ELSEVIER

Journal of Fluorine Chemistry 81 (1997) 205–210

JOURNAL OF FLUORINE CHEMISTRY

Organofluorine compounds and fluorinating agents Part 16 [1]: Monoalkylations and cycloadditions with *trans*-3,3,3-trifluoro-1-nitropropene

Oliver Klenz[a 2], Rainer Evers [a], Ralf Miethchen [a,*], Manfred Michalik [b]

[a] *Universität Rostock, Fachbereich Chemie, 18051 Rostock, Germany*

[b] *Institut für Organische Katalyseforschung an der Universität Rostock, 18055 Rostock, Germany*

Received 22 April 1996; accepted 31 July 1996

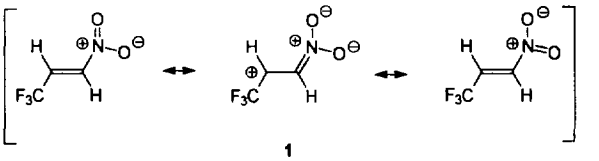
Abstract

Monoalkylations of different nucleophilic azoles were investigated with the electron-deficient *trans*-3,3,3-trifluoro-1-nitropropene (**1**) as alkylating reagent without addition of any catalyst. In each case, the bonding of the alkene at the azole occurs regioselectively at the trifluoromethyl-substituted C atom of the alkene, whereas the azoles react at different positions depending on the electron density of the heterocycles. Thus, 1-methyl-pyrrole (**2**) reacted with **1** under C–C bond formation giving the two regioisomers 2-(1-trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (**3**) (major product) and 3-(1-trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (**4**). The less nucleophilic pyrazole (**5**), 1,2,4-triazole (**7**), 3-bromo-1,2,4-triazole (**9**), and 3,5-dibromo-1,2,4-triazole (**12**) gave exclusively the corresponding *N*-alkyl azoles 1-(1-trifluoromethyl-2-nitroethyl)-pyrazole (**6**), 1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**8**), 3-bromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**10**)/5-bromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**11**), and 3,5-dibromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**13**), respectively. The enantiomeric pairs of the chiral monoalkyl-azoles could not be separated. Moreover, we used *trans*-3,3,3-trifluoro-1-nitropropene (**1**) as a dienophile in Diels-Alder cycloadditions with cyclopentadiene (**14**), cyclohexa-1,3-diene (**16**), and furan (**18**). Two diastereomeric products (**15A/15B, 17A/17B**, and **19A/19B**), which could not be separated by column chromatography, are formed from each diene. All compounds were characterized by ^{1}H, ^{13}C, and ^{19}F NMR data.

Keywords: Azoles; Alkylation; Trifluoromethyl derivatives; Cycloaddition; NMR spectroscopy

1. Introduction

The synthesis of organofluorine compounds using fluorine-containing 'building blocks' is an efficient alternative to the direct introduction of fluoride with fluorinating reagents. The prochiral *trans*-3,3,3-trifluoro-1-nitropropene (**1**), which was synthesized for the first time by Shechter et al. [2], meets the requirements of such a 'building block'. Recently, the compound was used for C-alkylations of pyrrole and indole working without addition of any catalyst [3]. The *trans*-3,3,3-trifluoro-1-nitropropene (**1**) can be considered as a higher reactive 'Michael acceptor' [3], i.e. it is regioselectively attacked by nucleophiles at the C atom 2 (Scheme 1). The electron-deficient alkene **1** can also be used as a dienophile/dipolarophile in cycloadditions.



1

Scheme 1.

Nitroalkanes have proven to be valuable intermediates because of their facile conversion into corresponding amines, nitroaldol reactions, and reductive cleavage of the nitro groups [3,4]. We would like to use the advantageous arrangement of *trans*-3,3,3-trifluoro-1-nitropropene (**1**) to build up condensed heterocycles, e.g. alkaloid-like active substances after reduction of the nitro group to an amino function. Given this background, we investigated further alkylations of some azoles with **1**. Pyrrole, pyrazole (**5**), 1,2,4-triazole (**7**), 3-bromo-1,2,4-triazole (**9**), and 3,5-dibromo-1,2,4-triazole (**12**) (having in this order successively lowered π-electron density [5]) were selected to study aspects of the reactivity and regioselectivity of the reactions. The tendency of the pK_a

* Corresponding author.

[1] For Part 15, see Ref. [1].

[2] In deep grief for our deceased young colleague Dipl. Chem. Oliver Klenz.

PII S0022-1139(96)03522-1

values of these weak acidic heterocycles (pyrrole 17.51 [6], **5** 14.18 [7], **7** 10.26 [8], **9** 8.00 [8], and **12** 5.23 [8]) correlates with the successive decrease in their nucleophilic potential.

Furthermore, some cycloadditions were investigated using the *trans*-3,3,3-trifluoro-1-nitropropene (**1**) as dienophile.

