

## On the reactions of tertiary carbanions with some nitroindazoles and nitrobenzotriazoles

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### Abstract

The vicarious nucleophilic substitution in some nitroindazole and nitrobenzotriazole derivatives with tertiary carbanions leads almost exclusively to products substituted *para* to the nitro group. As results from the theoretical calculations and structural evidences, such reaction outcome is due mainly to the stereoelectronic reasons in combination with the considerable shortening of the *C<sub>ortho</sub>*–CNO<sub>2</sub> bond. The presence of the chiral and prochiral centres (the methine and N-methylene groups, respectively) often gives rise to additional splitting of the methylene protons signal that is transmitted on a long distance provided there is no pyridinic nitrogen in the pathway of coupling.

**Keywords:** Indazoles, benzotriazoles, vicarious nucleophilic substitution, tertiary carbanions

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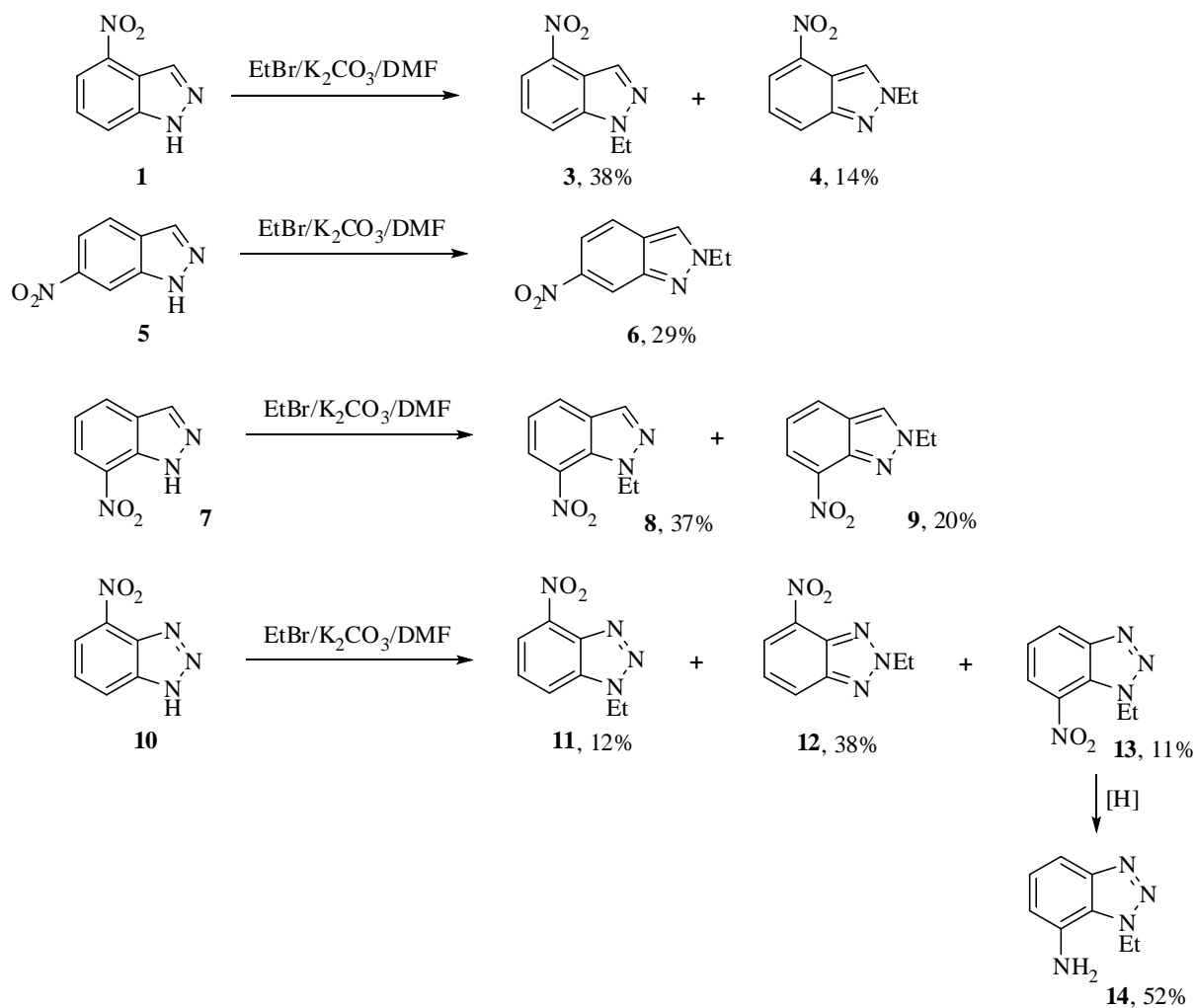
### Introduction

*Ortho*-substituted nitroarenes are useful starting materials for the synthesis of many heterocyclic compounds. One of the most practical methods that lead to the *ortho*-substituted derivatives of nitroarenes is the vicarious nucleophilic substitution (VNS). The VNS is a two-step reaction consisted in the addition of a carbanion, containing a leaving group X at the carbanionic centre, to a nitroarene followed by the base-induced  $\beta$ -elimination of HX from the  $\delta^H$ -adduct formed in the first step.<sup>1</sup> The reaction is the best practical method that allow introduction of a new substituent into an azole or benzazole ring by using nucleophilic reagents.<sup>2,3</sup> The VNS products with a functional alkyl substituent *ortho* to the nitro group are particularly useful for the synthesis of indole and quinoline derivatives.<sup>1,4,5</sup> Some VNS products are useful starting materials for the synthesis of biologically active compounds, like recently reported potent and selective 5-HT<sub>6</sub> antagonists.<sup>6</sup> We employed such VNS products to the synthesis of indazole and

condensed pyrazole derivatives that showed promising anticancer activity and were screened for anxiolytic effect.<sup>7,8</sup> However, in the synthesis of some *ortho*-substituted nitroderivatives, we encountered severe problems when using tertiary carbanions or secondary carbanions containing poorer leaving groups than the chloride or thiophenoxide ions.<sup>9,10</sup> In this paper we report our findings concerning the factors responsible for the VNS orientation in some nitrobenzazoles. Our results bear some relationship with those about the electrophilicity of nitroarenes and nitroheteroarenes published recently by the Mąkosza group.<sup>11,12</sup>

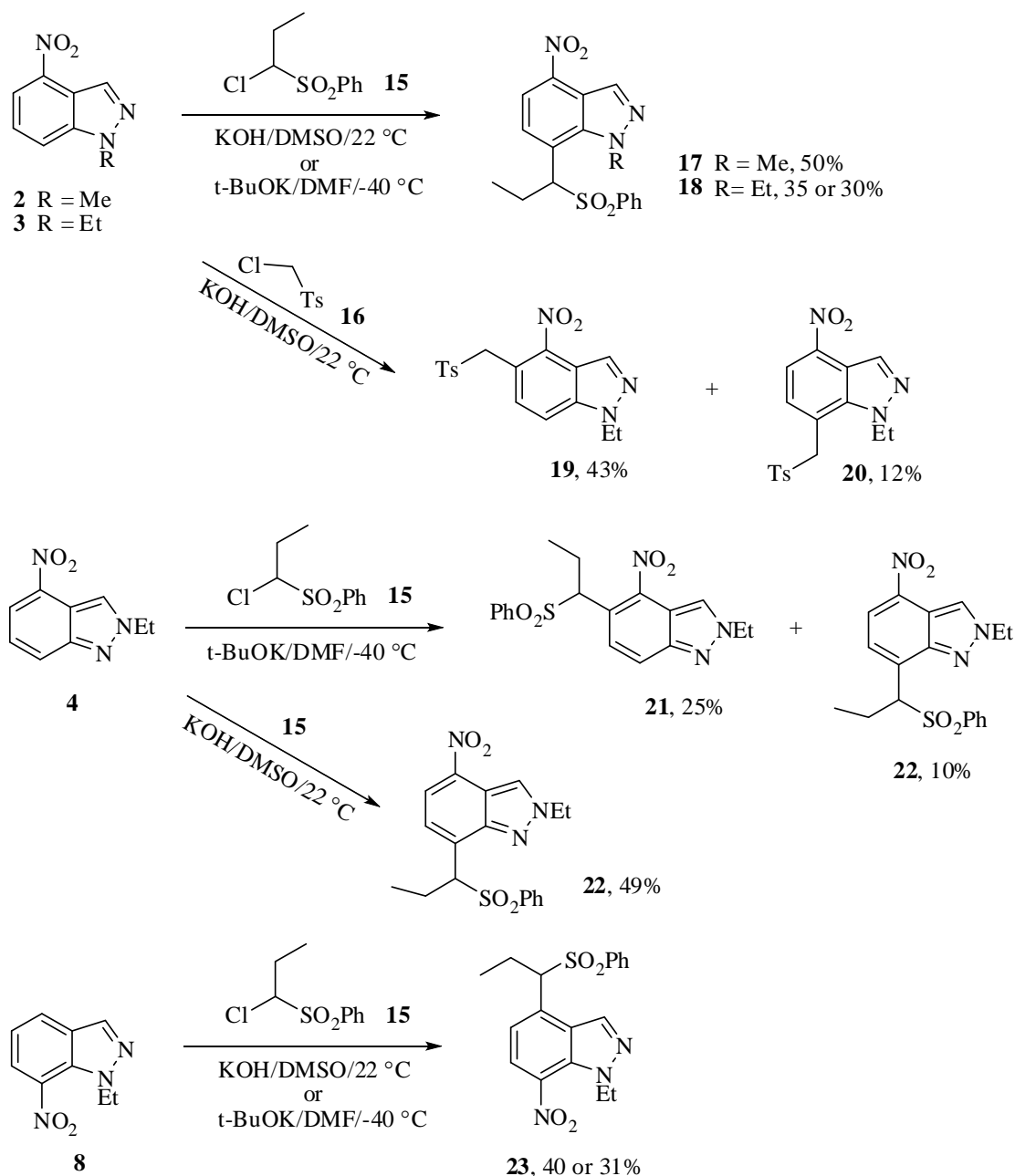
## Results and Discussion

The starting materials for the reactions described in the next paragraph were obtained by ethylation of nitroindazoles **1**, **5**, and **7**, as well as 4-nitrobenzotriazole **10** (Scheme 1).



