Introducing chirality in halogenated 3-arylsydnones and their corresponding 1-arylpyrazoles obtained by 1,3-dipolar cycloaddition†

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New 1-arylpyrazoles substituted with halogen atoms (Br, I) were synthesized from the corresponding sydnones by 1,3-dipolar cycloaddition. By introduction of a prochiral group such as isopropyl, in the ortho position of the benzene ring, in the starting phenylglycine the rotamers caused by the hindered rotation between the phenyl and the heterocyclic ring were detected by NMR spectroscopy for 1-arylpyrazoles and for the first time for 3-arylsydnones. The N-nitrosophenyglycines present E–Z stereoisomerism due to the partial C–N double bond character. All the new compounds were structurally characterized by NMR spectroscopy and confirmed by X-ray crystallography. The crystal structures of N-nitrosophenyglycines 2c and of the sydnone 3c present similar Br···Br type II halogen contacts.

Introduction

Mesionic compounds are versatile intermediates in the synthesis of bioactive pyrrole and pyrazole derivatives. Sydnones in particular, have been employed as 1,3-dipoles in obtaining N-arylpyrazoles by 1,3-dipolar cycloaddition reaction. N-Arylpyrazole derivatives have been shown to possess antithrombotic, anticancer, parathyroid dysfunction, antibiofilm, and antipain activity which makes them valuable targets for the pharmaceutical field.

Chirality is important in drug-target recognition processes and atropisomerism could be a useful tool for generating chiral drugs by blocking the free rotation about a bond axis through steric factors. The most studied systems are biaryl. The structure of N-arylpyrazoles implies the existence of axial chirality when the right substituents are grafting on their framework. By fine tuning of the substituents on the aryl or pyrazole rings the free rotation about the bond axis between the two rings could be hindered and thus leading to the existence of the two rotational isomers. Depending on the value for the energy of the free rotation about the two rings, the enantiomers can be detected by NMR spectroscopy or even the physical separation of the conformational isomers could be achieved. However, even in the case the free energy of rotation is smaller and the atropisomers are not easily separable in normal conditions but instead rotamers are detectable, the conformational analysis is still an important thing to be investigated under de drug-target interaction paradigm, for example.

Herein we present the synthesis of new halogenated 1-arylpyrazoles bearing in mind that halogen atoms could enhance their bioavailability due to halogen bonding formation with specific nucleophilic sites in proteins. The introduction of axial chirality in the new 1-arylpyrazoles was pursued and investigated during the synthesis steps starting with the N-nitrosodervatives and sydnone intermediates. The structures of the compounds were confirmed by X-ray single crystal diffraction analysis.

Results and discussions

Synthesis and characterization of N-nitrosophenyglycines 2

The synthesis of the 3-arylsydnone was achieved from corresponding N-nitroso-N-(2-isopropylphenyl)glycines obtained according to literature procedures. The starting N-arylglycine 1a (Scheme 1), precursor of the N-nitrosoglycines, was obtained from 2-isopropylaniline by condensation with monochloroacetic acid. Compound 1a was further brominated with Br2 to yield the N-arylglcines 1b,c (Scheme 1).
The $^1$H NMR spectra of the N-arylglycines 1a–c confirmed their structure. The isopropyl moiety appears as a doublet at 1.23–1.28 ppm with $J = 6.8$ Hz and a sextet at 2.96 ppm with the same value of the coupling constant. The aromatic region of the $^1$H NMR spectra of the compounds 1a–c presents the expected signals with the characteristic multiplicity (see Experimental section). The nitrosation of N-arylglycines 1a–c was made with NaN$_2$O in presence of hydrochloric acid according to Scheme 2. The nitroso derivatives 2a–c were obtained as crystalline solids in up to 90% yield.