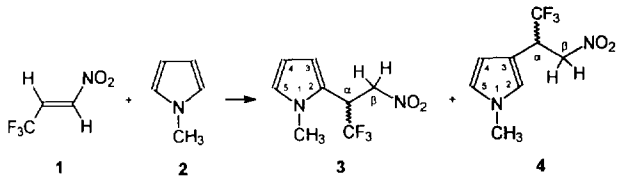
2. Results and discussion

1-Methyl-pyrrole (**2**), pyrazole (**5**), 1,2,4-triazole (**7**), 3-bromo-1,2,4-triazole (**9**), and 3,5-dibromo-1,2,4-triazole (**12**) could be alkylated with *trans*-3,3,3-trifluoro-1-nitropropene (**1**) without addition of a catalyst. The more nucleophilic azoles **2**, **5** and **7** reacted readily under very mild conditions (less than or equal to 20 °C), whereas the triazoles **9** and **12** required longer heating (24–48 h) of the reaction mixtures in an autoclave at 120 °C (argon, 70 bar). C-alkylations could only be achieved with 1-methyl-pyrrole (**2**) (moreover, pyrrole and indole [3]). The other azoles gave N-alkylated products. It is important to point out that the alkylations of the azoles with the alkene **1** run regioselectively with regard to the trifluoromethyl-substituted C atom of **1**. This centre is the most electrophilic because of the mesomeric effect of the nitro group (vinylogen system), Scheme 1. The electrophilic attack takes place on an electron-rich ring C atom or on a 'pyridine N atom' of the heterocyclic ring.

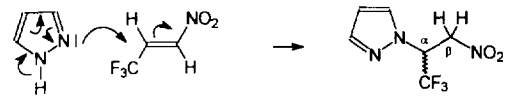
1-Methyl-pyrrole (**2**) reacted predominantly at the ring C atom 2(5) giving the 2-(1-trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (**3**) in a yield of 50%. In addition, only small amounts (4%) of the 3-(1-trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (**4**) were obtained (Scheme 2). The amount of the by-product decreased in favour of the major product **3** when the temperature of the reaction mixture was lowered.

The less nucleophilic azoles **5**, **7**, **9** and **12** were exclusively alkylated at a ring nitrogen atom giving the N-substituted products **6**, **8**, **10**, **11** and **13** in good to moderate yields; for the structure formulae see Schemes 3 and 4. With the exception of the monobromo derivative **9** which formed the two regioisomers **10** and **11**, these azoles gave only one product. However, each of these separated compounds is, of course, a pair of enantiomers.

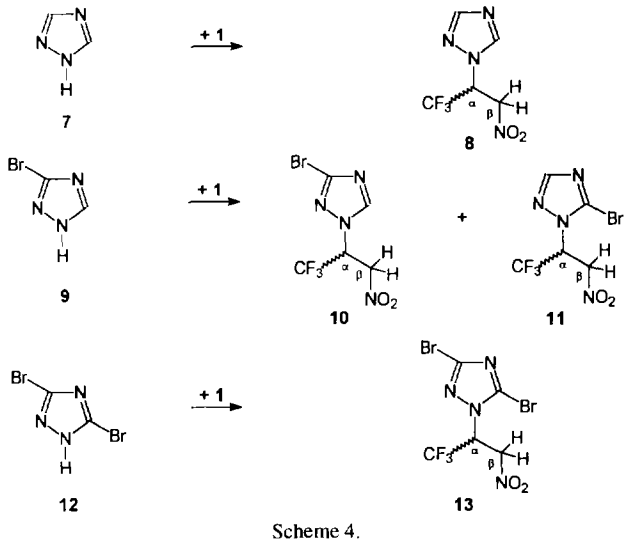
The structures of the alkylated azoles are supported by their NMR data. Thus, the location of the C atoms of the introduced alkyl chain relative to the heterocyclic ring can be given exactly by interpretation of the ^{1}H–^{1}H and ^{19}F–^{1}H couplings. The ^{1}H NMR spectra of the alkyl azoles show a doublet of doublets of quartets for a single proton. Such a signal can only result from couplings of the proton with a neighbouring trifluoromethyl group and with vicinal diastereotopic protons of the methylene group. Two doublets of doublets are additionally found in each spectrum, confirming the presence of the diastereotopic methylene protons. However, sometimes the doublets of doublets of the diastereotopic CH_2 protons are overlapped, e.g. in the case of the pyrazole derivative **6** ($\delta = 5.60$).



Scheme 2.



Scheme 3.



Scheme 4.

The position at the azole bearing the alkyl group was determined by checking the ^{1}H–^{1}H couplings of the ring protons. Additionally, an NOE experiment was necessary for characterization of the triazoles **10** and **11**.

The vicinal couplings of the heteroaromatic CH protons are indicated by coupling constants being generally larger than 2 Hz. In contrast, long-range couplings have values less than 2 Hz. Thus, the two regioisomeric pyrroles **3** and **4** can be distinguished by the H4 signal of isomer **3** ($\delta = 6.04$; $^{3}J_{H3/H4} \approx 4.0$ Hz, $^{3}J_{H4/H5} \approx 2.7$ Hz) showing the two vicinal couplings with H3 as well as H5, and by the H2 signal of isomer **4** ($\delta = 6.84$; $^{4}J_{H2/H5} = {}^{4}J_{H2/H4} \approx 1.9$ Hz) showing exclusively the expected long-range coupling for the 'isolated' H2. Long-range couplings ($^{4}J_{H3/H5} \approx 1.8$ Hz) were also found between the protons H3 and H5 of **3**. Furthermore, distinction between the regioisomers **3** and **4** was also possible on the basis of the ^{19}F–^{13}C couplings. Thus, the C2 signal of compound **3** is split into a quartet caused by the vicinal coupling ($^{3}J_{C2/CF3} \approx 2.0$ Hz). In the case of isomer **4** the C3 signal shows such a quartet ($^{3}J_{C3/CF3} \approx 2.0$ Hz).

