole

Lev M. Yagupolskii*, Dmitrij V. Fedyuk, Kirill I. Petko, Valeriya I. Troitskaya, Valentina I. Rudyk, Vitalij V. Rudyuk

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 5 Murmanskaya Street, Kiev 02094, Ukraine

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Abstract

1-Chlorodifluoromethyl- and 1-trifluoromethyl-substituted 2-methylbenzimidazoles and benzotriazoles were obtained by chlorination of the corresponding methyl 1-azoledithiocarboxylates and subsequent fluorination of the resulting 1-trichloromethyl derivatives. The condensation of *N*-sodium salts of 2-alkylbenzimidazoles and indazole with CF_2Br_2 was shown to afford the corresponding 1-bromodifluoromethylated compounds.

Keywords: Heterocycles; Dithiocarboxylates; Trihalomethylation; Azoles; Triazoles

1. Introduction

N-Trihalomethyl-substituted derivatives of nitrogen heterocyclic compounds are poorly known [1] and for benzimidazole, benzotriazole and indazole they have not been reported at all.

We have synthesized various *N*-trihalomethyl derivatives of the indicated heterocyclic bases which turned out to be useful intermediates for preparation of drug products, pesticides and dyestuffs [2,3].

2. Results and discussion

We have proposed a suitable method for substitution of hydrogen at the nitrogen atom of the heterocycles with trihalomethyl groups by the reaction of their *N*-sodium salts with carbon disulfide and methyl iodide followed by chlorination of the (methylthio)thiocarbonyl function and fluorination of the resulting trichloromethyl group (Scheme 1).

Compound **1** was previously described [4]. On chlorination, it affords the hydrochloride salt **2** in quantitative yield. The salt is storage-stable in the absence of moisture. In water it hydrolyzes to give, after treatment with ammonia, 2-methylbenzimidazole.

2-Methyl-1-trichloromethylbenzimidazole **3** was obtained by treatment of the salt **2** with triethylamine in THF. The compound is unstable in storage and easily hydrolyzed. On heating at reflux with SbF_3 in dioxane, **3** is transformed into 1-chlorodifluoromethyl-2-methylbenzimidazole **4**, a liquid stable in air and distillable in vacuo (Scheme 2).

The attempts at substituting all the chlorine atoms in **3** or **4** with fluorine by heating with SbF_3 in the absence or in the presence of catalysts ($SbCl_5$ or Br_2) were unsuccessful and led to tarring.

On treating with anhydrous HF at 20°C, the trichloromethyl group in **2** remains untouched. The resulting less stable hydrofluoride salt loses hydrogen fluoride in vacuo to give the base **3**.

The *N*-sodium derivative of benzotriazole is dithiocarboxylated with carbon disulfide at −10 to 0°C. The reaction is inhibited by water even in trace amounts. The resulting methyl dithiocarboxylate **5** is converted into 1-trichloromethylbenzotriazole **6** in good yield on treatment with chlorine in CCl_4. Since benzotriazole is a weaker base compared to benzimidazole, it gives on chlorination the free base **6** rather than the hydrochloride salt. On heating with anhydrous hydrogen fluoride, compound **6** converts into 1-trifluoromethylbenzotriazole **7**, a storage-stable liquid resistant to hydrolysis (Scheme 3).

* Corresponding author. Tel.: +38-044-559-03-49; fax: +38-044-573-26-43.
E-mail address: lev@fluor-ukr.kiev.ua (L.M. Yagupolskii).

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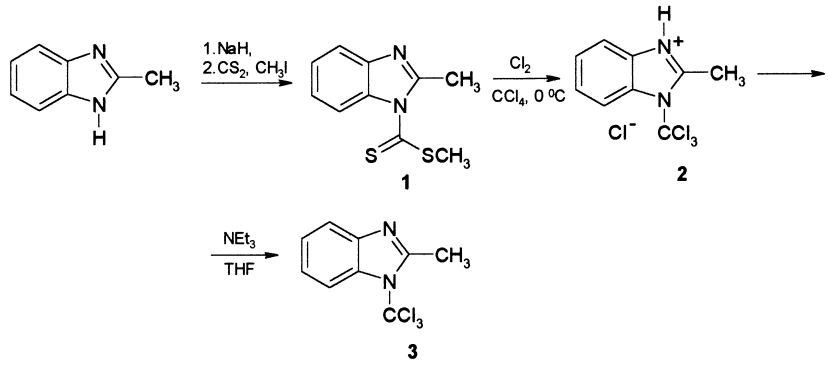
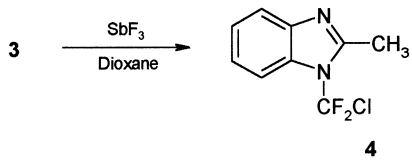


