

for 1 h. The resulting diazonium salt was then added with stirring to 0.13 g (0.001 mole) of p-chlorophenol in a saturated solution of Na_2CO_3 , and the mixture was allowed to stand for another hour (neutral medium). It was then extracted with CH_2Cl_2 , and the extract was evaporated in vacuo to give 0.2 g (54%) of a product with mp 288–290°C (from benzene). Found: C 60.8; H 3.8; N 14.0%. $\text{C}_{21}\text{H}_{15}\text{ClN}_4\text{O}_2$. Calculated: C 60.5; H 3.8; N 14.3%. IR spectrum 1675 (C=O), 1610 (C=N), and 3187–3400 cm^{-1} (NH).

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HETEROCYCLIC NITRO COMPOUNDS.

22.* NITRATION OF 1,2,4-TRIAZOLE AND ITS DERIVATIVES WITH NITRONIUM SALTS

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1,2,4-Triazole, 3(5)-R-1,2,4-triazoles (R = CH_3 , Cl, Br, NO_2), and their N-trimethylsilyl derivatives were nitrated with nitronium salts. The products were N-nitro-1,2,4-triazoles, which split out the nitro group under the influence of acids and undergo rearrangement to 3-nitrotriazoles when they are heated in inert solvents. When R = NO_2 , a dinitrotriazole is not formed, and the starting 3-nitro-1,2,4-triazole is recovered.

Attempts to synthesize 3(5)-nitro-1,2,4-triazoles by nitration of triazole derivatives with acidic nitrating agents have been unsuccessful because of the low reactivities of the ring carbon atoms with respect to electrophiles and the additional deactivation of the triazoles when they are protonated in acids [2–4]. The nitration of 1,2,4-triazol-5-one with nitric acid [4–7] constitutes an exception due to disruption of the aromatic ring. The only example of the nonacidic nitration of triazoles is the reaction of 3-phenyl-1,2,4-triazole with acetyl nitrate, which leads to the N-nitro derivatives; the latter then undergoes rearrangement to give the C-nitro compound [8].

We have observed that N-nitro-1,2,4-triazoles (VI–X) are formed in the reaction of 1,2,4-triazole (I) or 3-substituted 1,2,4-triazoles (II–V) with nitronium tetrafluoroborate in anhydrous acetonitrile. Because of their low stabilities, we were able to isolate only the derivatives of triazoles I and II (VI and VII). In the remaining cases the formation of the nitro derivatives can be judged from the PMR spectra of the reaction mixtures and from the

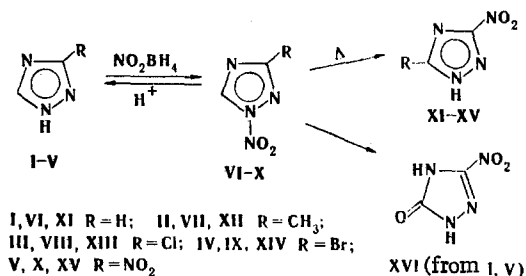
*See [1] for communication 21.

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results of thin-layer chromatography (TLC), as well as from their subsequent conversion to the C-nitro compounds.

Two signals at δ 7.95 and 9.05 ppm are observed in the PMR spectrum of N-nitrotriazole VI, but the signal of an N-H proton is absent; this makes it possible to assign the 1-nitro-1,2,4-triazole structure to VI. The IR spectra of the N-nitrotriazoles contain absorption bands of a nitro group at 1270-1295 and 1640-1670 cm^{-1} ; this is also characteristic for other N-nitro-triazoles [9, 10]. When N-nitrotriazoles VI and VII are heated, they undergo rearrangement to give the corresponding C-nitro compounds XI and XII (the formation of nitrotriazole XII was observed during the nitration); in addition, the starting triazoles are detected in the mixtures, and 3-nitro-1,2,4-triazol-5-one (XVI) is also detected in the case of unsubstituted 1,2,4-triazole.

N-Nitrotriazoles VIII and IX, which are not isolated from the reaction mixtures, also give mixtures of the starting triazoles and C-nitro compounds XIII and XIV when they are heated. When 1,3-dinitrotriazole (X) is heated, it is converted primarily to the starting

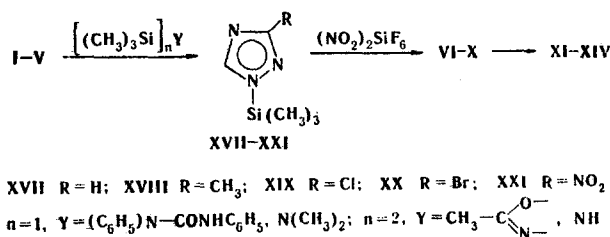


3-nitrotriazole (V); only traces of dinitrotriazole XV were found. In addition, nitrotriazolone XVI was detected in the mixture.

