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HETEROCYCLIZATION OF *trans*-1,2,3-TRIPHENYL-CYCLOPROPANE USING NITROUS ACID

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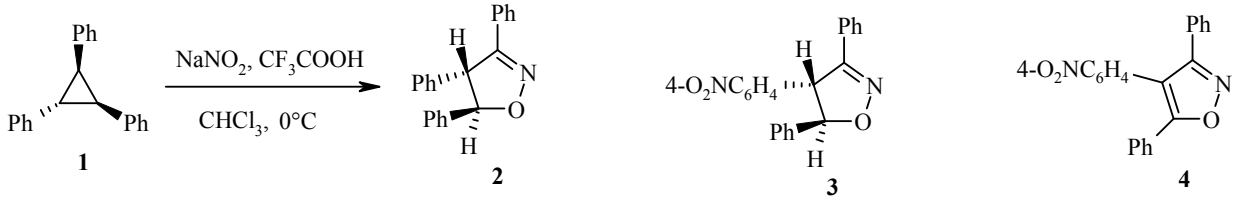
It is known that phenyl- and 1,2-diphenylcyclopropanes react readily with an equivalent of nitrous acid to form 5-phenyl- and 3,5-diphenyl-4,5-dihydroisoxazoles. The geometry of the benzene rings in the 1,2-diphenylcyclopropanes has virtually no effect on the yield of the corresponding heterocycles [1, 2]. Since not only mono- and disubstituted isoxazolines and isoxazoles but also triarylisoxazolines (and isoxazoles) are of interest for practical use [3], but synthetic methods of the latter are quite limited, we have tried to find out whether 1,2,3-triphenylcyclopropanes are converted to products of N=O fragment insertion into the three-carbon ring by the action of nitrous acid using the conditions reported in [1, 2].

It was shown that treatment of *trans*-1,2,3-triphenylcyclopropane (**1**) with an equivalent amount of sodium nitrite in trifluoroacetic acid gave only *trans*-3,4,5-triphenyl-4,5-dihydroisoxazole (**2**). This result shows that triphenylcyclopropanes can be used successfully in the synthesis of the corresponding isoxazolines.



1 **2** **3** **4**

We have previously reported that dihydroisoxazoles prepared from phenylcyclopropanes using an equivalent of HNO_2 can be oxidized to the corresponding isoxazoles using one equivalent of this reagent [4]. These same arylisoxazoles can also be directly formed from arylcyclopropanes if two equivalents of nitrous acid are used [4, 5]. It was found that reaction of hydrocarbon **1** with two equivalents of HNO_2 does not give rise to 3,4,5-triphenylisoxazole but, in this case, yields isoxazoline **2** (81%) and *trans*-3,5-diphenyl-4-(4-nitrophenyl)-4,5-dihydroisoxazole (**3**) (14%). Hence 3,4,5-triphenyl-4,5-dihydroisoxazole (**2**) behaves anomalously

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under nitrous acid oxidation conditions when compared with monophenylated analogs. It was interesting that treatment of the nitrophenylisoxazoline **3** with one equivalent of HNO_2 or of the hydrocarbon **1** with three equivalents of HNO_2 gave, in both cases, a high yield of the 4-(4-nitrophenyl)-3,5-diphenylisoxazole (**4**).

The experiment with the nitroisoxazoline **3** supports the formation of the nitroisoxazole **4** from hydrocarbon **1** through the preliminary stage of the isoxazoline **2** nitration.

Hence the corresponding triarylisoxazole derivatives can be synthesized from hydrocarbon **1** depending upon the ratio of substrate to HNO_2.

IR spectra were recorded on a UR-20 instrument in vaseline oil. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer using $CDCl_3$ with the residual $CHCl_3$ in the deuterated solvent as internal standard (δ 7.25 and 77.4 ppm respectively). Mass spectra were registered on a Finnigan SSQ 7000 instrument (GC-MS) using a capillary column (30 m×2 mm, DB-1 stationary phase), helium gas carrier (40 ml/min), temperature programming of 50-300ºC (10 deg/min), and ionization energy 70 eV. Separation of the reaction mixtures and monitoring of the reaction product purity were carried out on columns or on Silufol or alumina (Brockmann activity II grade) plates using the solvent system ether–petroleum ether (40-70ºC) (1:3).