Scheme 1.



Scheme 2.

The interaction of the *N*-sodium derivative of indazole with carbon disulfide and methyl iodide under the same conditions leads to a 1:3 mixture of methyl 1- and 2-indazoledithiocarboxylates **8** and **9** in good yield. The isomers were separated by chromatography on silica gel (Scheme 4).

The chlorination of these compounds in CCl_4 at 0°C gives a complex mixture of unidentified products.

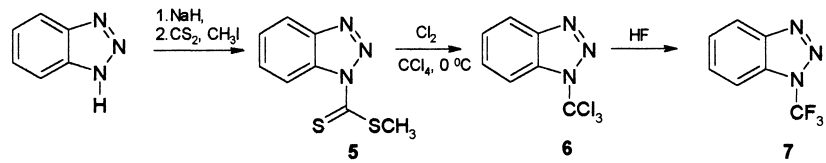
We used the same approach to prepare *N*-trichloromethylated carbazole. The reaction of its *N*-sodium derivative with carbon disulfide is less sensitive to moisture and temperature compared to the systems considered above. Sodium hydride can be replaced with sodium hydroxide, but the yield decreases from 90 to 30%. With other heterocycles sodium hydroxide is totally ineffective in the dithiocarboxylation reaction.

On chlorination, methyl 1-carbazoledithiocarboxylate **10** gives a mixture of products from which 3,3-dichloro-1-trichloromethyl-2,3-dihydrocarbazole **11** was isolated as crystals in 17% yield. After heating with 10% H_2SO_4, **11** was converted to the previously described 3-hydroxycarbazole [5] (Scheme 5).

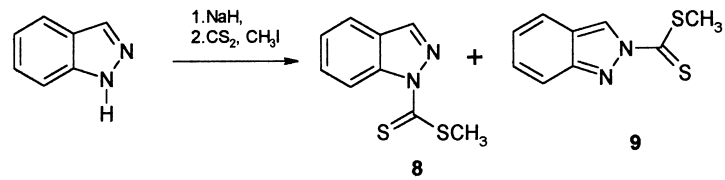
The structure of Compound **11** was confirmed by chemical analysis and ^{1}H NMR spectrum which, in addition to signals of the aromatic protons, displayed the signals of two protons in the 2-position (AB-system) and two doublets of the protons at the C^4=C^5 double bond.

One further approach to *N*-trihalomethyl derivatives of the indicated heterocyclic compounds was employed, that is, the condensation of their sodium salts with CF_2Br_2. Only one example of this reaction with 4-ethoxycarbonylpyrazole has been reported to date [1].

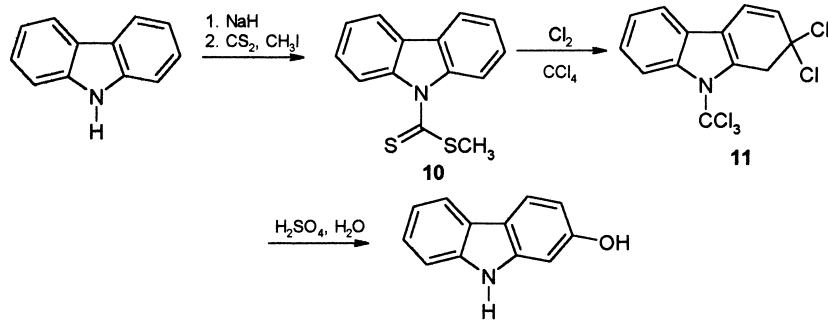
It was found that 2-methyl-, 2-propyl-, 2-benzylbenzimidazole and 2-methylnaphtho[2,3-*d*]imidazole give in this reaction the corresponding 1-bromodifluoromethylated benzimidazoles and naphthimidazole. The reaction of benzimidazoles having two electron-donor methoxy groups in positions 5 and 6 or two ethoxy substituents in positions 4 and 7 is accompanied by tarring and no individual product can be isolated from the reaction mixture (Scheme 6).