Scheme 1

The structures of benzotriazole derivatives **11-13** were confirmed by comparison of their  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra with the spectra for the corresponding N-methyl derivatives<sup>13</sup> and the NOE difference experiment performed for the amino derivative **14**; the latter was obtained by hydrogenation of **13** (Scheme 1). Irradiation of the amino protons resulted in enhancements of the neighbouring signals, namely 6-H doublet of doublets,  $\text{CH}_2$  quartet and  $\text{CH}_3$  triplet.



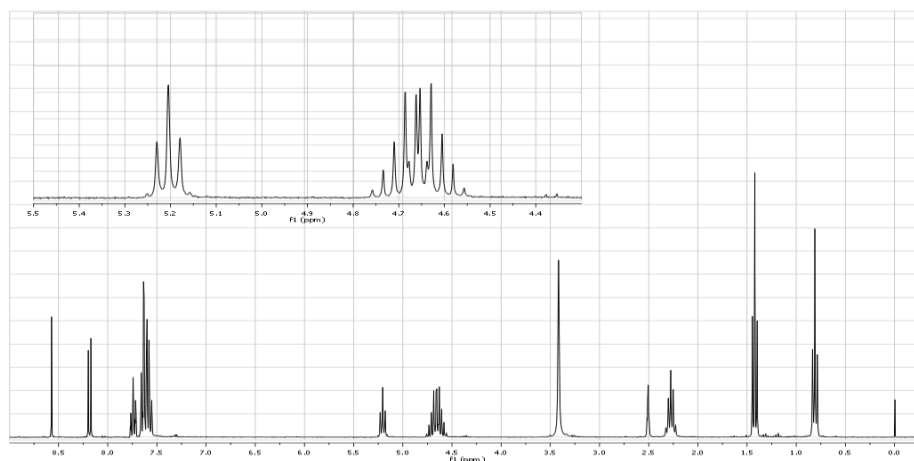
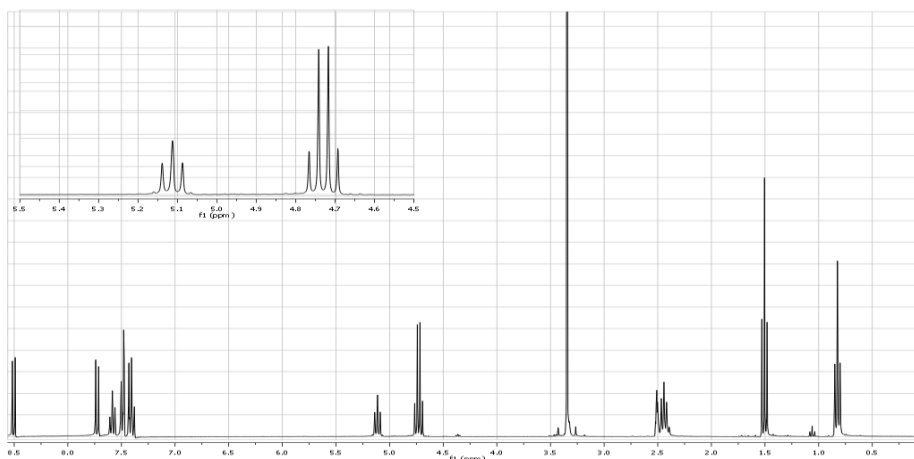
Scheme 2

In one of our initial experiments, we tried to obtain an *ortho*-substituted 4-nitroindazole derivative **18**. Under the typical for *ortho* substitution conditions, i.e. *t*-BuOK as a soluble base, DMF as a solvent and low temperature ( $-45\text{ }^{\circ}\text{C}$ ),<sup>1</sup> the synthesis led to a single isolable product (Scheme 2) but the reaction mixture contained a significant amount of tars. With only the  $^1\text{H}$  NMR spectrum at hand, we were convinced that compound **18** was the desired *ortho* isomer. However, when the reaction was repeated under the conditions favourable for the *para* orientation (KOH/DMSO at room temperature), its outcome was identical.

The  $^1\text{H}$  NMR spectrum of compound **18** (Figure 1) displays several signals in the aromatic region confirming the disubstituted benzene part of the indazole ring, namely a singlet at 8.58 ppm for the 3-H proton, a doublet at 8.20 ppm for the 5-H proton and two multiplets between 7.57 and 7.78 ppm for the  $\text{PhSO}_2$  group; the latter multiplet overlaps with the doublet for the remaining 6-H proton. The coupling constant for the doublet at 8.20 ppm ( $^3J$  8.2 Hz) could not be conclusive whether the benzene part of the indazole ring is *ortho*- or *para*-substituted, thus we decided to register a NOE difference spectrum. Irradiation of the methine proton at 5.22 ppm, gave a significant NOE on the N- $\text{CH}_2$  protons at 4.57-4.77 ppm as well as on the  $\text{CH-CH}_2$  (2.24-2.33 ppm) and  $\text{C-CH}_2\text{CH}_3$  (0.82 ppm) protons. A weak enhancement of the  $\text{CH}_3$  triplet of the N-ethyl group (1.43 ppm) was also observed. This clearly shows that the methine proton and N-ethyl group are in close proximity and the benzene ring is *para*-substituted. The signal for the N- $\text{CH}_2$  protons is particularly interesting due to its atypical splitting: instead of the expected quartet it appears as a complex multiplet (Figure 1). Also the methine signal is observed as a triplet with some residual splitting instead of a doublet of doublets. A part of the mystery was resolved by registering the NMR spectra for **18** at higher temperatures (Figure 2). At  $60\text{ }^{\circ}\text{C}$  the signal for methine proton appeared as a doublet of doublets and several lines disappeared from the complex N- $\text{CH}_2$  multiplet. The latter one was then observed as a clean nonet. The unusual splitting of the N- $\text{CH}_2$  signal is thus due to two factors: (i) hindered rotation and (ii) the presence of the chiral centre (the methine proton) in close proximity. The latter factor renders the N-methylene protons diastereotopic and not equivalent, and therefore they exhibit further splittings as they couple to each other.

To verify such reasoning, we obtained several indazole and benzotriazole derivatives with or without the chiral centre (Schemes 2 and 3).

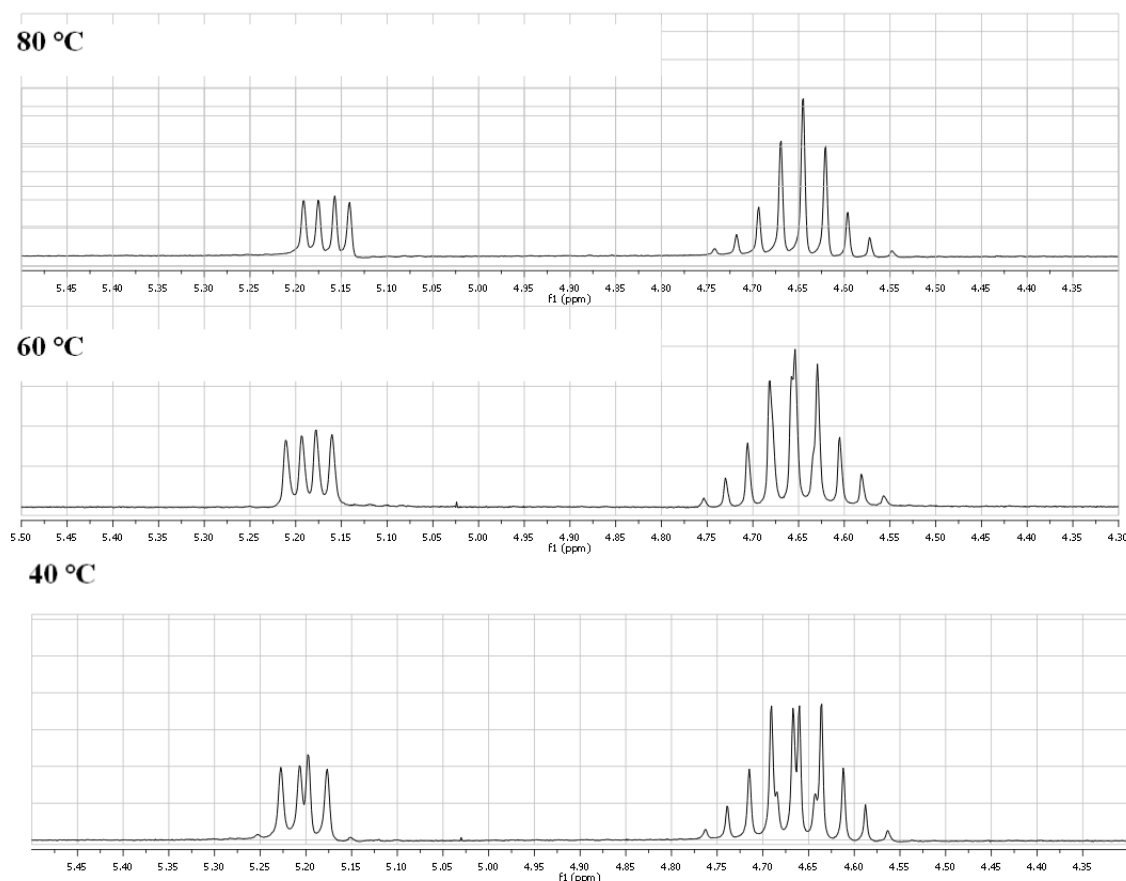
Similarly to the starting material **3**, the VNS in 1-methyl-4-nitroindazole (**2**) using the carbanion precursor **15** led to a single product **17** (Scheme 2) whereas, as expected, the reaction of compound **3** with **16** gave two isomers **19** and **20**. Compound **17** as well as isomers **19** and **20** contain neither prochiral methylene protons (**17**) nor a chiral centre (**19** and **20**). A normal singlet is observed for the N-methyl group in **17** and a typical quartet is seen for the methylene protons both in **19** and **20**.

