Mendeleev Commun., 1997, 7(1), 41–42

Selective synthesis of 2-(1-methylvinyl)tetrazoles

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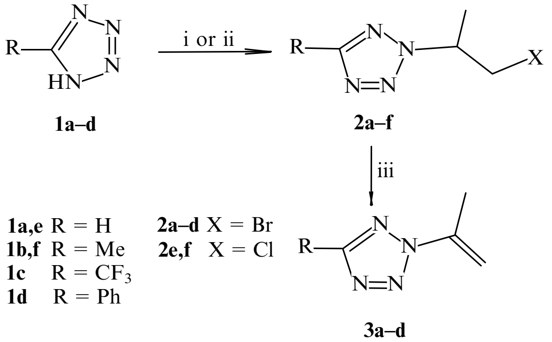
Hitherto unknown 2-(1-methylvinyl)tetrazoles have been obtained by regioselective alkylation of tetrazole and 5R-tetrazoles with 1-halogenopropan-2-ols and 3-bromopropene followed by dehydrohalogenation of the intermediate products.

Vinyltetrazoles having the general formula $CH_2{=}CRR'$, where R = H, alkyl, aryl; R′ = *C*- or *N*-tetrazolyl, are used as valuable intermediates in organic synthesis[1,2] and as starting materials for the preparation of various polymeric materials.[3] At the present time, a wide variety of 1- and 5-vinyltetrazoles have been synthesized. On the contrary, among 2-vinyl-5R-tetrazoles, only 2-vinyl-5*H*-tetrazole has been described as an individual compound.[4,5]

The syntheses of *N*-vinyltetrazoles starting with tetrazole, 5R-tetrazoles and chloroethanol[4] or 1,2-dichloroethane[5] have been described. However, the use of these methods is connected with the necessity to separate the isomeric 1- and 2-substituted tetrazoles, which is a result of the unselectivity of the alkylation process. Similarly, the direct interaction of 5-trifluoromethyltetrazole with arylacetylenes results in the formation of a mixture of the corresponding α-arylsubstituted vinyltetrazoles.[6] Several syntheses of 1-vinyltetrazoles have been developed, including vinylation of tetrazoles by vinylacetate,[7] interaction of vinylisocyanide with azides,[8] dehydration of the products which result from the interaction of 2-tributylstannyltetrazoles and epoxides[1] or by heterocyclisation of aminoethanol,[9] and the reaction between alkenes, nitriles, bromine and sodium azide in the presence of aluminium chloride followed by dehydrobromination.[10] However, selective preparations of 2-vinyltetrazoles have not yet been described.

Recently we have shown that tetrazole and 5-substituted tetrazoles are alkylated readily with secondary and tertiary aliphatic alcohols[11] and alkenes.[12] Alkylation in a concentrated sulfuric acid medium gave high yields only in the case of the corresponding 2-alkyl-5R-tetrazoles, independent of the size and electronic nature of substituent R at the 5-position of the heteroring; the formation of the isomeric 1-alkyl derivatives were not detected. It seemed appropriate to use the reaction of regioselective N2-alkylation for the preparation of 2-vinyltetrazoles, using halogen-containing alkylating agents (Scheme 1).

The reaction between tetrazoles **1** and 3-bromopropene or 1-bromopropan-2-ol in a concentrated sulfuric acid medium was found to proceed at room temperature giving the corresponding 2-(1-bromomethylethyl)tetrazoles **2** in high yields (Table 1) after 7 days reaction time. At the same time, alkylation of tetrazole **1a** with isopropanol leads to the formation of the corresponding 2-(1-methylethyl)tetrazole in 80% yield for 70 min.[11] According to the reaction mechanism,[11,13] such a distinction may be due to the essential difference between the rate-limiting step (generation of the intermediate carbocation from protonated alcohol or alkene) in the case of halogen-containing agents, which is a result of the strong electron-accepting properties of the halogen atoms.



1a–d **2a–f** **3a–d**

1a,e R = H **2a–d** X = Br
1b,f R = Me **2e,f** X = Cl
1c R = CF_3
1d R = Ph

Scheme 1 *Reagents*: i, $MeCH(OH)CH_2X{-}H_2SO_4$ (96%); ii, $CH_2{=}CHCH_2Br{-}H_2SO_4$ (96%); iii, KOH/EtOH.

