Cyclooctadecanedione (II) was prepared according to the procedure reported by Blomquist (*5*). Melting points were determined with a Thomas-Hoover Unimelt instrument and are uncorrected. NMR spectra were recorded on a Varian A-60 spectrometer using tetramethylsilane as an internal reference and shifts (δ) are reported in ppm.

1,1-Dibenzyl-5,5′:7,7′-bis(hexano)bis[6-(1H-cycloheptatriazolone] (III). A mixture of 1-benzyl-1*H*-triazole-4,5-dicarboxaldehyde (0.43 g, 0.002 mol), 1,10-cyclooctadecanedione (0.28 g, 0.001 mol), and 0.4 g of KOH in 50 mL of methanol was heated under reflux for 3 h. The mixture was cooled and the precipitate was collected by suction filtration. Crystallization from chloroform–petroleum ether afforded 0.52 g (66%) of III, mp 240–242 °C; NMR ($CDCl_3$) δ 7.70 (S, 4 H, H_4, and H_8), 7.10–7.40 (br, 10 H, ArH), 5.75 (S, 4 H, $ArCH_2$), 2.30–3.0 (br, 8 H, $C{=}C{-}CH_2$), and 0.90–1.70 (br, 16 H, CH_2). Elemental analysis (C, H, N) were obtained and submitted for review and were within ±0.3% of the theoretical values.

Registry No. I, 103532-75-8; II, 13747-10-9; III, 103532-76-9.

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Application of Dipolar Cycloaddition Reaction toward the Synthesis of Polyfunctionality Heterocycles

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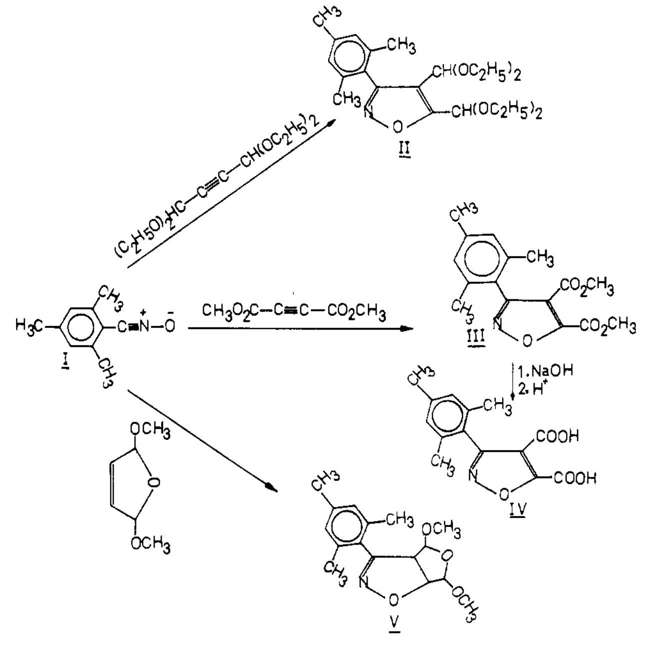
Dipolar cycloaddition reactions of 2,4,6-trimethylbenzonitrile oxide with two disubstituted acetylenes and with a disubstituted ethylene were used for the synthesis of polyfunctionality isoxazole and 2-isoxazoline ring systems.

The 1,3-dipolar cycloaddition reactions of nitrile oxides have been considered one of the best methods for the synthesis of isoxazole and 2-isoxazoline ring systems upon their reactions with substituted acetylenes (*1–5*) and ethylenes (*6–12*).

Most of the reported literature concern with the dialkylisoxazoles (*3–5*), dialkylisoxazolines (*6–10*) and with the monofunctional aldehydes (*2*, *11*, *12*) or esters (*1*, *8*). Yet, not much work have been reported on the synthesis of polyfunctional groups on the isoxazole ring. However, the lack of polyfunctional groups of the isoxazole and isoxazoline ring systems prompted us to the synthesis of isoxazoledicarboxaldehyde and isoxazole diester. I report in the present paper details on the reaction of the stable aromatic nitrile oxide, 2,4,6-trimethylbenzonitrile oxide (I), with two disubstituted acetylenes and with a disubstituted ethylene as shown in Scheme I.