(a) compound **18**(b) compound **26**

**Figure 1.** Examples of the  $^1\text{H}$  NMR spectra with expanded regions containing the signals for methine and N-methylene protons: (a) revealing the interaction between the chiral and prochiral centres; (b) devoid of this interaction due to suppression by the pyridinic nitrogen.

Only the *para* isomer **22** was detected and isolated from the reaction mixture containing compounds **4** and **15** as starting materials and KOH/DMSO as a base/solvent system (Scheme 2). Its  $^1\text{H}$  NMR spectrum shows a similar pattern concerning the signals for the N-methylene protons like that for compound **18**, i.e. a symmetrical multiplet, consisting this time of ten lines, instead of a typical quartet. However, in contrast to compounds **2** and **3**, the starting material **4** gave two isomers **21** and **22** when treated with the carbanion precursor **15** in t-BuOK/DMF at low temperature (Scheme 2). Moreover, the *ortho* isomer **21** was the major product of the reaction: 25% vs. 10% for isomer **22**. Such change in the VNS orientation is primarily caused by the presence of the *peri* unshared electron pair on the nitrogen atom N1. This electron pair retards both the approach of the carbanion to position 7 and the base attack in the elimination step, and thus forces the VNS at position 5. It is noteworthy that the  $^1\text{H}$  NMR spectrum of **21**

reveals an identical multiplet for the N-methylene protons like for the *para* isomer **22** regardless of the fact that the distance between these protons and the chiral centre is quite long.

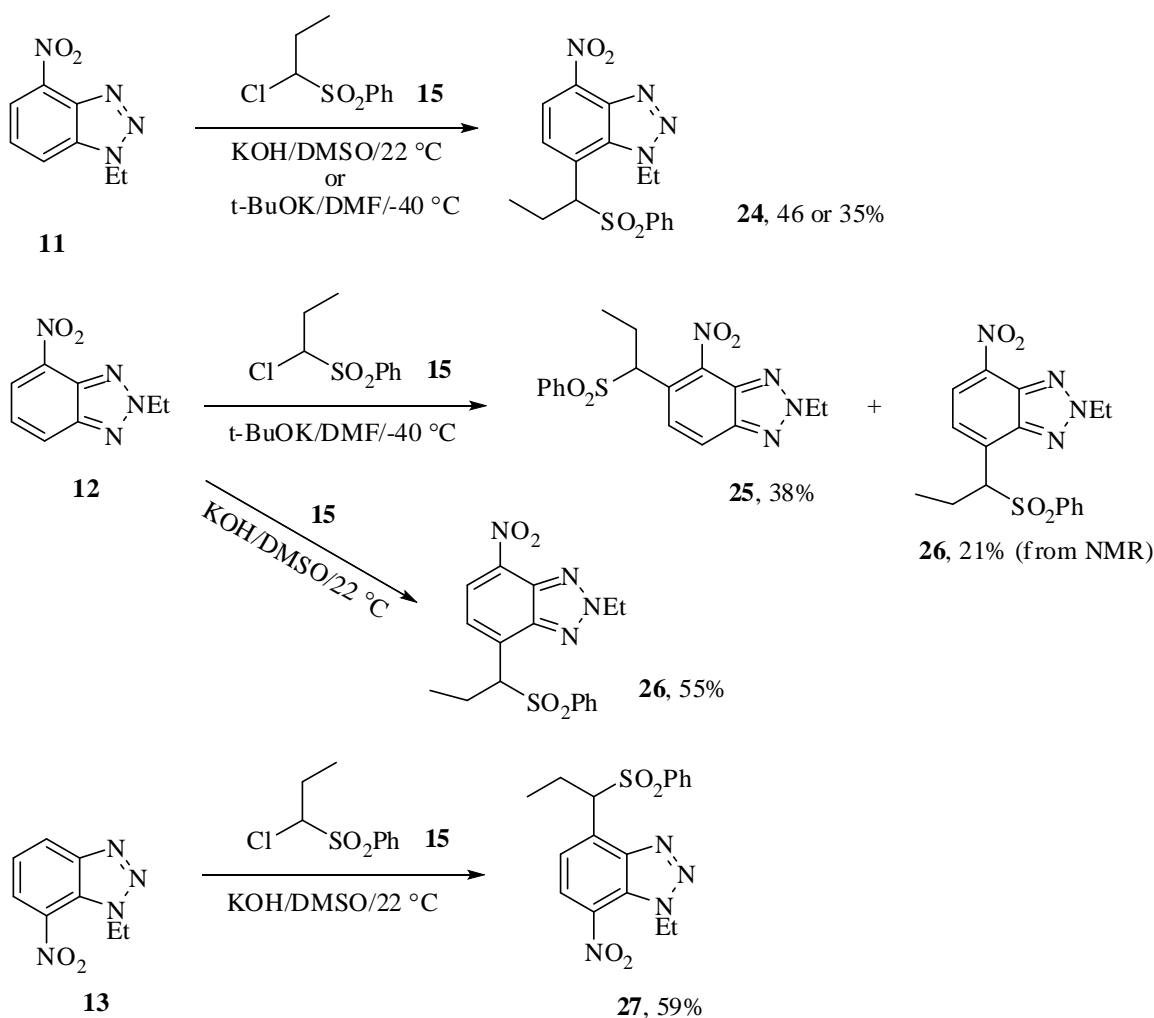


**Figure 2.** The  $^1\text{H}$  NMR spectra for compound **18** registered at 40, 60, and 80 °C, showing signals for the methine proton and N-methylene protons (the spectrum recorded at ambient temperature is shown in Figure 1a).

The VNS reaction of compound **6** with **15** did not lead to any isolable product. Despite using a variety of reaction conditions, we were able to recover only the starting material **6** (32-57%) from the reaction mixtures that contained usually significant quantities of tarry products. The most apparent rationale for the reaction failure is the stereoelectronic hindrance caused by the nitro group and unshared electron pair at N1, both in close proximity to the reaction site.

Likewise reactant **3**, compound **8** gave only the *para* substituted product **23** regardless of the conditions applied (Scheme 2). Strikingly, in the  $^1\text{H}$  NMR spectrum of **23**, the signal for N-CH<sub>2</sub> protons appears as a typical quartet rather than a complex multiplet as opposed to the N-CH<sub>2</sub> signals for indazoles **18**, **21**, and **22** described above (albeit some residual lines can be seen within this quartet), and the same signal in the spectrum of benzotriazole **24**. The latter compound was the sole product obtained from the reaction of nitrobenzotriazole **11** with the

carbanion precursor **15** in both base/solvent systems (Scheme 3). In its  $^1\text{H}$  NMR spectrum, an AB system – doublets at 7.72 and 8.33 ppm with *ortho* coupling  $^3J$  8.4 Hz – indicates a *para*-substituted benzene ring in benzotriazole rather than *ortho* as the coupling constant for the latter is substantially larger and close to 9 Hz.<sup>14</sup> The  $^1\text{H}$  NMR spectrum of **24** shows similar diastereotopism like the spectra for indazoles **18**, **21**, and **22**, i.e. the N-methylene protons signal takes shape of a symmetrical multiplet, this time consisting of 12 lines. The difference in number of lines present in the multiplets for N-methylene protons in compounds **18**, **21**, **22**, and **24** may be due not only to the hindered rotation (compound **18**) but also to overlapping of some lines within the multiplets.