Table 1 Some characteristics of tetrazoles **2** and **3** prepared according to Scheme 1.[†]

Tetrazole	Yield (%)	n_D^{20}	Bp/°C (mmHg)
2a	88[a]/88[b]	1.5028	52 (0.1)
2b	84[a]/86[b]	1.4984	61 (0.1)
2c	58[b]	1.4341	41 (0.02)
2d	72[b]	–	66 (mp)
2e	45[a]	1.4765	45 (0.1)
2f	15[a]	1.4749	40 (0.05)
3a	60[c]/57[d]	1.4833	51 (13)
3b	58[c]/55[d]	1.4816	74 (18)
3c	61[c]	1.4074	61 (13)
3d	69[c]	–	78 (mp)

[a] Synthesized using reagent i. [b] Synthesized using reagent ii. [c] Synthesized by dehydrohalogenation of corresponding bromoderivative **2**. [d] Synthesized by dehydrohalogenation of corresponding chloroderivative **2**.

The introduction of a trifluoromethyl group at the 5-position of the heteroring decreases the yield of the alkylation products. This is probably to be connected to the decrease of the electron density on the reaction centres, namely the N2 or N3 atoms of the intermediate 1,4-dihydro-5R-tetrazolium cation,[11,13] due to the electron-accepting character of the substituent. Owing to partial destruction of 1-chloropropan-2-ol in sulfuric acid media, 2-(1-chloromethylethyl)-5R-tetrazoles **2e**,**f** were obtained in low yields.

2-(1-Methylvinyl)-5R-tetrazoles **3** were synthesized in 55–69% yields by the dehydrohalogenation of **2**, which readily occurs in solutions of potassium hydroxide in ethanol (Table 1).

Synthesized compounds **2**, **3** were identified as 2-substituted tetrazoles according to their spectral and physico-chemical characteristics:[‡] the chemical shift of the C-5 protons of species **2a**,**e** and **3a** were independent of concentration unlike to 1-substituted tetrazoles, which are concentration dependent.[14] The presence of two multiplets of the phenyl group in the NMR spectra of compounds **2d** and **3d** are typical for 2-isomers.[11,15] Compounds **2a**–**c**,**e**,**f** and **3a**–**c** had lower boiling points in comparison to well-known

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[†] *General procedure for the synthesis of compounds* **2**. Alkylating agent (31 mmol) was added to 5R-tetrazole **1** (25 mmol) in concentrated sulfuric acid (96%, 20 ml) with stirring. After 7 days, the reaction mixture was poured into cold water (100 ml) and extracted with dichloromethane (4 × 25 ml). The combined extracts were washed with water (10 ml), aqueous sodium carbonate (5%, 10 ml), water (10 ml) and then dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was distilled *in vacuo*. Compound **2d** was recrystallized from ethanol.

The synthesis of compounds **3** was carried out by dehydrohalogenation of **2** according to the method described in ref. 4. Compound **3d** was recrystallized from ethanol.

1-vinyltetrazoles and their synthetic parents.[1,4–10]

It should be noted that compounds **3**, unlike 2-vinyl-5*H*-tetrazole,[4] are stable and safe to handle.

The research described in this publication was made possible in part by grant no. RWE000 from the International Science Foundation.

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Received: Moscow, 31st May 1996
Cambridge, 25th June 1996; Com. 6/03905G

[‡] All new compounds were identified by ^{1}H NMR data and elemental analyses consistent with the assigned structures.

Selected spectroscopic data for **2a**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.80 (d, 3 H, CH_3), 3.83 (m, 2 H, CH_2), 5.26 (sextet, 1 H, CH), 8.56 (s, 1 H, HC=N).

For **2b**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.69 (d, 3 H, CH_3), 2.49 (s, 3 H, CH_3), 3.72 (m, 2 H, CH_2), 5.09 (sextet, 1 H, CH).

For **2c**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.84 (d, 3 H, CH_3), 3.83 (m, 2 H, CH_2), 5.29 (sextet, 1 H, CH).

For **2d**: ^{1}H NMR (100 MHz, CD_3COCD_3) δ 1.81 (d, 3 H, CH_3), 4.08 (m, 2 H, CH_2), 5.38 (sextet, 1 H, CH), 7.46–7.60 (m, 3 H, *m*-,*p*-Ph), 8.06–8.20 (m, 2 H, *o*-Ph).

For **2e**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.78 (d, 3 H, CH_3), 3.98