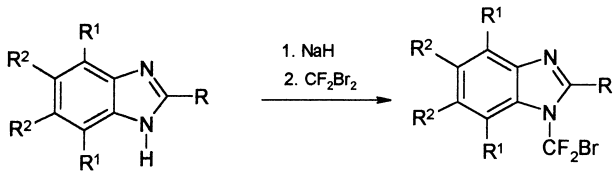
Scheme 3.



Scheme 4.

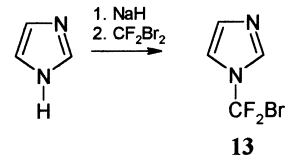


Scheme 5.



R= CH_3, R^1= R^2= H (**a**)
R= C_3H_7, R^1= R^2= H (**b**)
R= $CH_2C_6H_5$, R^1= R^2= H (**c**)
R= CH_3, R^1= H, R^2+ R^2= -CH=CH-CH=CH- (**d**)
R= CH_3, R^1= H, R^2= Cl (**e**)
R= CH_3, R^1= R^2= F (**f**)

Scheme 6.



Scheme 7.

The halogen substituents in the benzene ring of benzimidazole do not interfere with the reaction. Thus, 1-bromodifluoromethyl-5,6-dichloro-2-methylbenzimidazole **12e** and 1-bromodifluoromethyl-4,5,6,7-tetrafluoro-2-methylbenzimidazole **12f** were obtained in high yields. The reaction is accelerated in the presence of zinc dust.

The products **12** are crystallized from hexane as low melting solids. Some of them (**12a**, **b** and **f**) are distilled in vacuo.

We were able to prepare 1-bromodifluoromethylimidazole (**13**), but in small yield (9%), by conducting the condensation reaction in acetonitrile at a low concentration of the reagents. The sodium salt of imidazole is only difficultly soluble in this solvent (Scheme 7).

1-Bromodifluoromethyl-2-methylbenzimidazole was converted into the 1-trifluoromethyl derivatives 14 by refluxing with tetramethylammonium fluoride in anhydrous monoglyme. The reaction is accompanied by the formation of the 1-difluoromethylated product in significant amount which was separated by fractional distillation in vacuo (Scheme 8).

In contrast to **12a**, the substitution of the bromine for fluorine in 1-bromodifluoromethyl-4-dimethylaminopyridinium bromide with tetramethylammonium fluoride proceeds at room temperature in a dichloromethane solution [6].

Compound **12a** can be converted into **14** also by heating with SbF_3, but the end product is difficult to isolate from the reaction mixture.

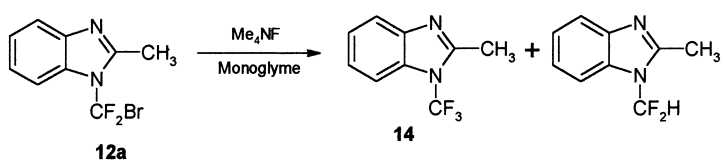
Compounds **12a** and **14** were transformed into tertiary salts **15** by treatment with methyl iodide and $AgBF_4$ (Scheme 9).

The sodium salt of benzotriazole does not react with dibromodifluoromethane under the indicated conditions. The reaction of more nucleophilic sodium derivatives of carbazole or alkoxybenzimidazoles with CF_2Br_2 is accompanied by heavy tarring.

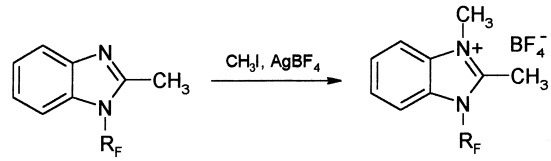
The sodium salt of indazole interacts with CF_2Br_2 to afford a 1:0.75 mixture of 1- and 2-bromodifluoromethylindazole **16** and **17** in about 60% overall yield. The isomers were not separated (Scheme 10).