Scheme 3

The effect of diastereotopic N-methylene protons is not observed for other benzotriazole derivatives **25**–**27** (Figure 1) obtained by the VNS from starting materials **12** and **13** (Scheme 3, we were unable to isolate an analytically pure sample of **26** but the  $^1\text{H}$  NMR of the reaction

mixture showed its presence in an about 21% yield). In the  $^1\text{H}$  NMR spectra registered for compounds **25-27**, the signal for these protons appears as a typical quartet.

The suppression of the additional splitting of N-methylene signal in the spectra of benzotriazole derivatives **25-27** is due to the presence of the pyridinic nitrogen N3 in the pathway of possible coupling. We tried to quantify the effect using theoretical calculations. Although we have not overly been successful, some of our findings are worthy of mention. The Natural Bond Orbitals (NBO) analysis showed the presence of a high-energy molecular Rydberg orbital  $\text{RY}^*$  on N3 with the following contribution of atomic orbitals: s 2.17%, p 93.10%, and d 4.73%. This analysis revealed also the presence of a two-centre Lewis orbital BD with a high occupancy value that connected atoms N2 and N3. The above features can be useful in the interpretation of the UV spectra of some benzotriazoles.

In summary, the presence of the chiral centre within a molecule of N-ethylindazole and N-ethylbenzotriazole often gives rise to further splitting of the N-methylene signal. The effect is transmitted through the  $\pi$  system on a long distance, even through seven bonds (compound **21**), provided that there is no pyridinic ring nitrogen in the way of possible coupling.

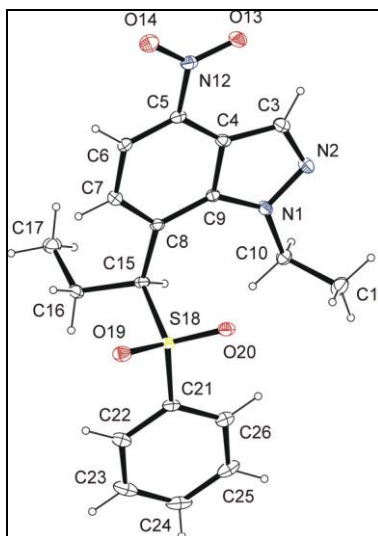
**Table 1.** The effective charges on atoms other than hydrogen in indazole and benzotriazole derivatives **3**, **4** and **11**, **12** calculated by the B3LYP/6-31G(d,p) method (CPCM/DMSO)

Atom	Indazole <b>3</b>	Indazole <b>4</b>	Benzotriazole <b>11</b>	Benzotriazole <b>12</b>
N1	-0.426	-0.431	-0.388	-0.376
N2	-0.282	-0.243	-0.049	-0.013
C3	0.111	0.130	-	-
N3	-	-	-0.418	-0.405
C3a	-0.023	-0.008	0.237	0.291
C4	0.200	0.211	0.273	0.270
C5	-0.095	-0.101	-0.102	-0.106
C6	-0.119	-0.124	-0.118	-0.116
C7	-0.058	-0.066	-0.061	-0.071
C7a	0.362	0.278	0.350	0.248
N(nitro)	0.377	0.372	0.372	0.372
O1	-0.400	-0.436	-0.426	-0.432
O2	-0.409	-0.443	-0.419	-0.426
C(H <sub>2</sub> )	-0.020	-0.057	-0.071	-0.052
C(H <sub>3</sub> )	-0.356	-0.323	-0.324	-0.326

To determine which factors are responsible for the practical lack of the substitution *ortho* to nitro group in nitroindazoles and nitrobenzotriazoles, we referred to theoretical calculations and X-ray crystallography. In nitroindazoles **3**, **4** and nitrobenzotriazoles **11**, **12**, the charge distribution obtained by the calculations is characterized by a noticeable withdrawal of the electron density from the benzene ring into the nitro group (Table 1). The electrons tend to

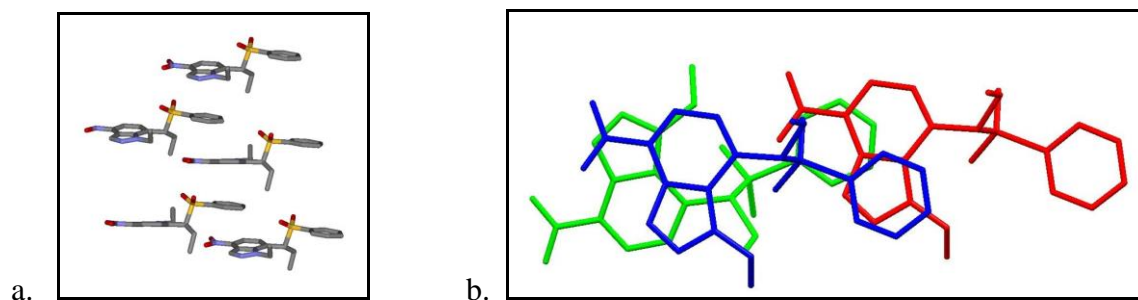


accumulate on the oxygen atoms and ring nitrogens. A particular low electron density is found on the carbons neighbouring the nitrogen atoms, i.e. the *ipso* carbon C4, bridge carbons C7a and C3a (the latter one only in benzotriazoles), and carbon C3 in indazoles. The calculations reveal small differences in charges between the *ortho* and *para* carbons, both in indazole and benzotriazole derivatives. Even though these dissimilarities, favouring the *para* positions by only 0.04 electrons, are not enough large to alter significantly the direction of carbanion attack, they may add some impact to the stereochemical discrimination between these positions described in the next paragraph.



**Figure 3.** ORTEP view of **18**. Ellipsoids are drawn at the 50% probability level.

Figure 3 shows the X-ray structure of compound **18**. As expected, the indazole ring is planar but the nitro group is not coplanar with the ring; it is twisted of the ring plane by 3.58°. The nitrobenzene ring of indazole derivative **18** reveals considerable deviations concerning some bonds in comparison with nitrobenzene. The C4-C5 bond is particularly short (1.35 Å vs. 1.3989 Å in nitrobenzene<sup>15</sup>). As a similar value for the C4-C5 bond length can be predicted for nitroindazole **3**, this bond shortening may be crucial for the orientation in the nucleophilic substitution. The other *exo* bond, namely C6-C7 is also significantly shorter than the C5-C6 *endo* bond (1.367 Å vs. 1.411 Å). This means that the antiperiplanar conformation required for the β-elimination is severely hindered in the *ortho* σ<sup>H</sup> adduct, hence the *ortho* substitution involving bulky tertiary carbanions is usually not observed for nitroindazole derivatives even when the reaction is carried out under the conditions more favourable for the kinetic *ortho* product (t-BuOK/DMF/low temperature). Only when using the 2-substituted nitrobenzazoles of dienoid structure **4** and **12** as starting materials, we were able to detect both *ortho* and *para* isomers in the reaction mixture (compounds **21** and **22** as well as **25** and **26**). This change in the VNS orientation is mainly due to the stereoelectronic hindrance of the *peri* unshared electron pair on N1.



**Figure 4.** (a) Cross section through the stacks of **18** (hydrogen atoms are omitted). (b) Superimposition of pyrazole and benzene rings in the stacks.

The crystallographic structure of **18** reveals some interesting features. The hydrogen atoms *ortho* to the sulfonyl group are engaged in a weak intramolecular hydrogen bonds with the oxygen atoms of the sulfonyl group; the distances  $C_{ortho}-H\cdots OS$  are 2.51 and 2.71 Å, respectively. Moreover, the oxygen atom O1S is an acceptor in the intermolecular hydrogen bond  $C5-H\cdots O1S$  having the following parameters:  $d = 2.56$  Å,  $D = 3.17$  Å, and  $\theta = 124^\circ$ . Another weak intermolecular hydrogen bond connects the  $NO_2$  oxygen atoms with the methine carbon and has the following parameters:  $d = 2.18$  Å,  $D = 3.38$  Å, and  $\theta = 152^\circ$ . All values listed above fit perfectly within the limits for weak hydrogen bonds:  $d = 2.0$ – $3.0$  Å,  $D = 3.0$ – $4.0$  Å, and  $\theta = 90$ – $180^\circ$ .<sup>16</sup> Worth mentioning is considerable lengthening of the bond between methine carbon and proton: 1.20 Å in comparison with the standard length for a  $Csp^3-H$  bond – 1.083 Å.<sup>17</sup> The intermolecular hydrogen bonds keep the molecules of **18** in a three-dimensional aggregation (Figure 4a). The unit cell contains four molecules. The indazole and phenyl rings from separate molecules are arranged alternatively forming infinite stacks. The extent of stacking is significant. Moreover, the stacking between the phenyl and pyrazole rings is considerably larger than the stacking between the phenyl and benzene rings (Figure 4b). Both above depicted interactions – the weak hydrogen bonding and  $\pi$ - $\pi$  stacking – may have an important value in the molecular recognition involving indazole ring.