Scheme I



Experimental Section

2,4,6-Trimethylbenzonitrile oxide was prepared according to the method reported by Grundmann (*13*). Acetylenedicarboxaldehyde bis(diethyl acetal) was prepared from acetylene and triethyl orthoformate by the method described by Wohl (*14*). Melting points were determined by using a Thomas-Hoover Unimelt instrument and are reported uncorrected. The nuclear magnetic resonance spectra were taken on a Varian A-60 spectrometer using tetramethylsilane as an internal reference and shifts (δ) are reported in ppm.

Preparation of 3-(2,4,6-Trimethylphenyl)-4,5-isoxazoledicarboxaldehyde Tetrakis(ethyl acetal) (II). To a solution of 4.83 g (0.03 mol) of 2,4,6-trimethylbenzonitrile oxide in 100 mL of tetrahydrofuran was added 6.90 g (0.03 mol) of acetylenedicarboxaldehyde bis(diethyl acetal). The resulting mixture was heated under reflux for 6 h. The solvent was removed on a rotary evaporator at diminished pressure. Distillation of the remaining liquid yielded 9.03 g (77%) of the product, bp 173–177 °C/1 mmHg. The product was solidified near room temperature, mp 44–45 °C; NMR ($CDCl_3$) δ 6.85 (2 H, s), 5.87 (1 H, s), 5.13 (1 H, s), 3.15–3.90 (8 H, m), 2.32 (3 H, s), 2.10 (6 H, s), 0.93–1.38 (12 H, m).

Dimethyl 3-(2,4,6-Trimethylphenyl)-4,5-isoxazoledicarboxylate (III). To a solution of 4.83 g (0.03 mol) of 2,4,6-trimethylbenzonitrile oxide in 80 mL of tetrahydrofuran was added 4.26 (0.03 mol) of dimethyl acetylenedicarboxylate. The mixture was heated under reflux for 1 h. After removal of the

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solvent, the residue was recrystallized from methanol–petroleum ether to give 5.18 g (57%) of III, mp 77–79 °C; NMR ($CDCl_3$) δ 7.15 (2 H, s), 4.0 (3 H, s), 3.7 (3 H, s), 2.30 (3 H, s), 2.10 (6 H, s).

3-(2,4,6-Trimethylphenyl)-4,5-isoxazoledicarboxylic Acid (IV). A solution of 3.03 g (0.01 mol) of dimethyl-3-(2,4,6-trimethylphenyl)-4,5-isoxazoledicarboxylate in 30 mL of 20% NaOH solution was heated under reflux for 2 h. The solution was cooled and then acidified with diluted HCl solution. The resulting solution was stirred vigorously for about 15 min, extracted with diethyl ether, and dried over anhydrous $CaCl_2$. After the ether was removed, the precipitated acid was collected and recrystallized from water to give 1.98 g (72%) of product IV, mp 212–214 °C; NMR (Me_2SO-d_6) δ 10.0 (2 H, s), 6.90 (2 H, s), 2.20 (3 H, s), 1.95 (6 H, s).

3a,4,6,6a-Tetrahydro-4,6-dimethoxy-3-(2,4,6-trimethylphenyl)furo[3,4-d]isoxazole (V). To a solution of 4.83 g (0.03 mol) of 2,4,6-trimethylbenzonitrile oxide in 70 mL of tetrahydrofuran was added 3.9 g (0.03 mol) of 2,5-dimethoxy-2,5-dihydrofuran. The resulting mixture was heated under reflux for 1 h. After the solvent was removed, the remaining solid was collected and recrystallized from methanol–petroleum ether to give 4.89 g (56%) of product V, mp 134–135 °C; NMR ($CDCl_3$) δ 6.90 (2 H, s), 5.10 (2 H, d), 4.80 (1 H, t), 4.20 (1 H, t), 3.45 (3 H, s), 3.25 (3 H, s), 2.35 (3 H, s), 2.20 (6 H, s).

Elemental analyses (C, H, N) for compounds II–V in agreement with theoretical values were obtained and submitted for review.

Registry No. I, 2904-57-6; II, 103884-79-3; III, 54470-38-1; IV, 103884-80-6; V, 103884-81-7; $(EtO)_2CHC{\equiv}CCH(OEt)_2$, 3975-08-4; $MeOC(O)C{\equiv}CC(O)OMe$, 762-42-5; 2,5-dimethoxy-2,5-dihydrofuran, 332-77-4.

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