Unusual reactions of vinyl ketones with tetranitromethane. The synthesis of 5-acyl-3-nitroisoxazoles

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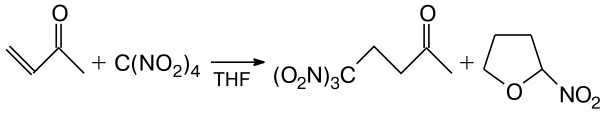
According to the literature data,[1] electrophilic alkenes are inert to tetranitromethane (TNM). Recently, we have studied three-component reactions of TNM with alkenes and showed[2,3] that nitronates, which are TNM—alkene adducts produced in the first step, are obtained only from olefins containing electron-donor substituents, while electrophilic alkenes participate only in subsequent [3+2] cycloaddition as dipolarophiles.

In our further investigations of reactions of alkenes with polynitromethanes, we found that methyl vinyl ketone (**1**) unusually reacts with TNM in THF to give 5,5,5-trinitropentan-2-one (**2**), a product of formal addition of trinitromethane to alkene **1**, and 2-nitrotetrahydrofuran (**3**) as a nitration product of THF (Scheme 1).

Scheme 1



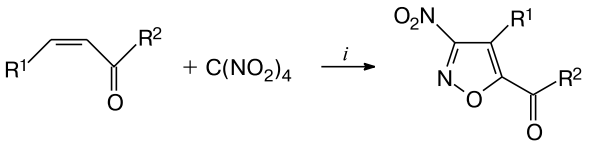
1 **2** (25%) **3** (21%)

In connection with this, we studied in more detail the reactivities of conjugated ketones toward TNM and found that the action of TNM on vinylic ketones **1** and **4**—**6** in the presence of triethylamine leads to 5-acyl-3-nitroisoxazoles **7**—**10** through a new pathway of heterocyclization of electrophilic alkenes (Scheme 2).

However, attempts to use other electrophilic alkenes in this reaction failed. Under these conditions, acrolein and acrylonitrile polymerized, (*E*)-4-phenylbut-3-en-2-one did not react with TNM, and 2,3,4,5,6-pentafluorostyrene and (*E*)-(2-nitrovinyl)benzene in reactions with TNM gave products of the formal addition of trinitromethane in trace amounts. Only with methyl acrylate (**11**) did we obtain trinitro derivative **12** [4] in low yield (Scheme 3).

Thus, we discovered an unusual reaction of vinyl ketones with TNM yielding 3-nitroisoxazoles. A possible precursor of nitroisoxazole could be an adduct of trinitromethane and a vinyl ketone, *e.g.*, compound **2** (see Scheme 1). To verify this assumption, we synthesized trinitro derivative **2** according to a known procedure.[5] However, treatment of adduct **2** with triethylamine under various conditions did not lead to isoxazole **7**.

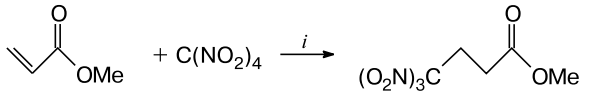
Scheme 2



1, **4**—**6** **7**—**10**

R^1 = H, R^2 = Me (**1**; **7**, 58%); R^1 = H, R^2 = Et (**4**; **8**, 47%); R^1 = H, R^2 = Ph (**5**; **9**, 85%); R^1, R^2 = —$(CH_2)_3$— (**6**; **10**, 45%); *i*. 1,4-Dioxane, Et_3N (2 equiv.).

Scheme 3



11 **12** (36%)

i. Et_3N, 1,4-dioxane—MeCN.

As a final remark, note that reactions of vinyl ketones with TNM demonstrate, as a way of example, that electrophilic alkenes can react with TNM. The presented method for the synthesis of 3-nitroisoxazoles is not versatile but it is feasible and involves accessible starting reagents. The mechanism of this reaction will be a subject of our further investigations.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ with chloroform as the internal standard (δ_H 7.28 and δ_C 77.1). The course of the reactions was monitored and the purity of the

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products was checked by TLC on Silufol UV-254 plates. Preparative column chromatography was carried out with SiO_2 as a sorbent (Acros, 60—200 mesh). Commercial alkenes **1**, **4**, and **5** and triethylamine were purified by distillation. Phenyl vinyl ketone (**7**) and tetranitromethane were prepared as described earlier.[6,7]

5,5,5-Trinitropentan-2-one (2). Tetranitromethane (0.49 g, 2.5 mmol) was added to a solution of methyl vinyl ketone (0.53 g, 7.5 mmol) in THF (8 mL) and the reaction mixture was stirred at 20 °C for 10 days. After the reaction was completed, the solvent was removed under reduced pressure and the product was isolated by column chromatography with light petroleum—EtOAc (5 : 1) as an eluent. The yield was 25%, m.p. 44 °C (*cf.* Ref. 8: m.p. 43—44 °C), R_f = 0.35 ($CHCl_3$). ^{1}H NMR, δ: 2.24 (s, 3 H, Me); 2.87—2.90 (m, 2 H, CH_2); 3.31—3.34 (m, 2 H, $CH_2C(NO_2)_3$). ^{13}C NMR, δ: 28.7 ($\underline{C}H_2CO$, $^1J_{C,H}$ = 137 Hz); 29.7 (CH_3, $^1J_{C,H}$ = 137 Hz); 37.3 ($\underline{C}H_2C(NO_2)_3$, $^1J_{C,H}$ = 130 Hz); 127.0 ($C(NO_2)_3$); 202.5 (CO).