## Experimental Section

**General.** Flash chromatography (FC) was performed using silica gel 60, 230–400 mesh (Merck), Low Pressure Liquid Chromatography (LPLC) – the Michael-Miller system and 15-40 silica gel (Merck), gradient chromatography – silica gel 60, 60-230 mesh (Merck). Melting points were determined on a Boetius apparatus and are uncorrected.  $^1H$  NMR were recorded at 300 (Varian Mercury 300), 400 (Varian VNMR-S), or 600 MHz (Bruker Avance 600) in  $DMSO-d_6$  with TMS as an internal standard. When necessary, the position of the phenylsulfonyl substituent attachment at the hetarene ring was proved by NOE differential spectra.  $^{13}C$  NMR spectra were registered at 100 or 150 MHz using Varian VNMR-S or Bruker Avance 600 spectrometers,

respectively. Low resolution mass spectra were recorded on an AMD Intectra Mass AMD 402 instrument operating at 75 eV. IR spectra were run in KBr on a Specord 75-IR apparatus. Elemental analyses were performed on a Vario EL III instrument. Starting materials, apart from those described below, were obtained by known procedures (**2**<sup>18</sup>, **15** and **16**<sup>19</sup>) or were commercially available.

**Alkylation of nitroindazoles.** A mixture of 4- or 6- or 7-nitroindazole (**1** or **5** or **7**) (4.9 g, 30 mmol), bromoethane (3.5 g, 32 mmol) and finely powdered K<sub>2</sub>CO<sub>3</sub> (14 g) was stirred vigorously in DMF (60 mL) at room temperature for 75 (compound **1**), 60 (compound **5**) or 120 (compound **7**) minutes. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was treated with water and the products were isolated as described below.

**1-Ethyl-4-nitro-1H-indazole (3) and 2-ethyl-4-nitro-2H-indazole (4).** The resulted yellow precipitate was filtered off. The solid was dried and crystallized twice from methanol to yield 1.55 g of compound **3** as orange plates, mp 107-109 °C. <sup>1</sup>H NMR (300 MHz): δ 1.45 (t, <sup>3</sup>J 7.5 Hz, 3H, CH<sub>3</sub>), 4.59 (q, <sup>3</sup>J 7.5 Hz, 2H, CH<sub>2</sub>), 7.66 (dd, <sup>3</sup>J<sub>67</sub> 8.2 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 6-H), 8.19 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>57</sub> 0.5 Hz, 1H, 5-H), 8.31 (dd, <sup>3</sup>J<sub>67</sub> 8.2 Hz, <sup>5</sup>J<sub>37</sub> 0.8 Hz, 1H, 7-H), 8.52 (d, <sup>5</sup>J<sub>37</sub> 0.8 Hz, 1H, 3-H). <sup>13</sup>C NMR (100 MHz): δ 14.9 (CH<sub>3</sub>), 43.8 (CH<sub>2</sub>), 115.8, 117.9, 118.4, 125.6, 131.4, 139.6, 140.4. Anal. Calcd for C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub> (191.18): C, 56.54; H, 4.74; N, 21.98%. Found: C, 56.37; H, 4.85; N, 22.01%.

The solution from crystallization was evaporated to dryness and the residue was flash-chromatographed twice using benzene – ethyl acetate 10 : 1 as an eluent to yield 0.65 g of compound **3**, mp 107-109 °C (methanol) (total yield: 2.20 g, 38%) and 0.83 g (14%) of 2-ethyl-4-nitroindazole (**4**) as yellow prisms, mp 78-79 °C (methanol) (lit.<sup>20</sup> 75-77 °C). <sup>1</sup>H NMR (300 MHz): δ 1.56 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>), 4.61 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>), 7.50 (dd, <sup>3</sup>J<sub>67</sub> 8.5 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 6-H), 8.20 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>57</sub> 0.5 Hz, 1H, 5-H), 8.21 (dd, <sup>3</sup>J<sub>67</sub> 8.5 Hz, <sup>4</sup>J<sub>57</sub> 0.5 Hz, 1H, 7-H), 8.92 (s, 1H, 3-H). <sup>13</sup>C NMR (100 MHz): δ 15.7 (CH<sub>3</sub>), 48.4 (CH<sub>2</sub>), 113.9, 120.3, 124.2, 124.3, 126.2, 140.0, 149.1.

**2-Ethyl-6-nitro-2H-indazole (6).** The resulted yellow precipitate was crystallized twice from methanol to give 1.67 g (29%) of compound **6** as yellow needles, mp 97-98 °C. <sup>1</sup>H NMR (300 MHz): δ 1.43 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>), 4.62 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>), 7.95 (dd, <sup>3</sup>J<sub>45</sub> 8.8 Hz, <sup>4</sup>J<sub>34</sub> 1.9 Hz, 1H, 4-H), 8.02 (dd, <sup>3</sup>J<sub>45</sub> 8.8 Hz, <sup>4</sup>J<sub>57</sub> 0.7 Hz, 1H, 5-H), 8.32 (d, <sup>4</sup>J<sub>57</sub> 0.7 Hz, 1H, 7-H), 8.76-8.78 (m, 1H, 3-H). <sup>13</sup>C NMR (100 MHz): δ 14.9 (CH<sub>3</sub>), 43.6 (CH<sub>2</sub>), 106.7, 114.7, 122.1, 126.5, 133.3, 137.4, 145.8. Anal. Calcd for C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub> (191.18): C, 56.54; H, 4.74; N, 21.98%. Found: C, 56.74; H, 4.80; N, 21.69%.

The filtrate from crystallization contained a mixture of compound **6** and its 1-ethyl isomer that was not further separated.

**1-Ethyl-7-nitro-1H-indazole (8) and 2-ethyl-7-nitro-2H-indazole (9).** The resulted yellow precipitate was flash-chromatographed using hexanes – ethyl acetate 5 : 1 as an eluent. The first fraction, after crystallization from dilute methanol, gave 2.11 g (37%) of compound **8** as yellow needles, mp 71-72 °C. <sup>1</sup>H NMR (300 MHz): δ 1.55 (t, <sup>3</sup>J 7.1 Hz, 3H, CH<sub>3</sub>), 4.52 (q, <sup>3</sup>J 7.1 Hz,

2H, CH<sub>2</sub>), 7.35 (dd, <sup>3</sup>J<sub>45</sub> 8.0 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 5-H), 8.20 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>46</sub> 0.8 Hz, 1H, 6-H), 8.26 (dd, <sup>3</sup>J<sub>45</sub> 8.0 Hz, <sup>4</sup>J<sub>46</sub> 0.8 Hz, 1H, 4-H), 8.44 (s, 1H, 3-H). <sup>13</sup>C NMR (100 MHz): δ 15.3 (CH<sub>3</sub>), 47.3 (CH<sub>2</sub>), 120.1, 124.6, 128.5, 128.7, 129.4, 134.8, 134.9. Anal. Calcd for C<sub>9</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub> (191.18): C, 56.54; H, 4.74; N, 21.98%. Found: C, 56.27; H, 4.63; N, 22.23%.

The second fraction was further flash-chromatographed using benzene – ethyl acetate 10 : 1 as an eluent. The separation resulted in recovery of the starting material **7**: 0.98 g (20%), mp 188-189 °C (lit.<sup>21</sup> mp 186.5-187.5 °C). The third fraction was flash-chromatographed using hexanes – ethyl acetate 2 : 1 as an eluent. Crystallization from methanol gave 1.12 g (20%) of 2-ethyl-7-nitroindazole (**9**) as yellow plates, mp 80-81 °C (lit.<sup>18</sup> 74-76 °C). <sup>1</sup>H NMR (300 MHz): δ 1.56 (t, <sup>3</sup>J 7.4 Hz, 3H, CH<sub>3</sub>), 4.58 (q, <sup>3</sup>J 7.4 Hz, 2H, CH<sub>2</sub>), 7.26 (dd, <sup>3</sup>J<sub>45</sub> 8.2 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 5-H), 8.27 (dd, <sup>3</sup>J<sub>45</sub> 8.2 Hz, <sup>4</sup>J<sub>46</sub> 0.8 Hz, 1H, 4-H), 8.31 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>46</sub> 0.8 Hz, 1H, 6-H), 8.82 (s, 1H, 3-H). <sup>13</sup>C NMR (100 MHz): δ 15.6 (CH<sub>3</sub>), 48.4 (CH<sub>2</sub>), 119.6, 124.6, 125.2, 126.3, 129.9, 136.5, 139.4.

**Alkylation of 4-nitro-1H-benzotriazole (10).** A mixture of 4-nitro-1H-benzotriazole (**10**) (2.46 g, 15 mmol), bromoethane (1.96 g, 18 mmol), finely powdered K<sub>2</sub>CO<sub>3</sub> (7.0 g), and tetrabutylammonium bromide (50 mg) was stirred vigorously in DMF (30 mL) at 40 °C for 90 minutes. The reaction mixture was diluted with water (200 mL) and the resulted precipitate was filtered off (solid A). The filtrate was extracted with dichloromethane (3 x 20 mL), the combined organic layers were washed with water and dried over MgSO<sub>4</sub>. The solvent was distilled off to give solid B as yellow crystals. Solid A consisted of two isomers while solid B contained, apart from these isomers, also a third compound.