1-Bromodifluoromethylbenzimidazoles react with aromatic aldehydes in the presence of tetrakis(dimethylamino)ethylene (TDAE) to form compounds **18** of potential interest for medicinal chemistry [7,8] (Scheme 11).

The difluoromethylene group in **18** is stable and is not hydrolyzed with dilute acids and bases at room temperature.



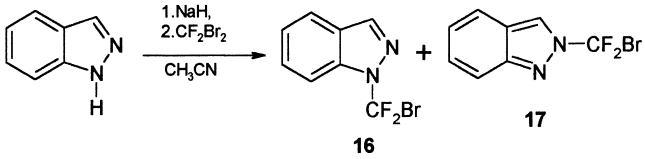
Scheme 8.



12a, 14 **15a-b**

R_F= CF_2Br (**a**), CF_3 (**b**)

Scheme 9.



Scheme 10.

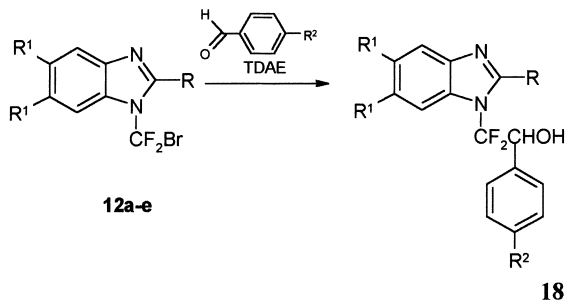
3. Experimental

3.1. General

Boiling and melting points are uncorrected. ^{1}H NMR: Varian VXR-300 (300 MHz) (TMS as internal standards). ^{19}F NMR: Varian VXR–300 (288 MHz) ($CFCl_3$ as internal standard). Mass spectra were obtained on a MX-1321 mass spectrometer at 70 eV.

3.2. 2-Methyl-1-trichloromethylbenzimidazole hydrochloride (2)

Through a stirred and cooled (−5°C) solution of methyl 2-methylbenzimidazole-1-dithiocarboxylate (11.6 g, 5.2 mmol) in CCl_4 (800 ml) was bubbled dry Cl_2 for 2 h at a temperature below 0°C. Then the mixture was warmed up to room temperature over 2 h. The precipitate was filtered under an atmosphere of dry argon, washed with anhydrous CCl_4 (3 × 100 ml), and dried in vacuo to afford 15 g (100%) of **2** as colorless crystals, mp 185–189°C. Found: Cl 48.90, calculated for $C_9H_8Cl_4N_2$:Cl 49.65%, Compound **2** was used without purification.



12a-e **18**

R= CH_3, C_3H_7, $CH_2C_6H_5$;
R^1= H, Cl; R^1+ R^1= -CH=CH-CH=CH- ;
R^2= H, F, Br, OCH_3

Scheme 11.

3.3. 2-Methyl-1-trichloromethylbenzimidazole (3)

A mixture of **2** (5 g, 18 mmol) and Et_3N (2.6 ml, 19.8 mmol) in dry THF (50 ml) was refluxed for 5 h. The solvent was evaporated under reduced pressure and the residue was extracted with hot hexane. The extract was evaporated to leave a crude product which was purified by crystallization from hexane to give 3.6 g (80%) of **3** as light yellow crystals, mp 83−84°C, ^{1}H NMR (acetone-D_6): $\delta = 2.58$ (s, 3H); 6.83–8.00 (m, 4H). Found: Cl 42.60, calculated for $C_9H_7Cl_3N_2$: Cl 42.62%.

3.4. 1-Chlorodifluoromethyl-2-methylbenzimidazole (4)

To a solution of **3** (1 g, 4 mmol) in dry dioxane (50 ml) was added SbF_3 (1.08 g, 6 mmol). The mixture was heated under reflux for 6 h and evaporated under reduced pressure. The residue was extracted with hexane. The extract was concentrated in vacuo and distilled to give 0.5 g (58%) of **4** as a colorless liquid, bp 68–70°C (0.1 Torr), $n_D^{18} = 1.5372$, ^{1}H NMR ($CDCl_3$): $\delta = 2.77$ (s, 3H); 7.3–7.8 (m, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -33.96$ (s, CF_2Cl). Found: Cl 16.15, calculated for $C_9H_7ClF_2N_2$: Cl 16.37%.