In general, the yields of C-nitrotriazoles XI-XV are low because of the dinitration of the intermediate N-nitro compounds formed during the reaction with the acid. In addition, it is difficult to isolate the nitro compounds for the reaction mixtures.

In order to avoid the development of acidity during the nitration we used N-trimethylsilyl-1,2,4-triazoles as the starting reagents with the expectation that the trimethylsilyl group would split out readily under the influence of the nitrating agent to give silyl derivatives that do not have acidic properties.

The silylation of triazoles I-V proceeds relatively readily (the products are obtained in greater than 80% yields) under the influence of various silylating agents - O,N-bis(trimethylsilyl)acetamide, N, N'-diphenyl-N-trimethylsilylurea, hexamethyl disilazan, and trimethylsilyldimethylamine.



The PMR spectrum of trimethylsilyltri azole XVII (two signals of the protons of the triazole ring are present) provides evidence that it has the structure of the 1-trimethylsilyl derivatives. The presence of only one signal of protons of the trimethylsilyl group in the spectra of XVII-XXI (at 0.4-0.5 ppm) and the absence of splitting of this signal at low temperatures (up to -60°C) are evidently due to the existence of these compounds in the form of one isomer.

The most convenient silylating agents are hexamethyldisilazan and trimethylsilyldimethylamine, since excess amounts of the reagents and their conversion products (ammonia and dimethylamine) can be easily removed from the reaction mixtures by evacuation and do not interfere with the carrying out of the subsequent nitration.

The analysis of N-trimethylsilyltri azoles is difficult because of their high sensitivity to air moisture, and the compounds are identified in most cases from the PMR spectra tak-

ing into account the intensity ratio of the signals of the protons of the trimethylsilyl group and the ring.

The nitration of silylated heterocyclic compounds at the N-Si bond has been described in the case of 2-isopropylimidazole [11]; nitration at the ring carbon atom is also observed along with the formation of the N-nitro compound.

Only the corresponding N-nitrotriazoles (according to monitoring by TLC and from the PMR spectra of the reaction mixtures) are formed in the reaction of N-silyl derivatives XVII-XXI with nitronium tetrafluoroborate or hexafluorosilicate in anhydrous solvents (acetonitrile, methylene chloride, and dichloroethane) at -30 to +10-15°C. The thermal rearrangement of N-nitrotriazoles to C-nitro compounds XI-XIV can be carried out after removal of the volatile products in vacuo. The yields of nitro compounds XI-XIV range from 70 to 90%, and only traces of dinitrotriazole XV are formed. The N-nitration of N-trimethylsilyltriazoles can also be carried out without isolation of the products in pure form. It is sufficient to remove the volatile reaction products by vacuum distillation after silylation, after which nitration is accomplished after addition of the appropriate solvent. It is interesting to note that, in contrast to the nitration of nonsilylated methyltriazole II, in the case of the nitration of N-silyl derivative XVIII two signals of protons of a methyl group (2.42 and 2.80 ppm) are observed in the PMR spectrum of the N-nitration product (VII). Isomeric N-nitro-3-methyltriazoles, one of which is unstable, are probably formed in this case, since the products of N-nitration undergo decomposition during isolation. At the same time, the N-nitration of methyltriazole II gives a relatively stable N-nitrotriazole, which can be isolated and characterized. Thus the nitration of N-trimethylsilyl-1,2,4-triazoles with subsequent rearrangement of the N-nitro compounds was found to be a convenient preparation method for the synthesis of various 3(5)-nitro-1,2,4-triazoles.

EXPERIMENTS

The PMR spectra of the compounds were recorded with a Perkin-Elmer R-12 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of films of the compounds were recorded with a UR-20 spectrometer.

Nitration of 1,2,4-triazole (I). A 3-g (0.044 mole) sample of triazole I was added in portions with stirring to a solution of 5.3 g (0.04 mole) of nitronium tetrafluoroborate in 50 ml of anhydrous acetonitrile at 0-10°C, and the mixture was maintained under these conditions for 30 min. It was then poured into ice water, and the aqueous mixture was neutralized to pH 8-9 and extracted with ethyl acetate. Evaporation of the extract gave 2.8 g (58%) of VI with mp 42-46°C (dec.), which decomposed rapidly in air with the evolution of nitrogen oxides. The product had R_f 0.85 (dioxane-hexane, 1:4). PMR spectrum (in CH_2Cl_2), δ : 9.05 and 7.95 ppm. IR spectrum: 1280 and 1640 cm^{-1} (N-NO₂). Found: C 21.8; H 1.7%. $C_2H_2N_4O_2$. Calculated: C 21.0; H 1.7%.