Solid A was treated with concd HCl (50 mL) and the resulted suspension was stirred at room temperature for 30 minutes. The insoluble part was filtered off and crystallized from ethanol to give 0.52 g of 2-ethyl-4-nitro-2H-benzotriazole (**12**) as yellow plates, mp 101-102 °C. <sup>1</sup>H NMR (400 MHz): δ 1.66 (t, <sup>3</sup>J 7.3 Hz, 3H, CH<sub>3</sub>), 4.93 (q, <sup>3</sup>J 7.3 Hz, 2H, CH<sub>2</sub>), 7.68 (dd, <sup>3</sup>J<sub>67</sub> 8.5 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 6-H), 8.46 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>57</sub> 0.8 Hz, 1H, 5-H), 8.49 (dd, <sup>3</sup>J<sub>67</sub> 8.5 Hz, 1H, <sup>4</sup>J<sub>57</sub> 0.8 Hz, 7-H). <sup>13</sup>C NMR (100 MHz): δ 14.8 (CH<sub>3</sub>), 52.1 (CH<sub>2</sub>), 124.7, 125.5, 126.5, 136.3, 137.1, 145.8. Anal. Calcd for C<sub>8</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub> (192.17): C, 50.00; H, 4.19; N, 29.16%. Found: C, 50.26; H, 4.38; N, 28.84%.

The filtrate after the separation of compound **12** was diluted with water (100 mL) and refluxed for a short time. After cooling, it was extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over MgSO<sub>4</sub>. The residue after evaporation of the solvent was chromatographed using hexane – ethyl acetate 3 : 1 as an eluent. The first fraction afforded 0.15 g of 1-ethyl-7-nitro-1H-benzotriazole (**13**) as yellow needles (ethanol), mp 98-99 °C. <sup>1</sup>H NMR (400 MHz): δ 1.51 (t, <sup>3</sup>J 7.1 Hz, 3H, CH<sub>3</sub>), 4.93 (q, <sup>3</sup>J 7.1 Hz, 2H, CH<sub>2</sub>), 7.63 (dd, <sup>3</sup>J<sub>45</sub> 8.2 Hz, <sup>3</sup>J<sub>56</sub> 7.9 Hz, 1H, 5-H), 8.44 (dd, <sup>3</sup>J<sub>56</sub> 7.9 Hz, <sup>4</sup>J<sub>46</sub> 0.9 Hz, 1H, 6-H), 8.58 (dd, <sup>3</sup>J<sub>45</sub> 8.2 Hz, <sup>4</sup>J<sub>46</sub> 0.9 Hz, 1H, 4-H). <sup>13</sup>C NMR (100 MHz): δ 16.0 (CH<sub>3</sub>), 47.0 (CH<sub>2</sub>), 123.7, 124.6, 125.6, 127.2, 134.9, 148.5. Anal. Calcd for C<sub>8</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub> (192.17): C, 50.00; H, 4.19; N, 29.16%. Found: C, 50.27; H, 4.02; N, 29.20%. The third fraction was crystallized from ethanol to yield 0.49 g of compound **12**, mp 101-102 °C.

Solid B (1.0 g) was chromatographed using hexane – ethyl acetate 3 : 1 as an eluent. The first fraction was crystallized from ethanol to yield 0.16 g of compound **13** (total yield: 0.31 g, 11%). The third fraction after crystallization from ethanol afforded 0.09 g of compound **12** (total yield: 1.10 g, 38%). The fourth fraction was crystallized from ethanol to give 0.35 g (12%) of 1-ethyl-4-nitro-1*H*-benzotriazole (**11**) as yellow plates, mp 146-147 °C. <sup>1</sup>H NMR (400 MHz): δ 1.56 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>), 4.87 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>), 7.80 (dd, <sup>3</sup>J<sub>67</sub> 8.2 Hz, <sup>3</sup>J<sub>56</sub> 7.7 Hz, 1H, 6-H), 8.33 (dd, <sup>3</sup>J<sub>56</sub> 7.7 Hz, <sup>4</sup>J<sub>57</sub> 0.8 Hz, 1H, 5-H), 8.47 (dd, <sup>3</sup>J<sub>67</sub> 8.2 Hz, <sup>4</sup>J<sub>57</sub> 0.8 Hz, 1H, 7-H). <sup>13</sup>C NMR (100 MHz): δ 14.9 (CH<sub>3</sub>), 43.5 (CH<sub>2</sub>), 118.7, 121.5, 126.8, 135.0, 137.5, 137.9. Anal. Calcd for C<sub>8</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub> (192.17): C, 50.00; H, 4.19; N, 29.16%. Found: C, 50.19; H, 4.35; N, 28.91%.

**Hydrogenation of 1-ethyl-7-nitro-1*H*-benzotriazole (13).** A solution of compound **13** (116 mg, 0.6 mmol) in ethanol (2 mL) was added to a suspension of iron (123 mg, 2.2 mmol) in acetic acid (3 mL). The resulted mixture was refluxed for 10 hours, ethanol was distilled off, and the residue was diluted with water (10 mL) and extracted with ethyl acetate (2 x 10 mL). The combined extracts were dried over MgSO<sub>4</sub>, the solvent was removed and the residue was chromatographed using CH<sub>2</sub>Cl<sub>2</sub> – methanol 10 : 1 as an eluent. Crystallization from dilute methanol afforded 52 mg (52%) of 7-amino-1-ethyl-1*H*-benzotriazole (**14**) as beige needles, mp 53-54 °C. <sup>1</sup>H NMR (400 MHz): δ 1.46 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>), 4.89 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>), 5.54 (s, 2H, NH<sub>2</sub>), 6.68 (dd, <sup>3</sup>J<sub>56</sub> 7.5 Hz, <sup>4</sup>J<sub>46</sub> 0.7 Hz, 1H, 6-H), 7.08 (dd, <sup>3</sup>J<sub>45</sub> 8.3 Hz, <sup>3</sup>J<sub>56</sub> 7.5 Hz, 1H, 5-H), 7.21 (dd, <sup>3</sup>J<sub>45</sub> 8.3 Hz, <sup>4</sup>J<sub>46</sub> 0.7 Hz, 1H, 4-H). <sup>13</sup>C NMR (100 MHz): δ 17.0 (CH<sub>3</sub>), 44.5 (CH<sub>2</sub>), 107.0, 110.3, 124.1, 125.1, 134.2, 147.5. Anal. Calcd for C<sub>8</sub>H<sub>10</sub>N<sub>4</sub> (162.19): C, 59.24; H, 6.21; N, 34.55%. Found: C, 59.13; H, 6.49; N, 34.38%.

**Vicarious nucleophilic substitution of hydrogen. Method A.** Finely powdered KOH (400 mg) was added in one portion to a stirred solution of carbanion precursor **15** or **16** (1 mmol) and nitrobenzazole (1 mmol) in dry DMSO (5 mL). The resulting dark coloured mixture was vigorously stirred for 30 min (unless otherwise stated) at 22 °C, quenched with 3% HCl (30 mL) and extracted twice with CH<sub>2</sub>Cl<sub>2</sub> (30 and 20 mL). The extract was washed with water, dried and the solvent was removed under vacuum. The purification procedure is given at the description of individual compounds.

**Method B.** A solution of carbanion precursor **15** (1 mmol) and nitrobenzazole (1 mmol) in dry DMF (4 mL) was added to a stirred solution of t-BuOK (336 mg, 3 mmol) in dry DMF (3 mL). The resulted mixture was stirred for 30 min (unless otherwise stated) at -40 °C, quenched with 3% HCl (30 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 and 20 mL). The extract was washed with water, dried over MgSO<sub>4</sub> and the solvent was removed under vacuum. The purification procedure is given at the description of individual compounds.

**Method C.** A solution of sulphone **15** (1 mmol) and nitroarene (1 mmol) in dry THF (7 mL) was added dropwise to a solution of t-BuOK (336 mg, 3 mmol) in dry THF (3 mL). The reaction was carried out as in method B.

**1-Methyl-4-nitro-7-[1-(phenylsulfonyl)propyl]-1*H*-indazole (17).** **Method A.** The residue was flash-chromatographed using hexanes – ethyl acetate 2 : 1 as an eluent to give compound **17** as

yellow needles, 179 mg (50%), mp 179-181 °C (ethanol).  $^1\text{H}$  NMR (300 MHz):  $\delta$  0.79 (t,  $^3J$  7.3 Hz, 3H,  $\text{CH}_3\text{C}$ ), 2.13-2.31 (m, 2H,  $\text{CH}_2$ ), 4.38 (s, 2H,  $\text{CH}_3\text{N}$ ), 5.41 (dd,  $^3J_{\text{syn}}$  10.4 Hz,  $^3J_{\text{anti}}$  4.7 Hz, 1H, CH), 7.58-7.80 (m, 6H, Ph and 6-H), 8.20 (d,  $^3J$  8.0 Hz, 1H, 5-H), 8.53 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  10.7 ( $\text{C-CH}_3$ ), 22.2 ( $\text{CH}_2$ ), 40.4 ( $\text{N-CH}_3$ ), 64.7 (CH), 117.6, 118.1, 122.9, 127.1, 128.9, 129.4, 131.1, 134.5, 136.4, 139.6, 140.6. Anal. Calcd for  $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_4\text{S}$  (359.39): C, 56.81; H, 4.77; N, 11.69%. Found: C, 57.04; H, 4.80; N, 11.52%.

