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1,3-Dipolar Cycloaddition of Nitrile-N-oxides with 3,5-Di-*tert*-butyl-1,2-benzoquinone: Facile Formation of Spiro-1,3-dioxazoles

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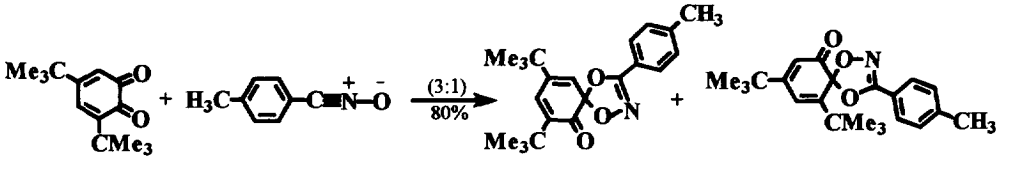
Abstract: *An efficient synthesis of novel spiro-dioxazole systems by the 1,3-dipolar cycloaddition reactions of 3,5-di-tert-butyl-1,2-benzoquinone with aryl nitrile oxides is described.*

The Diels-Alder reaction of *o*-benzoquinones has invoked considerable interest[1-6] and our own investigations[7-12] in this area have contributed to the understanding of the reactivity and synthetic potential of this fascinating class of compounds. During the course of this work, we became aware that 1,3-dipolar cycloaddition reactions[13-16] of *o*-benzoquinones have received very little attention. The scant information available is derived from the reaction of diazomethane[17] and certain mesoionic compounds[18] with 3,6-di-*tert*-butyl-1,2-benzoquinone and *o*-chloranil. In addition, there are two isolated reports on the cycloaddition of nitrile oxides to *o*-benzoquinone and *o*-bromanil[19,20]; the products have been assigned a tris and a bis adduct structure respectively, albeit with grossly inadequate supporting data.

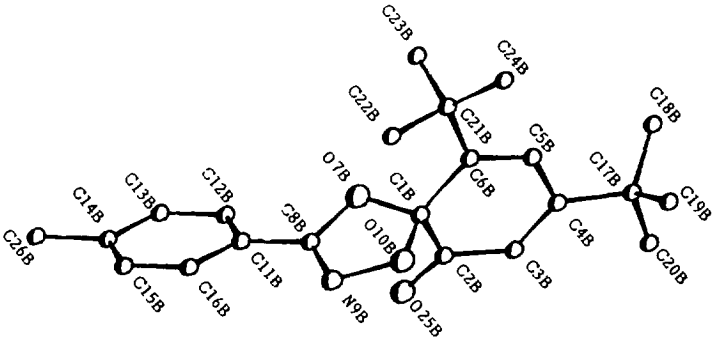
In view of the intrinsic interest in the 1,3-dipolar cycloaddition of *o*-quinonoid compounds and the untapped potential of such reactions for the synthesis of novel compounds, we have undertaken some work in this area and herein we report our preliminary results . Our studies were initiated with the cycloadditions of *p*-tolyl nitrile oxide[21] with 3,5-di-*tert*-butyl-1,2-benzoquinone. This reaction proceeded smoothly[22] to afford a regioisomeric mixture(3:1) of novel spiro-1,3-dioxazole derivatives as illustrated in the following scheme 1.



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

Scheme 1

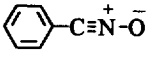
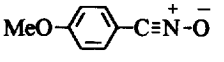
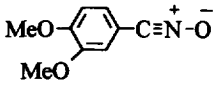
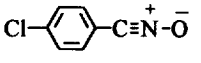
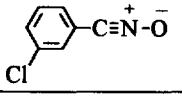
The two products obtained were separated by silica gel column chromatography. The IR spectra showed a single carbonyl group absorption at 1699 and 1685 cm^{-1} respectively for **3** and **4**[23]. The characteristic stretching frequency of C-O bond was observed at 1485 cm^{-1}. ^{13}C NMR spectrum of **3** and **4** showed the characteristic peak of the spiro carbon atom at δ 104 and 102 ppm respectively and that of C=N at δ 159 ppm. Final proof for the structure of the adducts was derived by single crystal X-ray analysis[24] of **4** utilizing SHELXS-86[25] and refined by SHELXL-93[26].