The solution remaining after extraction of nitrotriazole VI was acidified to pH 1 and extracted with ether. Evaporation of the ether gave 0.1 g of XVI with mp 252°C. IR spectrum: 1720 (C=O); 1360 and 1550 cm^{-1} (NO₂). Found: C 18.7; H 1.0; N 43.2%; M 134. $C_2H_2N_4O_3$. Calculated: C 18.5; H 1.5; N 43.0%; M 130. No melting-point depression was observed for a mixture of this product with an authentic sample of 3-nitro-1,2,4-triazol-5-one.

3-Nitro-1,2,4-triazole (XI). A 1.1-g sample of N-nitrotriazole VI was heated in 10 ml of benzonitrile at 120°C for 36 h until starting VI vanished (as monitored by TLC). The benzonitrile was removed by vacuum distillation, the residue was treated with petroleum ether, and the precipitated reaction product was removed by filtration and crystallized from ethanol to give 0.6 g (54%) of a product with mp 210-211°C (dec.) [12]. No melting-point depression was observed for a mixture of this product with a genuine sample. The IR and PMR spectra were identical to the spectra of 3-nitro-1,2,4-triazole.

Nitration of 3-methyl-1,2,4-triazole (II). The reaction was carried out under the same conditions as in the nitration of triazole I. After dilution with water and neutralization, the mixture was extracted with ether. Workup of the extract gave 1.9 g of a greasy substance, the extraction of which with heptane and subsequent evaporation yielded 0.35 g (7.5%) of N-nitrotriazole VII with mp 78°C (dec.). PMR spectrum (in DMSO), δ : 8.20 ppm. IR spectrum: 1645, 1285 cm^{-1} (N-NO₂). The product had R_f 0.90 [dioxane-hexane 1:4 plus one drop of acetic acid]. Found: C 27.8; H 3.2; N 43.2%; M 127. $C_3H_4N_4O_2$. Calculated: C 28.1; H 3.1; N 43.7%; M 128. The residue after extraction with heptane of N-nitrotriazole VII was

identified as 3-nitro-5-methyl-1,2,4-triazole (XII) with mp 194°C [12]; no melting-point depression was observed for a mixture of this product with a genuine sample, and the IR and PMR spectra were identical.

The thermal rearrangement of N-nitrotriazole VII to 3-nitrotriazole XII was carried out in the same way as the reaction of nitro derivative VI in benzonitrile solution. The yield of product with mp 194°C was 60%.

Silylation of Triazoles I-V. N-Trimethylsilyl-1,2,4-triazole (XVII), with bp 78-79°C (12 mm), was obtained in 89% yield by the method in [13].

N-Trimethylsilyl-3-methyl-1,2,4-triazole (XVIII). A 5-g sample of triazole II was refluxed in 25 g of disilazan for 2.5 h, after which the excess disilazan was removed by distillation, and the residue was vacuum-distilled to give 8.8 g (93%) of a product with bp 41-42°C (1 mm). Found: C 46.7%. $C_6H_{13}N_3Si$. Calculated: C 46.5%. PMR spectrum (in CH_2Cl_2), δ : 8.0 (1H), 2.25 (3H), and 0.40 ppm (9H).

N-Trimethylsilyl-3-chloro-1,2,4-triazole (XIX). A) A mixture of 3.5 g of chlorotriazole III and 20 g of hexamethyldisilazan was refluxed for 9 h, after which the mixture was vacuum-fractionated to give 4.8 g (81%) of silylation product XIX with bp 59-60°C (1.5 mm). PMR spectrum (in CH_2Cl_2), δ : 8.18 (1H) and 0.42 ppm (9H). Found: C 34.2%. $C_5H_{10}ClN_3Si$. Calculated: C 34.5%.

B) A 1.5-g sample of chlorotriazole was refluxed in a solution of 5.1 g of trimethylsilyl-dimethylamine for 30 min, after which the mixture was vacuum-fractionated. The yield of silylation product XIX, with bp 59°C (1.5 mm), was 2.35 g (93%).

C) A 2-g sample of O-N-bis(trimethylsilyl)acetamide was added dropwise at room temperature to a suspension of 1.1 g of chlorotriazole in 3 ml of dry CH_2Cl_2 , and the mixture was allowed to stand for 1 h. It was then fractionated to give 1.55 g (80%) of a product with bp 52°C (1 mm).

