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A One Step Transformation of the Sodium Salt of α-*aci*-Nitrotoluene into 3,4,5-Triphenylisoxazole

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Synopsis. 3,4,5-Triphenylisoxazole was produced by the reaction of the sodium salt of α-*aci*-nitrotoluene with the 1-cyano-1-methylethyl radical. The reaction was found to proceed *via* one electron transfer from α-*aci*-nitrotoluene anion to a 1-cyano-1-methylethyl radical.

Although a great number of works have been published on the reactivity of the 1-cyano-1-methylethyl radical,[1)] little was known of their one electron transfer reactions.[2)] We now report chemical evidence to support that one electron transfer is involved in the reaction of the 1-cyano-1-methylethyl radical generated by decomposition of 2,2′-azobisisobutyronitrile (AIBN) with the sodium salt of α-*aci*-nitrotoluene (**1**).

When a mixture of **1** and AIBN was heated in dimethyl sulfoxide (DMSO) at a bath temperature of 40—80 °C for 2—3 h, a crystalline product was obtained. The structure was confirmed to be 3,4,5-triphenylisoxazole (**2**) by the analysis of the spectra and a mixed melting point determination. From a number of experiments, it was found that the formation of **2** was accelerated with increasing of the reaction temperature (see Table 1). The kinetics of the decomposition of AIBN was studied in various solvents by Kulkarni *et al.*[3)] They suggested that AIBN does not decompose to 1-cyano-1-methylethyl radical up to a temperature of 40 °C, that the formation of the radical from AIBN follows first order kinetics and that the rate constant is directly proportional to the reaction temperature. The dependence of the efficiency of this reaction on the reaction temperature correlates well with the dependence of the formation of 1-cyano-1-methylethyl radical on the reaction temperature. These facts imply that this reaction is initiated by thermal evolution of 1-cyano-1-methylethyl radical but not by one electron transfer from **1** to AIBN.

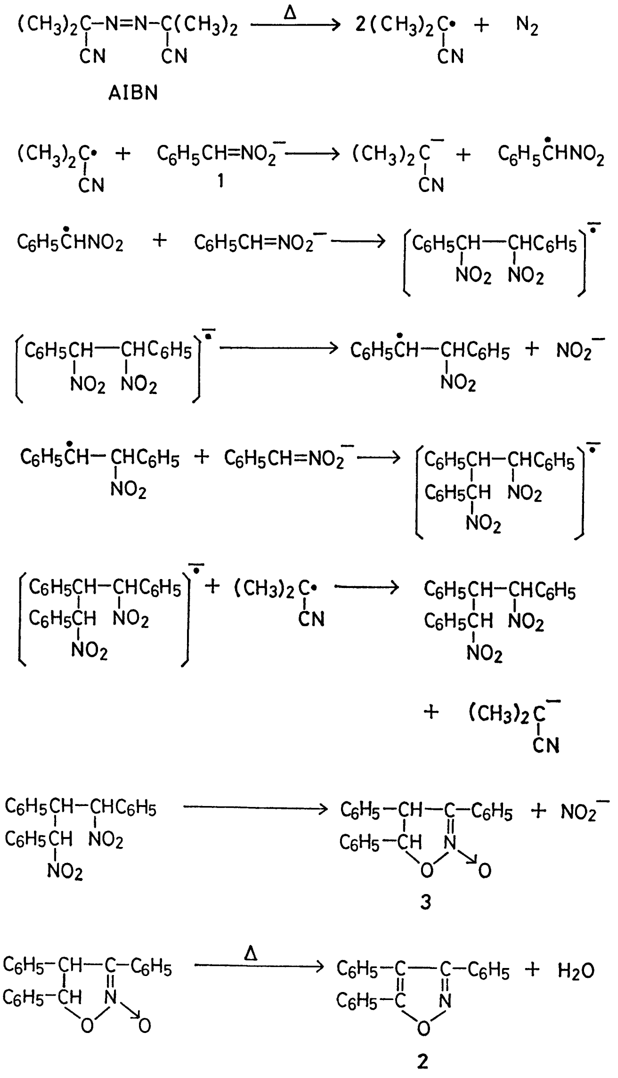
Analogous formation of 3,4,5-triphenyl-2-isoxazoline *N*-oxide (**3**) has been observed in the reaction of **1** with 2-bromo-2-nitropropane in DMSO at room temperature, for which a mechanism involving one electron transfer from **1** to 1-methyl-1-nitroethyl radical has been proposed.[4)] In the reaction of **1** with 1-cyano-1-methylethyl radical, a similar mechanism should operate.