**1-Ethyl-4-nitro-7-[1-(phenylsulfonyl)propyl]-1H-indazole (18). Method A.** Reaction time: 50 min. The residue was flash-chromatographed using hexanes – ethyl acetate 3 : 1 as an eluent. Crystallization from 80% ethanol gave compound **18** as small yellow prisms, 132 mg (35%), mp 119-121 °C.  $^1\text{H}$  NMR (300 MHz):  $\delta$  0.82 (t,  $^3J$  7.4 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{C}$ ), 1.43 (t,  $^3J$  7.1 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{N}$ ), 2.24-2.33 (m, 2H,  $\text{CH}_2\text{C}$ ), 4.57-4.77 (m, 2H,  $\text{CH}_2\text{N}$ ), 5.22 (dd,  $^3J$  7.7 and 7.4 Hz, 1H, CH), 7.57-7.78 (m, 6H, Ph and 6-H), 8.20 (d,  $^3J$  8.2 Hz, 1H, 5-H), 8.58 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  10.8 ( $\text{CH}_3$ ), 15.3 ( $\text{CH}_3$ ), 22.2 ( $\text{C-CH}_2$ ), 47.0 ( $\text{N-CH}_2$ ), 65.3 (CH), 117.8, 118.1, 122.8, 127.2, 129.0, 129.4, 131.7, 134.6, 136.2, 139.8, 139.9. MS  $m/z$  (%): 373 (4), 233 (15), 232 (100,  $\text{M} - \text{PhSO}_2$ ), 204 (4), 186 (6), 157 (4), 130 (3). Anal. Calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$  (373.44): C, 57.89; H, 5.13; N, 11.25%. Found: C, 58.01; H, 5.06; N, 11.50%.

**Method B.** Reaction time: 20 min. Purification procedure like in method A. Yield: 111 mg (30%).

**1-Ethyl-4-nitro-5-p-toluenesulfonylmethyl-1H-indazole (19) and 1-Ethyl-4-nitro-7-p-toluenesulfonylmethyl-1H-indazole (20). Method C.** Reaction time: 60 min. The residue was flash-chromatographed using hexane – ethyl acetate 2 : 1 as an eluent. Compound **20** (43 mg, 12 %) was obtained as orange plates, mp 201-203 °C (ethanol).  $^1\text{H}$  NMR (300 MHz):  $\delta$  1.47 (t,  $^3J$  7.2 Hz, 3H,  $\text{CH}_3\text{CH}_2$ ), 2.43 (s, 3H,  $\text{CH}_3\text{Ar}$ ), 4.71 (q,  $^3J$  7.2 Hz, 2H,  $\text{CH}_2\text{N}$ ), 5.29 (s, 2H,  $\text{CH}_2\text{SO}_2$ ), 7.29 (d,  $^3J$  8.0 Hz, 1H, 6-H), 7.44-7.46 (m, 2H, Ts), 7.66-7.69 (m, 2H, Ts), 8.09 (d,  $^3J$  8.0 Hz, 1H, 5-H), 8.61 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  15.2 ( $\text{CH}_3\text{CH}_2$ ), 21.1 ( $\text{CH}_3\text{Ar}$ ), 46.1 ( $\text{CH}_2\text{N}$ ), 57.8 ( $\text{CH}_2\text{SO}_2$ ), 117.7, 117.8, 119.4, 128.3, 129.9, 131.5, 131.8, 135.1, 139.2, 139.9, 145.1. Anal. Calcd for  $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_4\text{S}$  (359.39): C, 56.81; H, 4.77; N, 11.69%. Found: C, 57.02; H, 4.55; N, 11.49%.

**Compound 19** (156 mg, 43 %) was obtained as yellow needles, mp 167-168 °C (80% ethanol).  $^1\text{H}$  NMR (300 MHz):  $\delta$  1.42 (t,  $^3J$  7.1 Hz, 3H,  $\text{CH}_3\text{CH}_2$ ), 2.40 (s, 3H,  $\text{CH}_3\text{Ar}$ ), 4.53 (q,  $^3J$  7.1 Hz, 2H,  $\text{CH}_2\text{N}$ ), 5.26 (s, 2H,  $\text{CH}_2\text{SO}_2$ ), 7.36 (d,  $^3J$  8.7 Hz, 1H, 6-H), 7.39-7.42 (m, 2H, Ts), 7.53-7.57 (m, 2H, Ts), 8.12 (dd,  $^3J$  8.7 Hz,  $^5J$  0.5 Hz, 1H, 7-H), 8.29 (d,  $^5J$  0.5 Hz, 1H, 3-H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  14.8 ( $\text{CH}_3\text{CH}_2$ ), 21.1 ( $\text{CH}_3\text{Ar}$ ), 43.7 ( $\text{CH}_2\text{N}$ ), 57.0 ( $\text{CH}_2\text{SO}_2$ ), 115.4, 116.8, 117.3, 127.9, 129.9, 131.0, 131.6, 135.3, 140.1, 140.8, 144.8. Anal. Calcd for  $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_4\text{S}$  (359.39): C, 56.81; H, 4.77; N, 11.69%. Found: C, 56.87; H, 4.95; N, 11.83%.

**2-Ethyl-4-nitro-5-[1-(phenylsulfonyl)propyl]-2H-indazole (21) and 2-Ethyl-4-nitro-7-[1-(phenylsulfonyl)propyl]-2H-indazole (22). Method A.** The residue was flash-chromatographed using hexanes – ethyl acetate 2 : 1 as an eluent. The fraction containing compound **22** was treated with diethyl ether and the resulted solid was filtered off to give 178 mg (49%) of **22** as small yellow plates, mp 114-116 °C.  $^1\text{H}$  NMR (400 MHz):  $\delta$  0.81 (t,  $^3J$  7.3 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{C}$ ),

1.40 (t,  $^3J$  7.3 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{N}$ ), 2.29-2.50 (m, 2H,  $\text{CH}_2\text{C}$ ) 4.37-4.47 (m, 2H,  $\text{CH}_2\text{N}$ ), 5.14 (dd,  $^3J_{\text{syn}}$  11.3 Hz,  $^3J_{\text{anti}}$  4.4 Hz, 1H, CH), 7.34-7.54 (2 x m, 5H, Ph), 7.59 (d,  $^3J$  8.0 Hz, 1H, 6-H), 8.24 (d,  $^3J$  8.0 Hz, 1H, 5-H), 8.78 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  11.2 ( $\text{CH}_3$ ), 15.6 ( $\text{CH}_3$ ), 20.7 (C- $\text{CH}_2$ ) 48.4 (N- $\text{CH}_2$ ), 65.8 (CH), 113.3, 120.2, 123.8, 124.6, 128.5, 128.7, 130.9, 133.8, 137.2, 139.7, 148.9. Anal. Calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$  (373.44): C, 57.89; H, 5.13; N, 11.25%. Found: C, 58.09; H, 5.28; N, 11.12%.

**Method B.** Reaction time: 40 min. LPLC and hexanes - ethyl acetate 2 : 1 as an eluent was used to separate the reaction mixture. Compound **22** (36 mg, 10%) was obtained as yellow microcrystalline solid, mp 114-116 °C. Compound **21** (91 mg, 25%) was obtained as yellow prisms, mp 156-157 °C (ethanol).  $^1\text{H}$  NMR (600 MHz):  $\delta$  0.82 (t,  $^3J$  7.4 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{C}$ ), 1.52 (t,  $^3J$  7.3 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{N}$ ), 2.09-2.30 (m, 2H,  $\text{CH}_2\text{C}$ ) 4.50-4.56 (m, 2H,  $\text{CH}_2\text{N}$ ), 5.41 (dd,  $^3J_{\text{syn}}$  10.9 Hz,  $^3J_{\text{anti}}$  4.3 Hz, 1H, CH), 7.51-7.58 (m, 5H, Ph and 6-H), 7.67-7.70 (m, 1H, Ph), 8.11 (d,  $^3J$  9.0 Hz, 1H, 7-H), 8.61 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  10.9 ( $\text{CH}_3$ ), 15.5 ( $\text{CH}_3$ ), 20.9 (C- $\text{CH}_2$ ) 48.4 (N- $\text{CH}_2$ ), 64.5 (CH), 115.1, 121.2, 123.6, 124.4, 124.6, 128.2, 129.3, 134.2, 140.0, 142.5, 148.0. MS  $m/z$  (%): 373 (4), 233 (15), 232 (100, M -  $\text{PhSO}_2$ ), 204 (4), 186 (6), 157 (4), 130 (3). Anal. Calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$  (373.44): C, 57.89; H, 5.13; N, 11.25%. Found: C, 58.01; H, 5.06; N, 11.50%.