From a careful examination of the NMR spectra of the nitrosoderivatives 2a–c we concluded that these compounds were obtained as mixtures of E–Z isomers which were unquestionably observed at low temperatures due to the fact that in normal conditions the reaction leads to the most stable isomer as will be discussed further. The E–Z isomerism appears in nitrogen containing compounds in which C–N (i.e. amides, oximes, etc) or N–N (i.e. nitroso) presents partial double bond character due to conjugation.$^{39-44}$ However the E–Z isomerism in the case of nitrosoacids like 2a–c was less investigated. The activation parameters of the E–Z inter-conversion in the case of nitrosoamines were investigated by dynamic NMR techniques.$^{45,46}$

Also the E–Z configuration was attributed on the rationale that the most voluminous substituent must be in cis position in respect to the oxygen atom in the nitroso group. The $^1$H NMR spectrum of the compound 2a shows that the signals of the protons in the isopropyl moiety and the protons in methylene attached to the nitrogen atom appear as two distinctive sets with the integral ratio of 95 : 5 (Fig. 1). For each distinctive sets of signals the multiplicities are different: the methylene attached to the N atom appears as a singlet (for the 95% isomer) and as two doublets forming an AB system with $J = 17.8$ Hz for the 5% isomer. The same is valid for the isopropyl moiety, Table 1 presenting the signals in the aliphatic region and their corresponding multiplicities. The presence of two conformers is observed for Z-2a (Fig. 1) due to the hindered rotation about the C–N bond induced by the bulky isopropyl group and the contribution of the nitroso moiety. The different chemical shifts of the analogous atoms in the two rotamers are slightly different due to the magnetic anisotropy of the nitroso group which is in a different spatial relation with the interacting hydrogen atoms.

The Z–E isomerism was also observed for compounds 2b and 2c. For 2b the protons in the aromatic ring, present two sets of signals corresponding to the two stereoisomers (Table 1) while H-6 presents different chemical shifts also due to the spatial influence of the nitroso group.

The non-equivalence of the methyl protons of the isopropyl moiety suggests that Z-2a and Z-2b present axial isomerism which is induced by the hindered rotation about the C–N bond caused by the bulky isopropyl group. This is elegantly confirmed in the case of 2c, in which by introducing the bromine atom in the ortho position of the aryl ring with respect to the nitroso group gives the two E–Z stereoisomers in 58 : 42 ratio observed by $^1$H NMR spectroscopy (Fig. 1S). Both Z-2c and E-2c present the coexistence of two stable conformers in solution (Table 1). The NMR studies indicated that Z-2c transforms in E-2c in solution similar to 2a and 2b. Thus one can conclude that E-2c is the thermodynamically stable stereoisomer and Z-2c is obtained by the nitrosation reaction of 1c to 2c which goes under kinetic control. We were able to separate E-2c from the mixture and to characterize it separately by NMR (Fig. 2S) spectroscopy (see ESi†) and by single crystal X-ray diffraction analysis.

The structure of the N-nitrosophenylglycines 2 was investigated by X-ray single crystal diffraction of 2c as representative compound. Suitable crystals of 2c were grown by slow evaporation from acetonitrile. The X-ray diffraction analysis (Fig. 2)
such kind of compounds.

The crystal structure of 2c can be characterized as the parallel packing of the discrete infinite ribbons running along a crystallographic axis (Fig. 3†). The structure of one-dimensional ribbon-like supramolecular architecture is shown in Fig. 3 showing short Br···Br contacts. The value of the intermolecular Br···Br distance, 3.536(1) Å is under the sum of van der Waals radii (3.70 Å). Also the values of the angles C···Br···Br are 113.0° and 173.9°, respectively.

The Br···Br contacts are by definition included in the class of the halogen bonds of type II.†

The energy of the cyclic dimer made by the hydrogen bond in the carboxylic acid was calculated at HF/3-21 level as implemented in Crystal Explorer 17.48,49 The calculated value of ~73 kJ mol⁻¹ place the O–H–O=O=C bond strength as usual for such kind of compounds.50

Synthesis and characterization of the 3-arylsydnones 3–5

The new nitrosophenylglycines 2a–c were used further in the synthesis of the N-arylsydnones 3a–c (Scheme 2). The new sydnones were obtained in good yields (see ESI†). The sydnones 3a,b were then halogenated in position 4 to give 4-bromosydnones 4a,b and 4-iodosydnones 5a,b by using iodine monochloride or molecular bromine. Unfortunately the halogenation in the case of 3c did not give satisfactory results owing to prolonged reaction time or required higher temperatures which led to the decomposition of the reaction products.

The structure of the new compounds 3–5 (Table 2) was investigated and confirmed by NMR spectroscopy. The investigation of the NMR spectra showed that 1-arylsydnones 3a and 4b and 5a,b present also stable rotamers induced by the hindered rotation between the phenyl and sydnone ring given by the bulky isopropyl moiety and the voluminous halogen atom in position 4 of the sydnone ring in the case of 4 and 5. The diastereotopic isopropyl group has been used to probe the axial chirality which could be studied by NMR spectroscopy due to the magnetic non-equivalence of the methyl protons and carbon atoms caused by the hindered rotation around the C–N bond.