The ^{1}H NMR spectrum of 1-(1-trifluoromethyl-2-nitroethyl)-1H-pyrazole (**6**) shows the ring protons H3 ($\delta = 7.65$) and H5 ($\delta = 8.10$) as doublets with couplings to H4 ($^{3}J_{H3/H4} \approx 1.8$ Hz, $^{3}J_{H4/H5} \approx 2.4$ Hz), whereas the proton H4 ($\delta = 6.39$) gives expectedly a doublet of doublets. In the ^{13}C NMR spectrum of **6** three signals of ring C atoms were

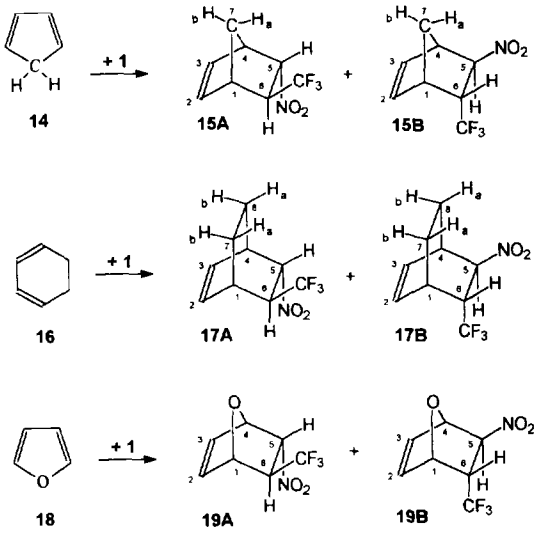
found which correspond to CH segments excluding any products of C-alkylation. 1-(1-Trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**8**) and 3,5-dibromo-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (**13**) show in the ^{13}C NMR spectra in each case different chemical shifts for their two ring C atoms 3 and 5 (δ=146.7, 152.8 and 134.9, 141.6, respectively). This indicates that the N-alkylation has occurred at N1 or N2 but not in the 4-position. Additionally, the two singlets at δ=8.20 and 8.90 in the ^1H NMR spectrum of **8** exclude an N-alkylation of the 4-position.

In order to assign the structures of the regioisomers **10** and **11**, we carried out additionally a NOESY experiment. The major product **10** shows a correlation between the ring proton (H5) and the exocyclic proton at the chiral C_α atom. Moreover, an NOE correlation was found between H5 and one of the diastereotopic methylene protons of the exocyclic β-position. In contrast to this, compound **11** did not show any couplings between the ring proton and one of the exocyclic protons. Furthermore, 3-substituted 1,2,4-triazoles are attacked by electrophilic reagents exclusively at the N atoms 1 or 2, never at N4 according to numerous examples in the literature [9]. Recently, analogous results were found for 3,5-bis(trifluoromethyl)-1,2,4-triazole [10].

In a second part of our investigations, we used *trans*-3,3,3-trifluoro-1-nitropropene (**1**) as a dienophile in Diels-Alder cycloadditions with cyclopentadiene (**14**), cyclohexa-1,3-diene (**16**), and furan (**18**). With regard to the regioselectivities and stereoselectivities of such reactions, the competition of the nitro and the trifluoromethyl group for an endo/exo-arrangement in the cycloadducts is especially interesting. The preferences of nitro groups for an endo-arrangement in cycloadducts has been observed [11].

Viktorova et al. [12] studied the cycloaddition of **1** with buta-1,3-diene. The authors described relatively drastic reaction conditions being necessary to achieve good yields. We found that cyclopentadiene (**14**) reacts with **1** in boiling etheric solution (3 h) to give the isomeric bicyclo[2.2.1]hept-2-enes **15A** and **15B** (overall yield 54%–55%) (Scheme 5). The two diastereomers could not be separated by column chromatography.

The NMR spectra of the purified colourless mixture of **15A/15B** shows two series of partly separated signals of the two compounds corresponding with the data expected for compounds formed by a [4+2]-cycloaddition. The assignment of the ^1H and ^{13}C signals was confirmed by recording the ^1H, ^1H COSY and ^{13}C, ^1H correlation spectra. Additionally, in a ^1H, ^1H NOESY spectrum, except other cross peaks, correlations between the protons at δ=5.63 (H5 (**15A**)) and 1.73 (H7a (**15A**)) as well as δ=3.70 (H6 (**15B**)) and 1.84 (H7a (**15B**)) were found, thus confirming the assignment of proton signals to the isomers **15A** and **15B**. The integration of corresponding signals indicates the ratio of the two diastereomers **15A** and **15B** to be nearly 1:1. This means that the nitro and the trifluoromethyl group compete with equal success for the favoured endo-position (Scheme 5).



Scheme 5.

The use of the cyclohexa-1,3-diene (**16**) instead of the diene **14** resulted in a lower yield in cycloaddition with the dienophile **1** under the same reaction conditions. Such a result was not surprising, because the cyclohexadiene **16** shows, in contrast to the co-planar cyclopentadiene **14**, a dihedral angle of nearly 20° [13]. The ratio of the diastereomeric 6-trifluoromethyl-5-nitro-bicyclo[2,2,2]oct-2-enes **17A** and **17B** was found to be 1:1. The details of the spectra correspond, in the range of expectation, to those of **15A** and **15B**, respectively. The assignment of the signals is based on the correlation spectra. Additionally, in a ^1H, ^1H NOESY spectrum, correlations between the protons H5 and H8a (isomer **17A**) as well as H6 and H7a (isomer **17B**) have been found.