2-Nitrotetrahydrofuran (3). Yield 21%, R_f = 0.78 ($CHCl_3$). ^{1}H NMR, δ: 2.05—2.17 (m, 2 H, CH_2); 2.20—2.30, 2.58—2.67 (both m, 1 H each, CH_2); 3.98—4.08 (m, 2 H, CH_2); 5.23 (t, 1 H, CH, ^3J = 7.6 Hz). ^{13}C NMR, δ: 25.6 (CH_2); 29.7 (CH_2); 71.1 (CH_2O); 79.7 (CH). MS, m/z = 71 $[M - NO_2]^+$. Compound **3** was not isolated in the analytically pure state.

Synthesis of 5-acyl-3-nitroisoxazoles 7—10 (general procedure). A solution of triethylamine (2.0 mmol) in dioxane (2.5 mL) was added dropwise to a cooled mixture of an alkene (1.0 mmol) and TNM (2.5 mmol) in dioxane (2.5 mL). Then the cooling was off and the reaction mixture was stirred at 20 °C for 12 h. If the reaction mixture separated into layers, acetonitrile (0.5 mL) was added. Then the solvent was removed under reduced pressure and the product was isolated by column chromatography with light petroleum—EtOAc (5 : 1) as an eluent.

1-(3-Nitroisoxazol-5-yl)ethanone[9] (7). Yield 58%, colorless crystals, m.p. 70—72 °C, R_f = 0.62 (light petroleum—EtOAc, 4 : 1). ^{1}H NMR, δ: 2.67 (s, 3 H, Me); 7.35 (s, 1 H, CH). ^{13}C NMR, δ: 26.8 (Me); 100.3 (CH); 163.3 (CNO_2); 165.7 (CON); 189.7 (C=O).

1-(3-Nitroisoxazol-5-yl)propan-1-one (8). Yield 47%, pale yellow crystals, m.p. 53—54 °C, R_f = 0.67 ($CHCl_3$). Found (%): C, 42.45; H, 3.54; N, 16.32. $C_6H_6N_2O_4$. Calculated (%): C, 42.36; H, 3.55; N, 16.47. ^{1}H NMR, δ: 1.20 (t, 3 H, Me, ^3J = 7.3 Hz); 3.07 (q, 2 H, CH_2, ^3J = 14.4 Hz); 7.34 (s, 1 H, CH). ^{13}C NMR, δ: 7.1 (Me); 33.2 (CH_2); 100.4 (CH); 162.9 (CNO_2); 165.7 (CON); 192.8 (CO).

(3-Nitroisoxazol-5-yl)phenylmethanone (9). Yield 85%, colorless crystals, m.p. 82—83 °C, R_f = 0.66 ($CHCl_3$). Found (%): C, 55.27; H, 2.63; N, 12.88. $C_{10}H_6N_2O_4$. Calculated (%): C, 55.05; H, 2.77; N, 12.84. ^{1}H NMR, δ: 7.53 (s, 1 H, CH); 7.56—7.60 (m, 2 H, Ph); 7.71—7.75 (m, 1 H, Ph); 8.31—8.33 (m, 2 H, Ph). ^{13}C NMR, δ: 102.9 (CH); 129.0 (CH, Ph); 130.8 (2 CH, Ph); 135.1 (CH, Ph); 134.3 (s, Ph); 163.5 (CON); 165.4 (CNO_2); 182.9 (CO).

3-Nitro-5,6-dihydro-1,2-benzoisoxazol-7(4*H*)-one (10). Yield 45%, yellow crystals, m.p. 114—115 °C, R_f = 0.25 ($CHCl_3$). Found (%): C, 46.21; H, 3.50; N, 15.19. $C_7H_6N_2O_4$. Calculated (%): C, 46.16; H, 3.32; N, 15.38. ^{1}H NMR, δ: 2.26—2.29, 2.78—2.81 (both m, 2 H each, CH_2); 3.17 (t, 2 H, CH_2, ^3J = 6.3 Hz). ^{13}C NMR, δ: 20.3, 22.3, 39.8 (all CH_2); 119.1 (s); 158.9 (CON); 160.9 (CNO_2); 189.2 (CO).

Methyl 4,4,4-trinitrobutanoate (12)[4] was obtained according to the general procedure for nitroisoxazoles. The yield was 36%, yellow substance, m.p. 25—26 °C, R_f = 0.51 (light petroleum—EtOAc, 4 : 1). ^{1}H NMR, δ: 2.75—2.78, 3.39—3.42 (both m, 2 H each); 3.75 (s, 3 H). ^{13}C NMR, δ: 27.9, 29.3 (both CH_2); 52.4 (Me); 129.2 ($C(NO_2)_3$); 169.8 (CO).

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