In the case of the sydnones 3a–c, we could detect the presence of the two rotamers at room temperature, only in the case

![Fig. 2 X-ray molecular structure of compound 2c with atom labeling and thermal ellipsoids at 50% level.](image)

![Fig. 3 1D supramolecular network in the crystal structure 2c. H-atoms not involved in hydrogen bonding are omitted. H-bonds and Br···Br contacts are shown in dashed-black lines.](image)

![Fig. 4 The two methyl protons in the isopropyl group become anisochronous due to the hindered rotation about the C–N group. The 1H NMR signals of the two methyl protons in 3c which coalesce at ~35 °C.](image)

### Table 1

| Isomer | CH₂, δ (ppm); J (Hz) | CH₁, δ (ppm); J (Hz) | CH₂, δ (ppm); J (Hz) | CH₁, δ (ppm); J (Hz) | H-6' | % |
|--------|---------------------|---------------------|---------------------|---------------------|------|---|
| E-2b   | 1.22, d, 6.9        | 2.90, sep., 6.9     | 4.49, s             | 7.28, s             | 95   |   |
| Z-2b   | 1.10, 1.16, 2d, 6.8 | 2.49, sep., 6.8     | 4.94, 5.53, 2d, 17.8| 6.95, s             | 5    |   |
| E-2c   | 1.18, 1.21, 2d, 6.9 | 3.38, sep., 6.9     | 3.95, 4.94, 2d, 16.8| —                   | 58   |   |
| Z-2c   | 1.10, 2d, 6.8       | 2.82, sep., 6.8     | 4.91, 5.78, 2d, 17.8| —                   | 42   |   |

### Table 2

| No.  | R     | X    | Yield (%) | Mp (°C) |
|------|-------|------|-----------|---------|
| 3a   | H     | H    | 87        | 68–69   |
| 3b   | 4-Br  | H    | 72        | 100–101 |
| 3c   | 4,6-Dibromo | H    | 54        | 169–171 |
| 4a   | H     | Br   | 85        | 91–92   |
| 4b   | 4-Br  | Br   | 82        | 142–144 |
| 5a   | H     | I    | 82        | 179–180 |
| 5b   | 4-Br  | I    | 82        | 195–197 |
of 3c which possess a Br atom attached to the other ortho position of the phenyl ring in respect to the sydnone and contributes by its volume to the steric hindrance between the phenyl and sydnone rings. Thus, in the $^1$H NMR spectrum of 3c the methyl protons of the isopropyl appear as two doublets at room temperature (Fig. 4) while the $^{13}$C NMR spectrum presents two distinctive signals for the non-equivalent methyl carbon atoms.

In the case of 4-bromosydrones 4a,b without a bromine in the position 6’ of the benzene ring the $^1$H NMR spectra does not provide relevant data regarding the presence of axial chirality at room temperature but the $^{13}$C NMR spectrum present the methyl groups C atoms as a broad singlet showing that at room temperature the energy barrier for the free rotation about the C–N bond is reached. Comparing the $^1$H and $^{13}$C NMR spectra of compounds 3c and 4a,b one can conclude that the presence of a Br atom on the ortho position of the phenyl ring has a greater influence upon the free rotation than in the case it is attached to the 4 position of the sydnone ring as the presence of the two rotamers is clearly distinguished in solution. For the 4-iodosydnone 5a,b the volume of iodine atom has an influence upon the signals of the methyl groups in the isopropyl moiety, the two methyl groups appearing as two distinct doublets in dilute solutions in $^1$H NMR. The $^{13}$C NMR spectra show also two distinct signals for the methyl groups.

The free rotation energy barrier about the single bond must be therefore a little higher than in the analogous 4-brominated sydrones but still the free rotation has an energy sufficiently low to make to separate them in usual conditions.

The results of X-ray diffraction investigation for 3c is depicted in Fig. 5, while bond distances and angles are summarized in Table 2S.† This compound exhibits a molecular crystal structure resulting from the packing of two-dimensional supramolecular double-layer in parallel orientation (as shown in Fig. 4S†). The self-assembling of two-dimensional layer occurs through the weak H-bonds where C2–H group of the phenyl acts as donor towards carbonyl oxygen atom O2 of adjacent molecule as acceptor of proton (Fig. 4S†).