Compound **1** was prepared by method [6]; mp 67ºC (EtOH) (mp 66.5-67.5ºC (heptane) [6]).

Reaction of *trans*-1,2,3-Triphenylcyclopropane (1) with Nitrous Acid (General Method). $NaNO_2$ was added over 30 min to a solution of compound **1** (2.70 g, 0.01 mol) in trifluoroacetic acid (5 ml) and chloroform (10 ml) at 0ºC. The reaction mixture was held at this temperature for 30 min, poured into water, and extracted with chloroform. The product was dried over magnesium sulfate, the extract was evaporated, and the residue was chromatographed on silica gel.

***trans*-3,4,5-Triphenyl-4,5-dihydroisoxazole (2)** was prepared using $NaNO_2$ (0.69 g, 0.01 mol). Yield 2.54 g (85%); mp 138ºC (EtOH) (mp 138-140ºC (heptane) [7]). ^1H NMR spectrum, δ, ppm (*J*, Hz): 4.74 (1H, d, *J* = 5.4, H-4); 5.56 (1H, d, *J* = 5.4, H-5); 7.26-7.37 (13H, m, H Ar); 7.59 (2H, dd, *J* = 1.5, *J* = 7.2, H Ar). ^{13}C NMR spectrum, δ, ppm: 62.3; 91.7; 125.3; 127.3; 127.5; 127.8; 128.2; 128.5; 128.8; 129.4; 129.8; 139.1; 140.8; 157.5. Mass spectrum, *m/z* (I_{rel}, %): 299 $[M]^+$ (2), 194 (13), 193 (100), 192 (10), 165 (20), 152(4), 116 (6), 103 (7), 89 (12), 77 (9), 51 (5). Found, %: C 84.17; H 5.58; N 4.21. $C_{21}H_{17}NO$. Calculated, %: C 84.25; H 5.72; N 4.68.

***trans*-3,4,5-Triphenyl-4,5-dihydroisoxazole (2)** (2.44 g, 81%) and ***trans*-4-(4-nitrophenyl)-3,5-diphenyl-4,5-dihydroisoxazole (3)** (0.48 g, 14%) were prepared similarly using $NaNO_2$ (1.38 g, 0.02 mol). Compound **3**: mp 197ºC (EtOH). IR spectrum, ν, cm^{-1}: 1540, 1345 (NO_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 4.79 (1H, d, *J* = 7.5, H-4); 5.72 (1H, d, *J* = 7.5, H-5); 7.26-7.37 (12H, m, H Ar); 7.59 (2H, d, *J* = 9.6, H Ar). ^{13}C NMR spectrum, δ, ppm: 62.7; 92.8; 123.8; 126.9; 127.5; 128.0; 128.4; 128.8; 129.0; 129.4; 129.7; 130.5; 140.8; 157.5; 166.5. Mass spectrum, *m/z* (I_{rel}, %): 344 $[M]^+$ (2), 194 (13), 193 (100), 192 (10), 165 (20), 152 (4), 116 (6), 103 (7), 89 (12), 77(9), 51 (5). Found, %: C 73.11; H 4.68; N 8.41. $C_{21}H_{16}N_2O_3$. Calculated, %: C 73.24; H 4.68; N 8.13.

4-(4-Nitrophenyl)-3,5-diphenylisoxazole (4) was prepared using $NaNO_2$ (2.07 g, 0.03 mol). Yield 3.12 g (92%); mp 223ºC (EtOH) (mp 221-222ºC [8]). IR spectrum, ν, cm^{-1}: 1535, 1340 (NO_2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.24 (2H, dd, *J* = 7.1, *J* = 1.5, H Ar); 7.53 (2H, dd, *J* = 7.1, *J* = 1.3, H Ar); 7.45-7.38 (10H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 113.3; 124.2; 127.0; 127.2; 128.2; 128.5; 128.7; 128.9; 129.8; 130.5; 131.3; 137.6; 147.6; 162.0; 166.6. Mass spectrum, *m/z* (I_{rel}, %): 342 $[M]^+$ (27), 180 (13), 165 (12), 134 (7), 106 (15), 105 (100), 78 (5), 77 (76). Found, %: C 73.43; H 4.38; N 8.01. $C_{21}H_{14}N_2O_3$. Calculated, %: C 73.68; H 4.12; N 8.18.

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