N-Trimethylsilyl-3-bromo-1,2,4-triazole (XX). This compound, with bp 73-74°C (2 mm), was obtained in 88% yield by a method similar to that used to prepare XIX (method A). PMR spectrum (in CH_2Cl_2), δ : 8.1 (1H) and 0.48 ppm (9H).

N-Trimethylsilyl-3-nitro-1,2,4-triazole (XXI). A) A mixture of 5 g of nitrotriazole I and 25 g of hexamethyldisilazan was refluxed for 2.5 h, after which the excess disilazan was removed by distillation, and the residue was vacuum-distilled to give 7.6 g (93%) of a product with bp 107-109°C (0.8 mm). PMR spectrum (in CH_2Cl_2), δ : 8.40 (1H) and 0.48 ppm (9H).

B) The silylation was carried out as in the case of chlorothiazole (method C), and the product was obtained in 80% yield.

C) A 0.7-g sample of diphenyltrimethylsilylurea was added at 20°C to 0.3 g of nitrotriazole V in 5 ml of CH_2Cl_2 . After 15-20 min, the precipitated diphenylurea was removed by filtration and washed with CH_2Cl_2 . The solvent was removed by distillation, and the residue was vacuum-distilled to give 0.4 g (81%) of silyl derivative XX with bp 108-109°C (0.8 mm).

Nitration of N-Trimethylsilyltriazole XVII. A) A solution of 3.4 g of derivative XVII in 8-10 ml of CH_2Cl_2 was added slowly at -30°C to a suspension of 2.8 g of nitronium hexafluorosilicate in 10 ml of dry CH_2Cl_2 , after which the temperature was raised to 0°C, and the mixture was allowed to stand for 30 min. The solvent and volatile reaction products were removed by vacuum distillation at 20°C, and the residue was dissolved in 10 ml of benzonitrile. The solution was heated at 120°C for 24 h, after which the solvent was removed by vacuum distillation, and the residue was treated with hexane to give 2.06 g (80%) of 3-nitro-1,2,4-triazole (XI) with mp 210°C.

B) A 1.72-g sample of nitronium tetrafluoroborate was added at -30°C to a solution of 1.83 g of XVII in 10 ml of dry CH_2Cl_2 , and the mixture was treated as in method A. Workup gave 1.15 g (78%) of nitrotriazole XI.

Nitration of Trimethylsilyltriazoles XVIII-XX. The reaction was carried out as in the nitration of XVII (method A). The yield of 3-nitro-5-methyl-1,2,4-triazole, with mp 194°C, was 48%; the yield of 3-nitro-5-chloro-1,2,4-triazole (XIII), with mp 132-133°C (from chloroform), was 80%. IR spectrum: 1570 and 1305 cm^{-1} (C-NO₂). PMR spectrum (in CH_2Cl_2), δ_{NH} : 12.75 ppm. Found: C 16.2; H 0.5; Cl 23.8; N 38.1; M 146. $C_2HClN_4O_2$. Calculated: C 16.1; H 0.7; Cl 23.9; N 37.7; M 148.5. The yield of 3-nitro-5-bromo-1,2,4-triazole (XIV), with mp 153-

154°C [14], was 75%; no melting-point depression was observed for a mixture of this product with an authentic sample.

The nitration of N-trimethylsilyl-3-nitro-1,2,4-triazole (XXI) and subsequent heat treatment in benzonitrile under similar conditions gave only traces of dinitrotriazole XV (it was detected by means of TLC). The principal reaction product was unsubstituted 3-nitro-1,2,4-triazole (V), which was isolated in virtually quantitative yield.

Silylation and Nitration of 3-Chloro-1,2,4-triazole without Isolation of the Intermediates. A mixture of 1 g of 3-chlorotriazole (III) and 5 g of trimethylsilyldimethylamine was refluxed for 30 min, after which the excess silylating agent and dimethylamine were removed by vacuum distillation, and 10 ml of dry dichloroethane was added to the residue. The latter mixture was cooled to -30°C, 1 g of nitronium hexafluorosilicate was added, the temperature was raised to 0°C, and the mixture was maintained at this temperature until the reaction was complete (as monitored from the PMR spectrum). The volatile reaction products and the solvent were then removed by distillation, 10 ml of benzonitrile was added to the residue, and the mixture was heated at 120°C for 12 h. The subsequent workup was the same as in the preceding examples. The yield of 3-nitro-5-chloro-1,2,4-triazole (XIII), with mp 133°C, was 1.05 g (75%).

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