3.5. General procedure for synthesis of methyl azoledithiocarboxylates

To a suspension of sodium hydride (60%, 1 g, 25 mmol) in anhydrous DMF (10 ml) was added under the inert atmosphere at −10°C a solution of the appropriate N–H azole (20 mmol) in dry DMF (10 ml). The mixture was stirred for 40 min at 0°C and cooled to −10°C in an argon stream. CS_2 (2 ml, 2.5 g, 35 mmol) was added dropwise and the resulting red solution was stirred for 20 min at 0°C and cooled again to −10°C. Methyl iodide (2 ml, 4.1 g, 27 mmol) was added in one portion with vigorous stirring. The color changed from red to yellow. The temperature was allowed to rise to +20°C and after 5 min the mixture was poured into water (150 ml).

3.6. Methyl 1-benzotriazoledithiocarboxylate (5)

The yellow crystals obtained, were filtered off, washed with water, dried at 30°C, and recrystallized from CCl_4. Yield 60%, mp 98–100°C, ^{1}H NMR ($CDCl_3$): $\delta = 2.57$ (s, 3H); 7.5–7.7 (m, 2H); 8.1–8.2 (m, 1H); 8.7–8.8 (m, 1H). Found: S 30.54, calculated for $C_8H_7N_3S_2$: S 30.64%.

3.7. Methyl 1- and 2-indazoledithiocarboxylates (8, 9)

The crystals were filtered off, washed with water, dried at 30°C and chromatographed on SiO_2 (MN-Kieselgel 60, eluent CCl_4/hexane 1:1).

8: Yellow crystals, $R_f = 0.25$, yield 17%, mp 88–89°C (from hexane), ^{1}H NMR ($CDCl_3$): $\delta = 2.67$ (s, 3H); 7.4–7.7 (m, 2H); 7.9–8.0 (m, 1H); 8.42 (s, 1H); 9.1–9.2 (m, 1H). Found S 30.42, calculated for $C_9H_8N_2S_2$:S 30.79%.

9: Yellow crystals, $R_f = 0.15$, yield 52%, mp 113–114°C (from hexane), ^{1}H NMR ($CDCl_3$): $\delta = 2.80$ (s, 3H); 7.1–7.2 (m, 1H); 7.4–7.5 (m, 1H); 7.6–7.7 (m, 1H); 7.9–8.0 (m, 1H); 9.25 (s, 1H). Found: S 30.37, calculated for $C_9H_8N_2S_2$: S 30.79%.

3.8. Methyl 1-carbazoledithiocarboxylate (**10**)

The mixture of crystals and oil was extracted with ether (3 × 30 ml), washed with water (2 × 30 ml), and dried ($CaCl_2$, 12 h). The solvent was evaporated, the product was crystallized from hexane, yield 87%, mp 55–57°C, ^{1}H NMR ($CDCl_3$): $\delta = 2.85$ (s, 3H); 7.3–7.5 (m, 4H); 8.0–8.1 (m, 2H); 8,5–8.6 (m, 2H). Found: S 25.14, calculated for $C_{14}H_{11}NS_2$: S 24.92%

3.9. 1-Trichloromethylbenzotriazole (**6**)

Chlorine-gas was bubbled through a suspension of **5** (6.3 g, 30 mmol) in CCl_4 (50 ml) at 0°C, with stirring, until a clear solution was formed. After stirring for 12 h at 20°C, the solvent was evaporated in vacuo, the residue was evacuated (2 h, 0.01 Torr), and crystallized from hexane to give 5.72 g (81%) of **6**, as colorless crystals, mp 55–57°C, ^{1}H NMR ($CDCl_3$): $\delta = 7.55-7.60$ (m, 1H); 7.65–7.70 (m, 1H); 8.05–8.10 (m, 1H); 8.10–8.15 (m, 1H). Found: Cl 44.20, calculated for $C_7H_4Cl_3N_3$: Cl 44.97%.