Furans show a significant lower reactivity to electrophilic reagents than pyrrole derivatives (factor of approximately 10^5 [14]), but have a more distinct diene character. In the literature, numerous [4+2]-cycloadditions of furan derivatives have been described with electron-deficient philodienes [15]. A cycloaddition of furan with methyl-3-nitroacrylate was of interest; Just et al. [16] obtained a diastereomeric mixture consisting of the *endo*-carbmethoxy derivative as major product (55%) and only 15% of the *endo*-nitro product.

We achieved a cycloaddition of furan (**18**) with 1,1,1-trifluoro-3-nitropropene (**1**) under very mild conditions. The diastereomeric 6-trifluoromethyl-5-nitro-7-oxabicyclo-[2.2.1]hept-2-enes **19A** and **19B** were isolated in 58%–59% yield. However, the isomers (ratio 1:1) could not be separated by column chromatography. [2+2]-Cycloadducts and products of substitution observed by Huisgen et al. [17–19] in the reaction of 2,3-bis-trifluoromethyl-but-2-ene-dinitril with alkoxy-furans, were not found.

The NMR spectra of the diastereomers **19A** and **19B** correspond to those of the cycloadducts **15A, 15B** and **17A, 17B** in essential parts. Owing to the O-bridge, the signals of H1 and H4 as well as C1 and C2 of the two diastereomers **19A** and **19B** are shifted significantly downfield compared with

the corresponding signals of compounds **15A, 15B** and **17A, 17B**, respectively.

3. Experimental details

The NMR spectra were recorded with the Bruker spectrometer AC-250. The chemical shifts δ are referred to TMS (^{1}H and ^{13}C) and $CFCl_3$ (^{19}F). The coupling constants J were determined using a first-order analysis. The elemental analysis were carried out with a Leco CHNS-932. Silica gel was used for chromatographic control, separation or purification. TLC, silica gel foils 60 F_{254}/Merck; column chromatography, silica gel 60, 63-200 μm/Merck; column, 300 mm/40 mm; eluents, see procedures.

Chemicals: Cyclopentadiene, cyclohexa-1,3-diene, 1-methyl-pyrrole (Janssen Chimica), pyrazole (Merck), and 1,2,4-triazole (EGA Chemie Steinheim). The *trans*-3,3,3-trifluoro-1-nitropropene (**1**) was prepared in two steps from trifluoroacetaldehyde methylhemiacetal using a modified procedure of Iwata et al. [3]. The hemiacetal, a gift of Hoechst AG, was purified via trifluoroacetaldehyde.

3.1. 2-(1-Trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (3), 3-(1-trifluoromethyl-2-nitroethyl)-1-methyl-pyrrole (4)

To a solution of 1.0 g (0.01 mol) of 1-methylpyrrole (**2**) in $CHCl_3$ (10 ml) or CH_2Cl_2 (10 ml), 1.4 g (0.01 mol) **1** [3] was added dropwise at −78 °C under stirring. Then, the mixture was allowed to warm up to room temperature within 5 h and the stirring was continued at this temperature for a further 12 h. After evaporation of the solvent, the crude product was purified by column chromatography (eluent, ethyl acetate:hexane 1:3; **3**, R_f = 0.5; **4**, R_f = 0.45) giving 1.20 g (50%) **3** and 100 mg (4%) **4** as a colourless oil.

3. $C_8H_9F_3N_2O_2$ (222.2): calculated C 43.28, H 4.05, N 12.61; found C 43.32, H 4.12, N 12.63. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ = 3.63 (s, 3H, CH_3); 4.78 (ddq, 1H, $^3J_{H\alpha/H\beta} \approx 8.9$ Hz, $^3J_{H\alpha/F} \approx 8.6$ Hz, $^3J_{H\alpha/H\beta'} \approx 6.0$ Hz, H_α); 5.15 (dd, 1H, $^2J_{H\beta/H\beta'} \approx 14.4$, $^3J_{H\alpha/H\beta} \approx 8.9$ Hz, H_β); 5.31 (dd, 1H, $^3J_{H\alpha/H\beta'} \approx 6.0$ Hz, $^3J_{H\beta/H\beta'} \approx 14.4$ Hz, $H_{\beta'}$); 6.04 (dd, 1H, $^3J_{H3/H4} \approx 4.0$ Hz, $^3J_{H4/H5} \approx 2.7$ Hz, H4); 6.29 (dd, $^4J_{H3/H5} \approx 1.8$ Hz, $^3J_{H3/H4} \approx 4.0$ Hz, 1H, H3); 6.79 (dd, $^3J_{H4/H5} \approx 2.7$ Hz, $^4J_{H3/H5} \approx 1.8$ Hz, 1H, H5). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 33.5 (CH_3); 38.9 (q, $^2J_{C\alpha/F} \approx 29.3$ Hz, C_α); 73.4 (q, $^3J_{C\beta/F} \approx 2.9$ Hz, CH_2); 107.2 (C4); 108.7 (C3); 121.6 (q, $^3J_{C2/F} \approx 2.0$ Hz, C2); 124.3 (C5); 124.8 (q, $^1J_{C/F} \approx 280.4$ Hz, CF_3). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −68.9 (s, CF_3).

4. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ = 3.60 (s, 3H, CH_3); 4.40 (ddq, 1H, $^3J_{H\alpha/H\beta} \approx {}^3J_{H\alpha/F} \approx 8.2$ Hz, H_α); 4.97 (dd, 1H, $^3J_{H\alpha/H\beta} \approx 8.2$ Hz, $^2J_{H\beta/H\beta'} \approx 13.7$ Hz, H_β); 5.17 (dd, 1H, $^2J_{H\beta/H\beta'} \approx 13.7$ Hz, $^3J_{H\alpha/H\beta'} \approx 6.7$ Hz, $H_{\beta'}$); 6.08 (br, 1H, H4); 6.68 (dd, 1H, $^3J_{H4/H5} \approx 2.4$ Hz, $^4J_{H2/H5} \approx 1.9$ Hz, H5); 6.84 (dd, 1H, $^4J_{H2/H5} \approx {}^4J_{H2/H4} \approx 1.9$ Hz, H2). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 35.8 (CH_3); 40.8 (q, $^2J_{C\alpha/F} \approx 28.1$ Hz, C_α); 74.5 (q, $^3J_{C\beta/F} \approx 2.4$ Hz, CH_2); 107.8 (C4); 111.7 (q, $^3J_{C/F} \approx 2.0$ Hz, C3); 121.8 (C2); 122.6 (C5); 125.8 (q, $^1J_{C/F} \approx 279.4$ Hz, CF_3). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −69.3 (s, CF_3).

3.2. 1-(1-Trifluoromethyl-2-nitroethyl)-1H-pyrazole (6)

0.7 g (0.01 mol) of pyrazole (**5**) dissolved in $CHCl_3$ (10 ml) was alkylated with 1.41 g (0.01 mol) **1** [3] as described for the compounds **3** and **4**, and the reaction mixture was worked up analogously. The yield was 1.5 g (71.4%) of **6** (colourless oil).

$C_6H_6F_3N_3O_2$ (209.1): calculated C 34.45, H 2.87, N 20.1; found C 34.43, H 3.06, N 19.94. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ = 5.60 (m, 2H, H_β, $H_{\beta'}$); 6.35 (m, 1H, H_α); 6.39 (dd, 1H, $^3J_{H4/H5} \approx 2.4$ Hz, $^3J_{H3/H4} \approx 1.8$ Hz, H4); 7.65 (d, 1H, $^3J_{H3/H4} \approx 1.8$ Hz, H3); 8.10 (d, 1H, $^3J_{H4/H5} \approx 2.4$ Hz, H5). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 58.3 (q, $^2J_{C\alpha/F} \approx 31.5$ Hz, C_α); 71.5 (CH_2); 106.8 (C4); 123.1 (q, $^1J_{C/F} \approx 283.2$ Hz, CF_3); 132.6 (C3); 141.1 (C5). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −72.5 (s, CF_3).

3.3. 1-(1-Trifluoromethyl-2-nitroethyl)-1,2,4-triazole (8)

0.70 g (0.01 mol) of 1,2,4-triazole (**7**) dissolved in CH_2Cl_2 (10 ml) was alkylated with 1.41 g (0.01 mol) of **1** [3] as described for the compounds **3** and **4**, and the reaction mixture was worked up analogously. The yield was 1.4 g (66.4%) of **8** (colourless oil).

$C_5H_5F_3N_4O_2$ (210.14): calculated C 28.57, H 2.38; found C 28.66, H 2.37. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ = 5.56 (dd, 1H, $^2J_{H\beta/H\beta'} \approx 15.3$ Hz, $^3J_{H\alpha/H\beta} \approx 9.2$ Hz, H_β); 5.66 (dd, 1H, $^3J_{H\alpha/H\beta'} \approx 4.3$ Hz, $H_{\beta'}$); 6.60 (m, 1H, H_α); 8.20, 8.90 (2s, 2×1H, H3, H5). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 56.3 (q, $^2J_{C\alpha/F} \approx 32.1$ Hz, C_α); 71.2 (CH_2); 122 (q, $^1J_{C/F} \approx 282.6$ Hz, CF_3); 146.7 (C5); 152.8 (C3). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −72.3 (s, CF_3).

3.4. 3-Bromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (10) and 5-bromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (11)

A solution of 1.41 g (0.01 mol) of **1** [3] and 1.5 g (0.01 mol) of 3-bromo-1,2,4-triazole (**9**) [20] in CH_2Cl_2 (50 ml) was heated under argon (70 bar) in an autoclave for 24 h at 120 °C. After concentration of the mixture, the residue containing the two isomers **10** and **11** (5:1[3]) was separated by column chromatography (eluent toluene; **10** R_f = 0.075; **11** R_f = 0.025). The yield was 1.45 g (50%) of **10**, colourless oil, and 0.29 g (10%) of **11**, colourless oil.

10. $C_5H_4BrF_3N_4O_2$ (289.02): calculated C 20.77, H 1.38, N 19.38; found C 20.95, H 1.48, N 19.30. ^{1}H NMR (250.1 MHz, $CDCl_3$): δ = 4.90 (dd, 1H, $^2J_{H\beta/H\beta'} \approx 15.6$ Hz, $^3J_{H\alpha/H\beta} \approx 3.0$ Hz, H_β); 5.40 (dd, 1H, $^2J_{H\beta/H\beta''} \approx 15.6$ Hz, $^3J_{H\alpha/}$

[3] Determined by NMR spectroscopy.