Each double-layer architecture is built-up from two 2D networks (Fig. 6), which is consolidated due to the C–H⋯O hydrogen bonding and halogen⋯halogen interactions at 3.6020(8) A for Br⋯Br distance (Fig. 6). In the sydnone 3c the intermolecular distance Br⋯Br 3.6020(8) is also under the value of vdW and values of the angles C–Br⋯Br of 119.57° and 169.39° respectively. The torsion angle between the plane of the phenyl ring and the plane of the sydnone ring has the value of 86.5°.

Beside the halogen Br⋯Br contacts in 3c we observed that 4-iodosydrones presented interesting halogen bonding affinity in solution in presence of different bases, and thus we envisaged that halogenated sydrones could provide ideal templates for studying the halogen bonding either in solution or solid state which will aim to investigate further.

**Synthesis and characterization of the 1-arylpyprazoles 6a–g**

The new halogenated 3-arylsydnones were employed in the final step in the synthesis of new halogenated 1-arylypyrazoles using the 1,3-dipolar cycloaddition reaction with activated acetylenic dipolarophiles. Thus, the new compounds 6a–g were obtained starting from the sydrones 3–5 at reflux temperature in toluene or xylene as solvent (Scheme 3).

The mechanism of the [3 + 2] addition of the DMAD to sydrones was investigated and generally accepted as going through a formation of a bicyclic intermediate 7 as presented in the Scheme 4 which leads to the final pyrazole compounds by elimination of one CO₂ molecule and further aromatization (Path A). Literature data suggest also another mechanism implying an acyclic intermediate of type 8 (Path B). In the case of the sydrones such intermediate was demonstrated to coexist
to a lesser extent with the bicyclic one, giving pyrazoles with another substitution pattern, a 1,3-dipole structure being suggested.

Table 3 presents the new synthesized pyrazoles 6a–g and their features.

Table 3  The new 1-arylpyrazoles 6a–g

| No. | R    | X    | Yield (%) | Mp (°C) |
|-----|------|------|-----------|---------|
| 6a  | H    | H    | 87        | 62–63   |
| 6b  | 4-Br | H    | 94        | 139–140 |
| 6c  | 2,4-DiBr | H | 67       | 113–115 |
| 6d  | H    | Br   | 87        | 92–93   |
| 6e  | H    | I    | 82        | 156–157 |
| 6f  | 4-Br | Br   | 86        | 103–104 |
| 6g  | 4-Br | I    | 80        | 128–131 |

Table 3 presents the new synthesized pyrazoles 6a–g and their features.

Compounds 6a–g where characterized by NMR spectroscopy and their structure was confirmed (Experimental section). The singlet in the range 8.03–8.06 belongs to H-5 proton in the pyrazole moiety while the protons in the phenyl group are in accordance with the substitution pattern. In the compounds 6a,b,d the two methyl groups in the isopropyl moiety appear as doublets due to the coupling with the adjacent methine hydrogen. In compounds 6c the presence of the bromine atom in the ortho position the phenyl ring is sufficient to increase the rotation barrier of the two rings about the single bond. This is reflected in the 1H NMR spectrum by the magnetic non-equivalence of the two methyl groups which appear as two doublets at 1.12 and 1.19 ppm (Fig. 7). In the 13C NMR spectra the methyl groups in the isopropyl moiety appear as a singlet for 6a,b,d and for 6c the spectrum shows two different signals highlighting the magnetic non-equivalence of the two protons in discussion. For the 5-bromopyrazoles 6d,f the most important proof of the hindered rotation is the 13C NMR which shows two signals for the methyl groups while the proton NMR being more sensible to dilution shows only one doublet. For the 5-iodopyrazoles 6e,g the magnetic non-equivalence of the two methyl groups is clear in both 1H and 13C NMR spectra. The NMR data suggests that the most effective hindrance of the free rotation about Ar–N bond is when the halogen atom and the isopropyl group are both grafted on the same ring, the phenyl ring in particular.

The compound 6e was studied by dynamic NMR and the resulted energy barrier of rotation was calculated at a coalescence temperature of 50 °C using the Gutowski relation. The energy was calculated to be 70.5 kJ mol, which is high enough to try the separation of the two enantiomers.