Table 1. Reactions of sodium salt of α-*aci*-nitrotoluene (**1**) with AIBN[a)]

Run	Amount of AIBN/mmol	Temp/°C	Time/h	Yield of **2**[b)]/%
1	25	25	6	trace
2	5	40	6	4
3	15	40	3	12
4	25	40	3	16
5	25	70	2	25
6	25	80	2	26
7[c)]	25	70	2	25

a) All the reactions were carried out using 3.95 g (25 mmol) of **1** in DMSO (25 ml). b) Pure isolated yield on **1**. c) The reaction was carried out under nitrogen.

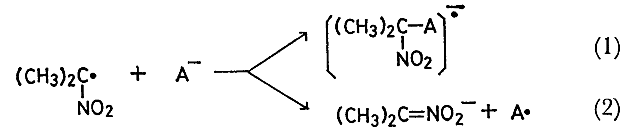
The above assumptions were strongly suggested by the fact that the reaction of **1** with 2-bromo-2-nitropropane under conditions similar to those employed for the reaction of **1** with AIBN resulted in the exclusive formation of **2** (see Experimental). It is surprising that relatively mild heating (70 °C, 2 h) of **3** in the reaction mixture afforded **2**, because it has been known that heating of **3** in a boiling ethanolic sodium hydroxide solution or without solvent under a reduced



Scheme 1.

pressure above its melting point give rise to **2**.⁵⁾ Thus, reactions of 1-methyl-1-nitroethyl radical and 1-cyano-1-methylethyl radical with **1** give essentially the same product. The process outlined in Scheme 1 may explain the formation of **2**: here an intermolecular cyclization of the resulting 1,3-dinitro-1,2,3-triphenylpropane could lead to **3** which give **2** by thermal dehydration.

It is well known that the scope of the S_{RN} 1 reaction involving the 1-methyl-1-nitroethyl radical is limited by the competition between reaction (1) (leading to substitution) and reaction (2) (leading to the 2-nitropropane dimer) as shown in Scheme **2**.



Scheme 2.

When the anion A⁻ contains a conjugated phenyl group which can lead to a substituted benzyl radical A, reaction (2) greatly predominates.⁶⁾ This may be the reason why 2-bromo-2-nitropropane fails to yield cross-coupling product with **1**.⁴⁾

In order to generalize the preparative route for isoxazoles from nitroalkane, similar reactions of anions of *aci*-nitroalkanes, such as the lithium salt of *aci*-2-nitropropane or *aci*-nitrocyclohexane, with AIBN were studied. However, the reactions under comparable conditions were unsuccessful.

Apparently similar to 1-methyl-1-nitroethyl radical, the 1-cyano-1-methylethyl radical has a sufficiently high electron affinity that electron transfer take preference to the addition reaction. Thus, trapping of the radical A· by the anion A⁻ is greatly facilitated by the presence of phenyl and nitro groups which will stabilize the resulting radical anion $[A\text{–}A]^{\overline{\cdot}}$.

Experimental

General. Melting points were determined in capillary tubes in a liquid bath and are uncorrected. The IR spectra were recorded with a Hitachi 215 grating spectrophotometer. Mass spectra were determined with a Hitachi RMU-6C spectrometer.

Materials. Commercial DMSO was distilled prior to use. Commercial AIBN was recrystallized from methanol. The sodium salt of α-*aci*-nitrotoluene was prepared by addition of methanol solution of phenylnitromethane⁷⁾ to an equivalent amount of sodium methoxide in methanol. 2-Bromo-2-nitropropane was prepared as described previously.⁴⁾

*General Procedure for Reaction of **1** with AIBN:* To a stirred suspension of **1** (3.95 g, 25 mmol) in DMSO (25 ml), AIBN (4.11 g, 25 mmol) was added in portions at 40 °C and the mixture was stirred at 70 °C for 2 h. The mixture was then poured into cold water to give a slightly yellow precipitate, which was collected by filtration, washed with water and dried. To the solid thus obtained methanol (30 ml) was added and the mixture was heated under reflux for 0.5 h, and then cooled to room temperature. The solid was again collected by filtration and recrystallized from ethanol to give **2** as colorless needles in 25% yield; mp 209—210 °C (lit,⁸⁾ mp 212 °C); MS 297.4 (M⁺); IR (KBr) 1430, 1400, 920 cm⁻¹ (C=C), 1210, 1010 cm⁻¹ (–O–).

*Reaction of **1** with 2-Bromo-2-nitropropane:* To a stirred suspension of **1** (3.95 g, 25 mmol) in DMSO (25 ml), 2-bromo-2-nitropropane (2.10 g, 12.5 mmol) was added dropwise at room temperature. The resulting solution was stirred at 70 °C for 2 h, and then poured into cold water. The mixture was extracted with chloroform (100 ml). The extract was washed with water, dried over magnesium sulfate, and concentration gave a solid material. The crude material was twice recrystallized from ethanol to give **2** in 24% yield.

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