3.10. 1-Trifluoromethylbenzotriazole (**7**)

Compound **6** (2 g, 8.5 mmol) was placed in a platinum cylinder in anhydrous HF (3 ml). The cylinder was held in a stainless steel bomb at 50°C for 5 h. The volative products were evaporated and the residue was extracted with hexane (20 ml). The extract was washed with 1 M aq K_2CO_3 (2 × 20 ml) and water (2 × 20 ml). The organic layer was dried over $CaCl_2$ for 10 h, evaporated under reduced pressure and the residue was distilled in vacuo. A drop of pyridine was added to the distillate (1.07 g, 77%) and within 2 h, the product was distilled once again to give 0.82 g (52%) of pure **7** as a colorless stable liquid, bp 77–78°C (15 Torr), ^{1}H NMR ($CDCl_3$): $\delta = 7.71-7.78$ (m, 1H); 7.89–7.95 (m, 1H); 7.98–8.02 (m, 1H); 8.28–8.34 (m, 1H). ^{19}F NMR ($CDCl_3$): $\delta = -57.68$ (s, CF_3). Found: C 44.76; H 2.76; N 22.31, calculated for $C_7H_4F_3N_3$: C 44.93; H 2.15; N 22.46%.

3.11. 3,3-Dichloro-1-trichloromethyl-2,3-dihydrocarbazole (**11**)

Chlorine-gas was bubbled through a solution of **10** (1.3 g, 5 mmol) in dry CCl_4 (10 ml) at 0°C for 2 h. The reaction mixture was allowed to stand for 12 h at 20°C, the solvent was evaporated in vacuo and the residue was evacuated (0.01 Torr, 30°C, 2 h). The oily mixture of the chlorination products was dissolved in hexane (5 ml) and held at 0°C for 24 h. The white precipitate was filtered off and washed with hexane to give 0.3 g (17%) of **11**, mp 167–170°C, ^{1}H NMR ($CDCl_3$): $\delta = 4.95$ (double, AB-system, 2H); 5.97 (d, $J = 5$ Hz, 1H); 6.37 (d, $J = 5$ Hz, 1H); 7.35–7.55 (m, 2H); 7.61–7.68 (m, 1H); 8.19–8.26 (m, 1H). Found: Cl 50.24, calculated for $C_{13}H_8Cl_5N$: Cl 49.87%.

3.12. General procedure for synthesis 1-bromodifluoromethyl-2-alkylbenz- and naphthimidazoles (**12a–f**)

To a stirred solution of 2-alkylbenzimidazole (20 mmol) in 50 ml of anhydrous acetonitrile cooled to −15°C, was added zinc dust (0.1 g, 1.5 mmol) under an argon atmosphere, followed by sodium hydride (0.53 g, 22 mmol) added in portions. After the addition, the mixture was stirred at −10 to −5°C for 3 h, cooled to −15°C and to a stirred solution dibromodifluoromethane (2.74 ml, 30 mmol) was added dropwise. The mixture was warmed to room temperature over 2 h and stirred for 14 h. The solvent was evaporated under reduced pressure and the residue was extracted with hot hexane (3 × 50 ml). The exstract was filtered and evaporated to leave a brown oil, which was purified by vacuum distillation or by crystallization from hexane.

3.13. 1-Bromodifluoromethyl-2-methylbenzimidazole (**12a**)

Yield 76%, mp 29–30°C, bp 80–82°C (0.01 Torr), ^{1}H NMR ($CDCl_3$): $\delta = 2.77$ (s, 3H); 7.3–7.9 (m, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -27.76$ (s, –CF_2Br). Found: C 41.88; H 2.56; N 10.41, calculated for $C_9H_7BrF_2N_2$: C 41.41; H 2.70; N 10.73%.