The structure of the highly substituted pyrazoles has been also confirmed by single crystal X-ray diffraction analysis. The molecular structure of the representative compound 6b is shown in Fig. 8 and bond distances and angles in Table 1S.†

The analysis of the crystal packing shows the presence of two-dimensional supramolecular layers, which are formed by a system of intermolecular C–H⋯O hydrogen bonding. A view of this layer is depicted in Fig. 5S.† The crystal structure essentially results from the packing of these layers parallel to 011 plane, as shown in Fig. 6S.† The torsion angle between the plane of the phenyl ring and the plane of the pyrazole ring has the value of 75.57°.

We have investigated recently the propensity of halogen bonding in halogenated 1-arylpyrazoles and we found them as versatile structures for study of this interesting interaction.54

Conclusions

In conclusion, new halogenated 3-(2-isopropylphenyl)sydnones and 1-(2-isopropylphenyl)pyrazoles were obtained from the corresponding N-nitrosoderivatives. The bulky halogen atoms on the phenyl or the five membered rings (sydnone and pyrazole) and the presence of the isopropyl on the ortho position of the phenyl ring induced a hindered rotation about the C–N bond, two stable rotamers being confirmed by NMR.
Experimental

The synthesis of N-(2-isopropyl)phenylglycine (1a)

M.p. 139–141 °C. Yield 46%. 30 mL (0.21 mol) of 2-isopropylaniline is mixed with 17 g (0.18 mol) of monochloroacetic acid in 200 mL water and 10 mL ethanol. The reaction mixture is kept under reflux for 3 h. The reaction mass is cooled with water and then stirred for 1 h on an ice bath. The formed precipitate is removed by filtration and then washed with water and with benzene after drying to remove any unreacted 2-isopropylaniline. Anal. for C11H14BrNO2 (272.14): found: C 48.87; H 5.47; Br 29.76; N 5.42.

The synthesis of N-phenylglycines 1b, c

N-(2-Isopropyl)phenylglycine 3.9 g (20 mmol) are suspended in 20 mL glacial acetic acid. Over this solution is added 20 mmol Br2 for 1b or 40 mmol Br2 for 1c dissolved in 5 mL acetic acid. The reaction is kept under stirring for cca. 15–20 min and then the reaction mass is poured over cold water and then stirred on an ice bath for 20 min and then the reaction mass is poured over cold water and then stirred for 1 h on an ice bath. The formed precipitate is removed by filtration and then washed with water and with filter paper, and then the solution is dried over cold water. The stirred mixture is filtered and then washed with water on the filter paper, and then the compound is dried.

N-(4-Bromo-2-isopropylphenyl)glycine (1b). White powder crystallized from ethyl acetate. Yield 94%, mp 191–193 °C. Anal. for C11H12Br2N2O3 (380.03): found: C 35.12; H 3.50; Br 42.44; N 5.42.

N-(4-Bromo-2-isopropylphenyl)glycine (1c). White powder crystallized from cyclohexane. Yield 76%; mp 103–105 °C. Anal. for C11H12Br2N2O3 (380.03): found: C 35.12; H 3.50; Br 42.44; N 7.69.

Procedures for obtaining N-nitroso-N-phenylglycines

N-(2-Isopropylphenyl)glycine 20 mmol is dissolved in 40 mL solution of 5% NaOH and 21.5 mmol of NaNO2 are added. Over this mixture 10 mL conc. HCl are added under vigorous stirring and cooling on an ice bath, until the pH will reach a value of 1.5–2. The stirring continues for another 15 min while the nitrosoderivative precipitates. The N-nitroso-phenylglycine is filtered washed with water on the filter and let to dry in air.

N-Nitroso-N-(2-isopropylphenyl)glycine (2a). White crystals obtained from ethanol-benzene mixture; yield 94%; mp 104–106 °C (desc.). Anal. for C11H12BrN2O2 (301.14): found: C 44.09; H 4.72; Br 26.94 N 9.59. Calcd: C 43.87; H 4.35; Br 26.53; N 9.30. 

N-Nitroso-N-(4-bromo-2-isopropylphenyl)glycine (2b). The same procedure as for 2a is employed. The compound precipitates as oil which is extracted twice with 15 mL CH2Cl2. This solution is dried over CaCl2 and then the amorphous mass is crystallized from ethyl acetate-benzene. Yield 89%; mp 121–123 °C (desc.). Anal. for C11H12BrN2O2 (301.14): found: C 44.09; H 4.72; Br 26.94 N 9.59. Calcd: C 43.87; H 4.35; Br 26.53; N 9.30.