$_{H\beta'}$ ≈ 9.5 Hz, $H_{\beta'}$); 5.60 (m, 1H, H_α); 8.10 (s, 1H, H5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 58.3 (q, $^2J_{C\alpha/F}$ ≈ 33.4 Hz, C_α); 70.0 (CH_2); 122.5 (q, $^1J_{C/F}$ ≈ 283.2 Hz, CF_3); 142.2 (C3); 146.7 (C5). ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = −72.4 (s, CF_3).

11. ^1H NMR (250.1 MHz, $CDCl_3$): δ = 4.90 (dd, 1H, $^2J_{H\beta/H\beta'}$ ≈ 15.6 Hz, $^3J_{H\alpha/H\beta}$ ≈ 3.0 Hz, H_β); 5.40 (dd, 1H, $^2J_{H\beta/H\beta'}$ ≈ 15.6 Hz, $^3J_{H\alpha/H\beta'}$ ≈ 9.5 Hz, $H_{\beta'}$); 5.80 (m, 1H, H_α); 8.00 (s, 1H, H5). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 56.5 (q, $^2J_{C\alpha/F}$ ≈ 33.4 Hz, C_α); 70.1 (CH_2); 124.8 (q, $^1J_{C/F}$ ≈ 283.2 Hz, CF_3); 132.5 (C3); 154.0 (C5). ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = −72.0 (s, CF_3).

3.5. 3,5-Dibromo-1-(1-trifluoromethyl-2-nitroethyl)-1,2,4-triazole (13)

A solution of 1.41 g (0.01 mol) of **1** [3] and 2.27 g (0.01 mol) of 3,5-dibromo-1,2,4-triazole (**12**) [21] in CH_2Cl_2 (50 ml) was heated under argon (70 bar) in an autoclave for 150 h at 120 °C. After concentration of the mixture the residue (3.0 g) was purified by column chromatography (ethyl acetate:heptane 1:3) giving 1.10 g (30%) of colourless crystals; mp 110–111 °C (ethyl acetate–heptane).

$C_5H_3Br_2F_3N_4O_2$ (367.91): calculated C 16.32, H 0.82, N 15.22; found C 16.53, H 0.86, N 15.14. ^1H NMR (250.1 MHz, DMSO-d_6): δ = 5.54 (m, 2H, CH_2); 6.43 (m, 1H, H_α). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 56.7 (q, $^2J_{C\alpha/F}$ ≈ 32.4 Hz, C_α); 70.1 (CH_2); 122 (q, $^1J_{C/F}$ ≈ 283.2 Hz, CF_3); 134.9, 141.6 (2C, C3, C5). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −71.8 (s, CF_3).

3.6. 6-Trifluoromoethyl-5-nitro-bicyclo[2.2.1]hept-2-ene (15A and 15B)

A solution of 1.41 g (0.01 mol) of cyclopenta-1,3-diene (**14**) and 0.65 g (0.01 mol) of **1** [3] in diethyl ether (15 ml) was refluxed for 3 h and then concentrated using a rotary evaporator. After purification of the residue by column chromatography (eluent ethyl acetate:hexane 1:3), 1.30 g (54.2%) of the pure mixture **15A** and **15B** (1:1) was obtained as a colourless oil. $C_8H_6F_3NO_2$ (206.04): calculated C 46.61, H 3.42, N 6.79; found C 46.39, H 3.65, N 6.40.

15A. ^1H NMR (250.1 MHz, DMSO-d_6): δ = 1.57 (dm, 1H, $^2J_{H7a/H7b}$ ≈ 9.8 Hz, H7b); 1.73 (dm, 1H, $^2J_{H7a/H7b}$ ≈ 9.8 Hz, H7a); 2.91 (m, 1H, H6); 3.15 (m, 1H, H1); 3.60 (b, 1H, H4); 5.63 (dd, 1H, $^3J_{H5/H6}$ ≈ 4.4 Hz, $^3J_{H4/H5}$ ≈ 4.0 Hz, H5); 6.14 (dd, 1H, $^3J_{H2/H3}$ ≈ 5.6 Hz, $^3J_{H3/H4}$ ≈ 2.8 Hz, H3); 6.58 (dd, 1H, $^3J_{H3/H2}$ ≈ 5.6 Hz, $^3J_{H2/H1}$ ≈ 3.2 Hz, H2). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 43.6 (q, $^3J_{C1/F}$ ≈ 1.8 Hz, C1); 45.7 (C7); 46.9 (C4); 47.6 (q, $^2J_{C6/F}$ ≈ 23.6 Hz, C6); 85.4 (q, $^3J_{C5/F}$ ≈ 1.6 Hz, C5); 126.7 (q, $^1J_{C/F}$ ≈ 279.0 Hz, CF_3)[4]; 134.0 (C3); 140.1 (C2). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −66.4 (s, CF_3)[5].

15B. ^1H NMR (250.1 MHz, DMSO-d_6): δ = 1.66 (dm, 1H, $^2J_{H7a/H7b}$ ≈ 9.4 Hz, H7b); 1.84 (dm, 1H, $^2J_{H7a/H7b}$ ≈ 9.4 Hz, H7a); 3.19 (m, 1H, H1); 3.53 (b, 1H, H4); 3.70 (m, 1H, H6); 4.64 (dm, 1H, $^3J_{H5/H6}$ ≈ 4.5 Hz, H5); 6.29 (m, 2H, H2, H3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 42.8 (q, $^3J_{C1/F}$ ≈ 1.8 Hz, C1); 47.4 (C7); 48.7 (q, $^2J_{C6/F}$ ≈ 27.3 Hz, C6); 49.1 (C4); 85.4 (q, $^3J_{C5/F}$ ≈ 1.6 Hz, C5); 126.5 (q, $^1J_{C/F}$ ≈ 278.0 Hz, CF_3)[6]; 134.4 (C3); 137.6 (C2). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −64.9 (s, CF_3)[7].