3.14. 1-Bromodifluoromethyl-2-propylbenzimidazole (**12b**)

Yield 80%, mp 44–45°C, bp 102–103°C (0.01 Torr), ^{1}H NMR (acetone-D_6): $\delta = 0.98$ (t, 3H); 1.79 (spt, 2H); 2.28 (t, 2H); 7.2–7.9 (m, 4H). ^{19}F NMR (acetone-D_6): $\delta = -27.51$ (s, –CF_2Br). *m/z* 290 ($M^+ + 1$, 9.7); 288 ($M^+ - 1$, 9.9); 260 (M^+–C_2H_5, 15.2); 209 (M^+–Br, 100.0); 159 (M^+–CF_2Br, 7.7); 43 ($C_3H_7^+$, 2.5).

3.15. 1-Bromodifluoromethyl-2-benzylbenzimidazole (**12c**)

Yield 72%, mp 44–45°C, ^{1}H NMR ($CDCl_3$): $\delta = 4.35$ (s, 2H); 7.1–7.9 (m, 9H). ^{19}F NMR ($CDCl_3$): $\delta = -27.24$ (s, –CF_2Br). *m/z* 338 ($M^+ + 1$, 16.0); 336 ($M^+ - 1$, 15.9); 257 (M^+–Br, 73.1); 207 (M^+–CF_2Br, 3.2); 91 ($PhCH_2^+$, 100.0).

3.16. 1-Bromodifluoromethyl-2-methylnaphth[2,3-d]imidazole (**12d**)

Yield 81%, mp 93–95°C, ^{1}H NMR ($CDCl_3$): δ=2.80 (t, $J_{H-F} = 3$ Hz, 3H); 7.4–8.2 (m, 6H). ^{19}F NMR ($CDCl_3$): $\delta = -26.81$ (s, $-CF_2Br$). *m/z* 312 ($M^+ + 1$, 26.7); 310 ($M^+ - 1$, 26.3); 232 (M^+–Br, 47.0); 231 (M^+−1–Br, 100.0); 181 (M^+–CF_2Br, 5.4).

3.17. 1-Bromodifluoromethyl-5,6-dichloro-2-methylbenzimidazole (**12e**)

Yield 70%, mp 76−78°C, ^{1}H NMR ($CDCl_3$): $\delta = 2.66$ (t, $J_{H-F} = 3$ Hz, 3H); 7.61 (s, 1H); 7.71 (s, 1H). ^{19}F NMR ($CDCl_3$): $\delta = -28.04$ (s, CF_2Br). *m/z* 330 (M^+, 17.1); 295 (M^+–Cl, 1.4); 261 ($M^+ + 1$–Cl–Cl, 100.0); 251 ($M^+ + 1$–Br, 47.7); 250 (M^+–Br, 14.0); 200 (M^+–CF_2Br, 36.5).

3.18. 1-Bromodifluoromethyl-4,5,6,7-tetrafluoro-2-methylbenzimidazole (**12f**)

Yield 86%, bp 94–95°C (0.05 Torr), ^{1}H NMR ($CDCl_3$): $\delta = 2.73$ (t, $J_{H-F} = 4$ Hz, 3H). ^{19}F NMR ($CDCl_3$): $\delta = -161.8-161.5$ (m, 1F); −160.0–159.7 (m, 1F); −151.6–151.0 (m, 1F); −153.66 (t, $J = 1.4$ Hz, 1F); −28.21 (d, $J_{H-F} = 4$ Hz, CF_2Br). *m/z* 333 (M^+, 16.2); 252 (M^+−1–Br, 100.0); 253 (M^+–Br, 11.6); 203 (M^+–CF_2Br, 12.0); 79 (Br, 1.6).

3.19. 1-Bromodifluoromethylimidazole (**13**)

To a solution of imidazol (1 g, 15 mmol) in dry acetonitrile (100 ml), was added sodium hydride (60%, 0.6 g, 15 mmol). The reaction mixture was stirred for 1 h at room temperature. After cooling to −15°C, zinc powder (0.1 g, 1.5 mmol) was added and, over 10 min CF_2Br_2 (4.2 g, 20 mmol) was added dropwise. The mixture was stirred for 4 h at room temperature and evaporated in vacuo at 0°C. The residue was extracted with hot hexane. The residue after evaporation of the extractant at atmospheric pressure, was distilled in vacuo to give 0.23 g (9%) of **13**. ^{19}F NMR ($CDCl_3$): $\delta = -28.80$ (s, CF_2Br). Found: N 14.70, calculated for $C_4H_3BrF_2N_2$: N 14.22%.