X-ray structure of **4**

The experiment was repeated with various nitrile oxides and in all cases the reaction proceeded smoothly to afford the spirodioxazoles. The results are summarised in Table 1.

Table 1 . Cycloaddition of nitrile oxides with 3,5-di-*tert*-butyl-1,2-benzoquinone

Entry	Nitrile-N-Oxide	Product (Ratio)	M.P	Yield (%)[1]
1		**5,6** (1:1)	**5** 144-146 °C **6** 120-122 °C	98
2		**7,8** (1:1)	**7** 128-130 °C **8** 156-158 °C	100
3		**9,10**(1:1)	**9** 110-112 °C **10** 166-168 °C	100
4		**11,12**(1.6:1)	**11** 150-152 °C **12** 146-148 °C	83
5		**13,14**(2:1)	**13** 125-127°C **14** 129-131 °C	83

[1]Isolated yield.

In conclusion, aryl nitrle oxides undergo facile cycloaddition to 3,5-di-*tert*-butyl-1,2-benzoquinone thus offering an efficient method for the synthesis of novel spirodioxazole systems. Preliminary results indicate that the reaction is general in scope and it may be be pointed out that the products are potentially amenable to a number of synthetic transformations. It is also worthy of note that the mono spirodioxazole formation reported here may be viewed as a means to obtain partially protected *o*-quinones. Further work is in progress.

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22. Typical Experimental procedure.
4-Methyl benzohydroximoyl chloride[21](0.250 g,1.50 mmol) in benzene (10 mL) was added to a solution of 3,5-di-*tert*-butyl-1,2-benzoquinone (0.220 g, 1.0 mmol) and triethyl amine (0.152 g, 1.5 mmol) in benzene at room temperature and stirred. When the reaction was complete (as indicated by TLC,30 min.), the reaction mixture was filtered to remove triethyl amine hydrochloride and the solvent was evaporated *in vacuo*. The residue obtained was

chromatographed on a silica gel column. Elution with 1% and 2% ethyl acetate in hexane afforded **3** (60% m.p 116-118°C) and **4** (20% m.p 120-122°C) as yellow crystalline solids.

23. Spectral data for illustrative example **4**.
Orange yellow crystalline solid m.p 120-122°C.
I R(KBr)- 2979, 1685, 1631,1485,1473,1351,1189,1119,1092,830,659 Cm^{-1}
^{1}H NMR in $CDCl_3$ (δ) : 7.79-7.2 (q, 4H), 6.5(d, 1H),5.9(d, 1H), 2.4(s, 3H),1.3(s, 9H), 1.15(s, 9H) ppm. ^{13}C NMR in $CDCl_3$ (δ): 193.41,163.79,159.76 151.17,142.2129.36,127.03,125.27,119.63,115.39,104.29,36.93,35.91,29.92,27.89, 21.53 ppm.
CHN analysis: Found C-74.4362 %, H-7.69411 %, N-3.72221 % (calculated-74.76 %, H- 7.7%, N-3.96 %)

24. Single crystal X-ray analysis co-ordinates and parameters.
Crystal data for **4**: $C_{22}H_{27}NO_3$, orange yellow crystals, 0.32x 0.28x0.16 mm, monoclinic, space group p 21/c, unit cell dimensions: a =18.207(7)°A,α = 90 deg, b =9.921(5)°A, β =106.03(4) deg, c = 23.42(11)°A, γ =90 deg. RI = 0.960, WR2 = 0.1572, Z = 8, density = 1.155 mg/ m-3, F(000) =1520, n=0.076 mm-1.

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