3.7. 6-Trifluoromethyl-5-nitro-bicyclo[2.2.2]oct-2-ene (17A and 17B)

A solution of 1.41 g (0.01 mol) of **1** [3] and 0.8 g (0.01 mol) of cyclohexa-1,3-diene (**16**) in diethyl ether (15 ml) was refluxed for 3 h. The workup procedure was the same as described for the isolation of the compounds **15A** and **15B**. The yield was 1.0 g (38.3%) of the diastereomeric mixture of **17A** and **17B** (1:1). $C_9H_{10}F_3NO_2$ (221.2): calculated C 48.87, H 4.52, N 6.33; found C 49.14, H 4.34, N 6.33.

17A. ^1H NMR (250.1 MHz, DMSO-d_6): δ = 1.04 (m, 1H, H7b); 1.33–1.48 (m, 2H, H8b, H8a (**17B**)); 1.60–1.72 (m, 2H, H7a, H8a); 2.99 (dq, 1H, $^3J_{H1/H2}$ ≈ 6.9 Hz, $^3J_{H1/F}$ ≈ 2.7 Hz, H1); 3.15 (m, 1H, H6); 3.41 (m, 1H, H4); 5.12 (dd, 1H, $^3J_{H5/H6}$ ≈ 5.1 Hz, $^3J_{H4/H5}$ ≈ 2.7 Hz, H5); 6.15 (dd, 1H, $^3J_{H2/H3}$ ≈ 8.0 Hz, $^3J_{H3/H4}$ ≈ 6.0 Hz, H3); 6.54 (dd, 1H, $^3J_{H2/H3}$ ≈ 8.0 Hz, $^3J_{H1/H2}$ ≈ 6.9 Hz, H2). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.7 (C7); 21.1 (C8); 29.1 (q, $^3J_{C1/F}$ ≈ 2.2 Hz, C1); 34.3 (C4); 44.6 (q, $^2J_{C6/F}$ ≈ 26.0 Hz, C6); 83.4 (C5); 126.7 (q, $^1J_{C/F}$ ≈ 280.5 Hz, CF_3)[8]; 129.7 (C3); 135.9 (C2). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = −69.6 (s, CF_3)[9].

17B. ^1H NMR (250.1 MHz, DMSO-d_6): δ = 1.15–1.33 (m, 2H, H7b, H8b); 1.33–1.48 (m, 2H, H8a, H8b (**17A**)); 1.78 (m, 1H, H7a); 2.91 (m, 1H, H1); 3.36 (m, 1H, H4); 3.48 (m, 1H, H6); 4.69 (dd, 1H, $^3J_{H5/H6}$ ≈ 5.8 Hz, $^3J_{H4/H5}$ ≈ 3.0 Hz, H5); 6.25–6.40 (m, 2H, H2, H3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.6 (C8); 24.2 (C7); 28.7 (q, $^3J_{C1/F}$ ≈ 2.2 Hz, C1); 34.8 (C4); 44.3 (q, $^2J_{C6/F}$ ≈ 27.0 Hz, C6); 84.3 (C5); 126.4 (q, $^1J_{C/F}$ ≈ 279.0 Hz, CF_3)[10]; 130.1 (C3); 134.1 (C2). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ = 67.0 (s, CF_3)[11].

3.8. 6-Trifluoromethyl-5-nitro-7-oxa-bicyclo[2.2.1]hept-2-enes (19A and 19B)

To a solution of 1.60 g (0.02 mol) of furan (**18**) in $CHCl_3$ (20 ml) or CH_2Cl_2 (20 ml), 2.80 g (0.02 mol) of **1** [3] were added dropwise at −78 °C under stirring. Then, the mixture was allowed to warm up to room temperature within 5 h and

[4] Exchangeable pairs (**15A** or **15B**).
[5] Exchangeable pairs (**15A** or **15B**).
[6] Exchangeable pairs (**15A** or **15B**).
[7] Exchangeable pairs (**15A** or **15B**).
[8] Exchangeable pairs (**17A** or **17B**).
[9] Exchangeable pairs (17A or 17B).
[10] Exchangeable pairs (**17A** or **17B**).
[11] Exchangeable pairs (**17A** or **17B**).

the stirring was continued at this temperature for a further 12 h. After concentration in a rotary evaporator, the crude product was purified by column chromatography (eluent ethyl acetate:heptane 1:3) giving 2.4 g (58.5%) of the pure mixture **19A** and **19B** (1:1) as a colourless oil. $C_7H_6F_3NO_2$ (209.1): calculated C 40.19, H 2.87, N 6.70; found C 39.93, H 2.80, N 6.74.