**1-Ethyl-7-nitro-4-[1-(phenylsulfonyl)propyl]-1H-indazole (23).** **Method A.** Flash-chromatography using hexanes – ethyl acetate 2 : 1 as an eluent afforded 148 mg (40%) of compound **23** as light orange prisms, mp 134-135 °C (methanol).  $^1\text{H}$  NMR (300 MHz):  $\delta$  0.76 (t,  $^3J$  7.4 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{C}$ ), 1.27 (t,  $^3J$  7.1 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{N}$ ), 2.20-2.36 (m, 2H,  $\text{CH}_2\text{C}$ ) 4.42 (q,  $^3J$  7.1 Hz, 2H,  $\text{CH}_2\text{N}$ ), 5.28 (dd,  $^3J_{\text{syn}}$  10.4 Hz,  $^3J_{\text{anti}}$  4.7 Hz, 1H, CH), 7.36 (d,  $^3J$  8.0 Hz, 1H, 5-H), 7.44-7.49 (m, 2H, Ph), 7.56-7.66 (m, 3H, Ph), 8.20 (d,  $^3J$  8.0 Hz, 1H, 6-H), 8.50 (s, 1H, 3-H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  10.8 ( $\text{CH}_3$ ), 15.1 ( $\text{CH}_3$ ), 21.0 (C- $\text{CH}_2$ ) 47.3 (N- $\text{CH}_2$ ), 67.1 (CH), 120.0, 124.5, 128.5, 129.0, 129.9, 133.4, 133.8, 134.0, 134.5, 136.9. As one quaternary signal was missing, the  $^{13}\text{C}$  NMR spectrum (150 MHz) was additionally registered in acetone- $d_6$ :  $\delta$  11.4 ( $\text{CH}_3\text{CH}_2\text{C}$ ), 15.6 ( $\text{CH}_3\text{CH}_2\text{N}$ ), 22.3 ( $\text{CH}_2\text{C}$ ), 48.5 ( $\text{CH}_2\text{N}$ ), 69.4 (CH), 121.1, 125.0, 129.1, 129.7, 130.3, 131.2, 134.1, 134.66, 134.70, 136.0, 138.7. Anal. Calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$  (373.44): C, 57.89; H, 5.13; N, 11.25%. Found: C, 58.11; H, 5.01; N, 11.40%.

Method B. Purification as in method A afforded 117 mg (31%) of compound **23**.

**1-Ethyl-4-nitro-7-[1-(phenylsulfonyl)propyl]-1H-benzotriazole (24).** **Method A.** Flash-chromatography using hexanes – ethyl acetate 1 : 2 as an eluent gave 175 mg (46%) of compound **24** as pale yellow needles, mp 160-162 °C (ethanol).  $^1\text{H}$  NMR (400 MHz):  $\delta$  0.83 (t,  $^3J$  7.4 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{C}$ ), 1.56 (t,  $^3J$  7.2 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{N}$ ), 2.24-2.36 (m, 2H,  $\text{CH}_2\text{C}$ ) 4.84-4.99 (m, 2H,  $\text{CH}_2\text{N}$ ), 5.21 (dd,  $^3J_{\text{syn}}$  8.9 Hz,  $^3J_{\text{anti}}$  6.4 Hz, 1H, CH), 7.57-7.66 (m, 4H, Ph), 7.72 (d,  $^3J$  8.4 Hz, 1H, 6-H), 7.72-7.78 (m, 1H, Ph), 8.33 (d,  $^3J$  8.4 Hz, 1H, 5-H).  $^{13}\text{C}$  NMR (100 MHz):  $\delta$  10.7 ( $\text{CH}_3$ ), 15.3 ( $\text{CH}_3$ ), 21.9 (C- $\text{CH}_2$ ) 45.9 (N- $\text{CH}_2$ ), 65.3 (CH), 121.2, 123.4, 128.1, 129.1, 129.4, 134.68, 134.74, 135.8, 138.1, 138.3. Anal. Calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}_4\text{S}$  (374.41): C, 54.53; H, 4.85; N, 14.96%. Found: C, 54.28; H, 4.99; N, 14.76%.

**Method B.** Flash-chromatography using hexanes – ethyl acetate 2 : 1 as an eluent gave 133 mg (35%) of compound **24**.

**2-Ethyl-4-nitro-5-[1-(phenylsulfonyl)propyl]-2H-benzotriazole (25) and 2-ethyl-4-nitro-7-[1-(phenylsulfonyl)propyl]-2H-benzotriazole (26).** **Method A.** The residue was chromatographed using hexanes – ethyl acetate 1 : 2 as an eluent to yield 215 mg (55%) of compound **26** as pale yellow needles, mp 134-136 °C (ethanol). <sup>1</sup>H NMR (400 MHz): δ 0.83 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>C), 1.51 (t, <sup>3</sup>J 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>N), 2.44 (quintet, 2H, CH<sub>2</sub>C) 4.74 (q, <sup>3</sup>J 7.1 Hz, 2H, CH<sub>2</sub>N), 5.11 (dd, <sup>3</sup>J 7.7 and 7.4 Hz, 1H, CH), 7.39-7.61 (3 x m, 5H, Ph), 7.73 (d, <sup>3</sup>J 8.1 Hz, 1H, 6-H), 8.51 (d, <sup>3</sup>J 8.1 Hz, 1H, 5-H). <sup>13</sup>C NMR (100 MHz): δ 11.1 (CH<sub>3</sub>), 14.7 (CH<sub>3</sub>), 20.4 (C-CH<sub>2</sub>) 52.1 (N-CH<sub>2</sub>), 67.4 (CH), 124.6, 125.8, 128.7, 128.9, 131.5, 134.0, 135.8, 136.8, 136.9, 145.8. Anal. Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S (374.41): C, 54.53; H, 4.85; N, 14.96%. Found: C, 54.59; H, 4.62; N, 14.79%.

**Method B.** The residue was chromatographed using hexanes – ethyl acetate 4 : 1 as an eluent to yield 150 mg (38%) of compound **25** as small yellow plates, mp 107-109 °C (ethanol-hexanes). <sup>1</sup>H NMR (400 MHz): δ 0.80 (t, <sup>3</sup>J 7.4 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>C), 1.61 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>N), 2.22-2.36 (m, 2H, CH<sub>2</sub>C) 4.86 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>N), 4.90 (dd, <sup>3</sup>J<sub>syn</sub> 10.9 Hz, <sup>3</sup>J<sub>anti</sub> 4.4 Hz, 1H, CH), 7.53-7.76 (2 x m + d, 6H, Ph + 6-H), 8.39 (d, <sup>3</sup>J 9.0 Hz, 1H, 7-H). <sup>13</sup>C NMR (100 MHz): δ 10.8 (CH<sub>3</sub>), 14.6 (CH<sub>3</sub>), 21.0 (C-CH<sub>2</sub>) 52.2 (N-CH<sub>2</sub>), 65.0 (CH), 123.0, 123.8, 125.4, 128.4, 129.5, 134.5, 136.2, 136.6, 140.0, 144.6. Anal. Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S (374.41): C, 54.53; H, 4.85; N, 14.96%. Found: C, 54.80; H, 4.58; N, 14.84%.

The fraction containing a mixture of isomers **25** and **26** was not further separated.

**1-Ethyl-7-nitro-4-[1-(phenylsulfonyl)propyl]-1H-benzotriazole (27).** **Method A.** The residue was chromatographed using hexanes – ethyl acetate 1 : 2 as an eluent to yield 230 mg (59%) of compound **27** as pale yellow needles, mp 143-145 °C (ethanol). <sup>1</sup>H NMR (400 MHz): δ 0.79 (t, <sup>3</sup>J 7.4 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>C), 1.45 (t, <sup>3</sup>J 7.2 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>N), 2.34-2.47 (m, 2H, CH<sub>2</sub>C) 4.87 (q, <sup>3</sup>J 7.2 Hz, 2H, CH<sub>2</sub>N), 5.40 (dd, <sup>3</sup>J<sub>syn</sub> 9.6 Hz, <sup>3</sup>J<sub>anti</sub> 6.0 Hz, 1H, CH), 7.44-7.64 (2 x m, 5H, Ph), 7.68 (d, <sup>3</sup>J 8.1 Hz, 1H, 5-H), 8.48 (d, <sup>3</sup>J 8.1 Hz, 1H, 6-H). <sup>13</sup>C NMR (100 MHz): δ 11.1 (CH<sub>3</sub>), 15.9 (CH<sub>3</sub>), 20.9 (C-CH<sub>2</sub>) 47.1 (N-CH<sub>2</sub>), 66.0 (CH), 123.4, 124.2, 125.5, 128.5, 129.1, 132.1, 134.1, 134.7, 136.7, 148.5. Anal. Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S (374.41): C, 54.53; H, 4.85; N, 14.96%. Found: C, 54.69; H, 4.76; N, 15.17%.

**X-ray structure analysis of 18.** Crystal data for C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>S: monoclinic, space group Cc, a=13.5565(6) Å, b=15.689(3) Å, c=8.1832(3), β=97.851(3), V=1712.90(12) Å<sup>3</sup>, Z=1, λ=0.71073 Å. Data were collected at 130 K for a crystal with dimensions 0.25 x 0.2 x 0.1 mm with a KM4-CCD Oxford diffractometer using graphite monochromated Mo Kα radiation. Cell parameters were obtained from 2852 independent reflections. The crystal structures have been solved with the SHELXS-97 and refined with the SHELXL-97 program packages.<sup>22</sup>

Crystallographic data for the structure of **18** in CIF format have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 869881.



**Theoretical calculations.** Density functional calculations were executed and the geometries of compounds were optimized at the DFT level of theory using the Gaussian 09 program,<sup>23</sup> B3LYP functional, 6-31 G (d,p) basis set, and Conductor-like Polarizable Continuum Model (CPCM, DMSO as solvent).<sup>23-26</sup> NBO calculations were carried out as implemented in the Gaussian 09.

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## Graphical Abstract

**On the reactions of tertiary carbanions with some nitroindazoles and nitrobenzotriazoles**

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