N-Nitroso-N-(4,6-dibromo-2-isopropylphenyl)glycine (2c). The same procedure as for 2a white crystals were crystallized from cyclohexane; yield 78%; mp 170–172 °C (desc.). Anal. for C11H12BrN2O2 (301.14): found: C 35.12; H 3.50; Br 42.44; N 7.69. Calcd: C 34.76; H 3.18; Br 42.05; N 7.37.

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General procedure for the synthesis of 3-(2-isopropylphenyl)sydnone 3–5

N-nitroso-N-(2-isopropylphenyl)glycine 20 mmol was dissolved in 30 mL acetic anhydride. On this solution is added 1 mL of dried pyridine. The reaction mixture is gently heated on a water bath at reduced pressure in order to evaporate the excess acetic anhydride and the acetic acid resulted from the reaction. The sydnone precipitates as oil which crystallizes upon cooling.

3-(2-Isopropylphenyl)sydnone (3a). White crystals were crystallized from ethanol; yield 87%; mp 68–69 °C. Anal. for C11H8BrN2O2 (240.22): Found: C 55.21; H 3.36; N 14.80. Calcd: C 55.64; H 3.36; N 14.80.

4-Bromo-3-(2-isopropylphenyl)sydnone (4a). White crystals were crystallized from isopropanol; yield 85%; mp 91–92 °C. Anal. for C11H7BrN2O2 (261.20): Found: C 57.13; H 3.50; N 14.12. Calcd: C 57.13; H 3.50; N 14.12.

5-Isodo-3-(2-isopropylphenyl)sydnone (5a). 3-(2-Isopropylphenyl)sydnione 10 mmol and 15 mmol anhydrous sodium acetate are dissolved in 15 mL acetic acid glacial. A solution of 12 mmol ICl in 5 mL acetic acid is added under stirring and then the reaction mixture is stirred for 10 min at room temperature and another 1 h at 50–60 °C. After this, the reaction mixture is poured over 150 mL of cold water. The precipitated 4-iodosydnone is filtered and washed with water triturated with ethyl ether and crystallized from ethanol as white crystals. Yield 82%; mp 179–180 °C. Anal. for C11H11BrN2O2 (310.12): Found: C 46.38; H 3.67; N 13.83. Calcd: C 46.38; H 3.67; N 13.83.

6-Dibromo-3-(2-isopropylphenyl)sydnone (6a). 10 mmol sydnone 4a and 12 mmol DMAD are heated under reflux in 20 mL toluene for 8 h. The solvent is evaporated and the resulting oil is eluted on an Al2O3 column using CH2Cl2 as solvent. The sydnone 6a is crystallized from methanol as white crystals. Yield 87%; mp 62–63 °C. Anal. for C13H8Br2N2O2 (302.30): Found: C 63.87; H 6.33; N 9.55. Calcd: C 63.56; H 6.00; N 9.27. 1H NMR (CDCl3, δ ppm, J Hz): 1.24 (dd, 6H, 6.9; CH3); 2.63 (sep., 1H, 6.9; CHMe2); 5.15 (dd, 1H, 8.4, 6.9; H-5’); 2.77 (dd, 1H, 8.4, 6.9; H-6’); 7.70 (d, 1H, 1.0; H-3’); 13C NMR (CDCl3, δ ppm): 32.6; 24.3 (2CH3); 105.9 (C-4’); 132.3 (C-3’); 128.7 (C-3’); 129.7 (C-3’); 130.9 (C-1’); 133.4 (C-3’); 148.9 (C-3’); 168.5 (CO).

General procedure for obtaining 4-brom-3-(2-isopropylphenyl) sydonenes (4a,b)

3-(2-Isopropylphenyl)sydnione 10 mmol and 12 mmol sodium acetate anhydrous are dissolved in 15 mL glacial acetic acid. Over the reaction mixture are added under stirring and on an ice bath 11 mmol Br2 dissolved in 15 mL glacial acetic acid. The stirring is kept 10–15 minutes at room temperature and then the reaction mixture is poured over 150 mL of cold water. The formed precipitate is removed by filtration and washed with water on the filter paper.

4-Bromo-3-(2-isopropylphenyl)sydnone (4a). White crystals were crystallized from isopropanol; yield 85%; mp 91–92 °C.
Conflicts of interest

There are no conflicts to declare.

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