19A. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ=3.26 (dq, $^3J_{H5/H6}\approx$3.6 Hz, $^3J_{H6/F}\approx$9.5 Hz, H6); 5.31 (m, 1H, H1); 5.53 (m, 1H, H4); 5.72 (dd, 1H, $^3J_{H5/H4}\approx$4.5 Hz, $^3J_{H5/H6}\approx$3.6 Hz, H5); 6.51 (dd, 1H, $^3J_{H2/H3}\approx$5.7 Hz, $^3J_{H3/H4}\approx$1.7 Hz, H3); 6.82 (dd, 1H, $^3J_{H2/H3}\approx$5.7 Hz, $^3J_{H1/H2}\approx$2.0 Hz, H2). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=47.6 (q, $^2J_{C6/F}\approx$28.4 Hz, C6); 78.1 (C4); 79.7 (q, $^3J_{C1/F}\approx$2.0 Hz, C1); 82.3 (C5); 125.0 (q, $^1J_{C/F}\approx$278.0 Hz, CF_3)[12]; 134.1 (C3); 139.4 (C2). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ=−63.9 (s, CF_3)[13].

19B. ^{1}H NMR (250.1 MHz, DMSO-d_6): δ=3.84 (m, 1H, H6); 5.05 (d, 1H, $^3J_{H4/H5}\approx$3.9 Hz, H5); 5.33 (m, 1H, H1); 5.63 (m, 1H, H4); 6.64 (m, 2H, H2, H3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=47.9 (q, $^2J_{C6/F}\approx$28.6 Hz, C6); 77.4 (q, $^3J_{C1/F}\approx$2.0 Hz, C1); 83.5 (C4); 85.0 (q, $^3J_{C5/F}\approx$2.0 Hz, C5); 126.2 (q, $^1J_{C/F}\approx$278.0 Hz, CF_3)[14]; 134.9; 139.6 (C2, C3). ^{19}F NMR (235.4 MHz, DMSO-d_6): δ=−66.8 (s, CF_3)[15].

Acknowledgements

The authors thank the 'Fonds der Chemischen Industrie' for financial support and Hoechst AG for the gift of trifluoroacetaldehyde.

[12] Exchangeable pairs (**19A** or **19B**).
[13] Exchangeable pairs (**19A** or **19B**).
[14] Exchangeable pairs (**19A** or **19B**).
[15] Exchangeable pairs (**19A** or **19B**).

References

[1] R. Miethchen, M. Hein, D. Naumann and W. Tyrra, *Liebigs Ann. Chem.*, (1995) 1717.
[2] H. Shechter, D.E. Ley and E.B. Roberson, *J. Am. Chem. Soc., 78* (1956) 4984.
[3] S. Iwata, Y. Ishiguro, M. Utsugi, K. Mitsuhashi and K. Tanaka, *Bull. Chem. Soc. Jpn., 66* (1993) 2432.
[4] G. Rosini and R. Ballini, *Synthesis,* (1988) 833.
[5] G.C. Levy and R.L. Lichter, *Nitrogen-15 Nuclear Magnetic Resonance for Organic Chemists,* Wiley, New York, 1979.
[6] G. Yagil, *Tetrahedron, 23* (1967) 2855.
[7] J. Catalan, R.M. Claramunt, J. Elguero, J. Laynez, M. Menendez, F. Anvia, J.H. Quian, M. Taagepera and R.W. Taft, *J. Am. Chem. Soc., 110* (1988) 4105.
[8] W. Freiberg and C.-F. Kröger, *Chimia, 21* (1967) 159.
[9] E. Nachbaur and G. Faleschini, 1,2,4-Triazole. In *Houben-Weyl, Methoden der Organischen Chemie*, Vol. E8d, Georg Thieme Verlag, Stuttgart, 1994, pp. 479–598.
[10] M.M. Abdul-Ghani and A.E. Tipping, *J. Fluorine Chem., 72* (1995) 135.
[11] E.E. van Tamelen and R.J. Thiede, *J. Am. Chem. Soc., 74* (1952) 2615.
[12] N.M. Viktorova, S.P. Knyazev and N.S. Zefirov, *Zh. Org. Khim., 8* (1972) 944; English translation in H. Feuer and A.T. Nielsen, *Nitro Compounds*, VCH Verlagsgesellschaft, Weinheim, 1990, p. 949.
[13] H. Wollweber, Diels-Alder Reaktion. In *Houben-Weyl, Methoden der Organischen Chemie*, Vol. 5/1c, Georg Thieme Verlag, Stuttgart, 1970, p. 1025 ff.D. Craig, J.J. Shipman and R.B. Fowler, *J. Am. Chem. Soc., 83* (1961) 2885.
[14] A.R. Katritzky and C.W. Rees, *Comprehensive Heterocyclic Chemistry*, Vol. 4, Pergamon, Frankfurt, 1984, p. 42 ff.
[15] R.P. Kreher, Hetarene Teil I. In *Hoyben-Weyl, Methoden der Organischen Chemie*, 4 Aufl., Vol. E6a, Georg Thieme Verlag, Stuttgart, 1994, p. 163 ff.
[16] G. Just, A. Martel, K. Grozinger and M. Ramjeesingh, *Can. J. Chem., 53* (1975) 131.
[17] R. Huisgen and G. Mloston, *Tetrahedron Lett., 35* (1994) 4981.
[18] G. Mloston and R. Huisgen, *J. Heterocycl. Chem., 31* (1994) 1279.
[19] G. Urrutia-Desmaison, R. Mloston and R. Huisgen, *Tetahedron Lett., 35* (1994) 4977.
[20] W. Manchot and R. Noll, *Liebigs Ann. Chem., 343* (1905) 1.
[21] C.-F. Kröger and R. Miethchen, *Chem. Ber., 100* (1967) 2250.