3.20. 2-Methyl-1-trifluoromethylbenzimidazole (**14**)

A mixture of **12a** (5 g, 19 mmol) and tetramethylammonium fluoride (3.6 g, 38 mmol) in monoglyme (30 ml) was refluxed for 5 h and evaporated under reduced pressure. The residue was extracted with hexane. Hexane was removed in vacuo. The mixture of 1-trifluoromethyl- and 1-difluoromethyl-2-methylbenzimidazoles, obtained after evaporation of the extract was separated by fractional distillation to give 1.5 g (40%) of **14** and 1.2 g (35%) of 1-difluoromethyl-2-methylbenzimidazole; b.p. 135–137°C/12 Torr, ([9] 120–122°C/4 Torr).

14: bp 80–82°C (12 Torr), ^{1}H NMR ($CDCl_3$): $\delta = 2.74$ (s, 3H); 7.3–7.8 (m, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -57.97$ (s, CF_3). Found: C 53.88; H 3.46; N 13.44, calculated for $C_9H_7F_3N_2$: C 54.01; H 3.52; N 14.00%.

3.21. 2,3-Dimethyl-1-trihalomethylbenzimidazolium tetrafluoroborates (**15a**–**b**)

To a stirred solution of $AgBF_4$ (1 g, 5 mmol) in dichloroethane (2 ml) was added 2-methyl-1-trihalomethylbenzimidazole **12a** or **14** (1 mmol) in dichloroethane (1 ml) and CH_3I (0.6 ml, 1 mmol). The mixture was stirred at room temperature for 6 h, then AgI was filtered off and washed with dichloroethane (1 ml). The combined filtrate was concentrated in vacuo and triturated with diethyl ether to afford **15a** or **15b**, respectively, as white powders.

3.22. 1-Bromodifluoromethyl-2,3-dimethylbenzimidazolium tetrafluoroborate (**15a**)

Yield 0.160 g (44%), mp 225–227°C. ^{19}F NMR (acetone-D_6): $\delta = -149.96$ (s, BF_4^-); −34.07 (s, CF_2Br). Found C: 33.87; H 2.44; N 7.34, calculated for $C_{10}H_{10}BBrF_6N_2$: C 33.09; H 2.76; N 7.72%.

3.23. 1-Trifluoromethyl-2,3-dimethylbenzimidazolium tetrafluoroborate (**15b**)

Yield 0.241 g (80%), mp 167–169°C. ^{19}F NMR (acetone-D_6): $\delta = -149.54$ (s, BF_4^-), −54.60 (s, CF_3). Found: C 40.66; H 3.58; N 9.13, calculated for $C_{10}H_{10}BF_7N_2$: C 40.06; H 3.31; N 9.27%.

3.24. 1- and 2-Bromodifluoromethylindazoles (**16**, **17**)

To a solution of indazole (1.18 g, 10 mmol) in dry acetonitrile (15 ml) was added sodium hydride (60%, 0.6 g, 15 mmol) at 0°C. After stirring for 1 h the reaction mixture was cooled to −15°C, and Zn powder (0.1 g, 1.5 mmol) was added. After 10 min CF_2Br_2 (3.1 g, 15 mmol) was added dropwise and the mixture was stirred for 1 h at 0°C and 2 h at 20–30°C. The solvent was evaporated in vacuo and the residue was extracted with hot hexane. The extract was filtered, evaporated under reduced pressure and the residue was distilled in vacuo to give 1.48 g (61%) of the mixture of isomers **16** and **17**, bp 69–77°C (0.1 Torr); 125–135°C (20 Torr), ^{1}H NMR ($CDCl_3$): $\delta = 7.2-7.9$ (m, 4H); 8.27 and 8.37 (s, 1-isomer and s, 2-isomer in the ratio 1:0.75, 1H). ^{19}F NMR ($CDCl_3$): $\delta = -33.37$ and −31.38 (s, 1-isomer and s, 2-isomer in the ratio 1:0.75, CF_2Br). Found: C 39.21; H 2.45, calculated for $C_8H_5BrF_2N_2$: C 38.90; H 2.04%.

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