

Synthesis of Novel Diazeniumdiolate and Sydnone-N-oxide Products

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Abstract

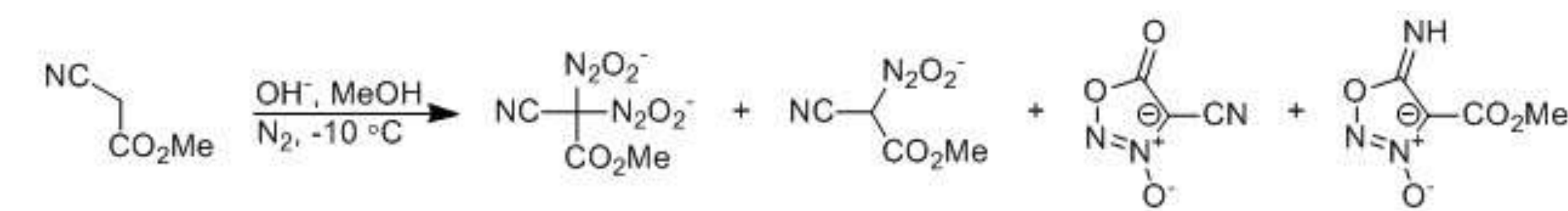
Methyl cyanoacetate reacts with NO in the presence of ammonium hydroxide or alkali hydroxides forming an unstable and reactive diazeniumdiolate. The poorly characterized product decomposes in aqueous solutions releasing NO and forming a stable sydnone-N-oxide. The final product is stable, and is characterized by UV-Vis, IR and NMR spectroscopic data, and single crystal X-ray diffraction analysis as potassium trimethyl 1,3-dinitrilopropenyl-1,2,3-tricarboxylate. The release of NO from the less stable diazeniumdiolate in aqueous media at pH 7.4 under ambient conditions is verified by the trapping of the free radical with the well-known NO-trapping reagent Fe(MGD)₂. EPR spectral data measured for the NO adduct of Fe(MGD)₂ exhibits the expected three-line pattern.

Introduction

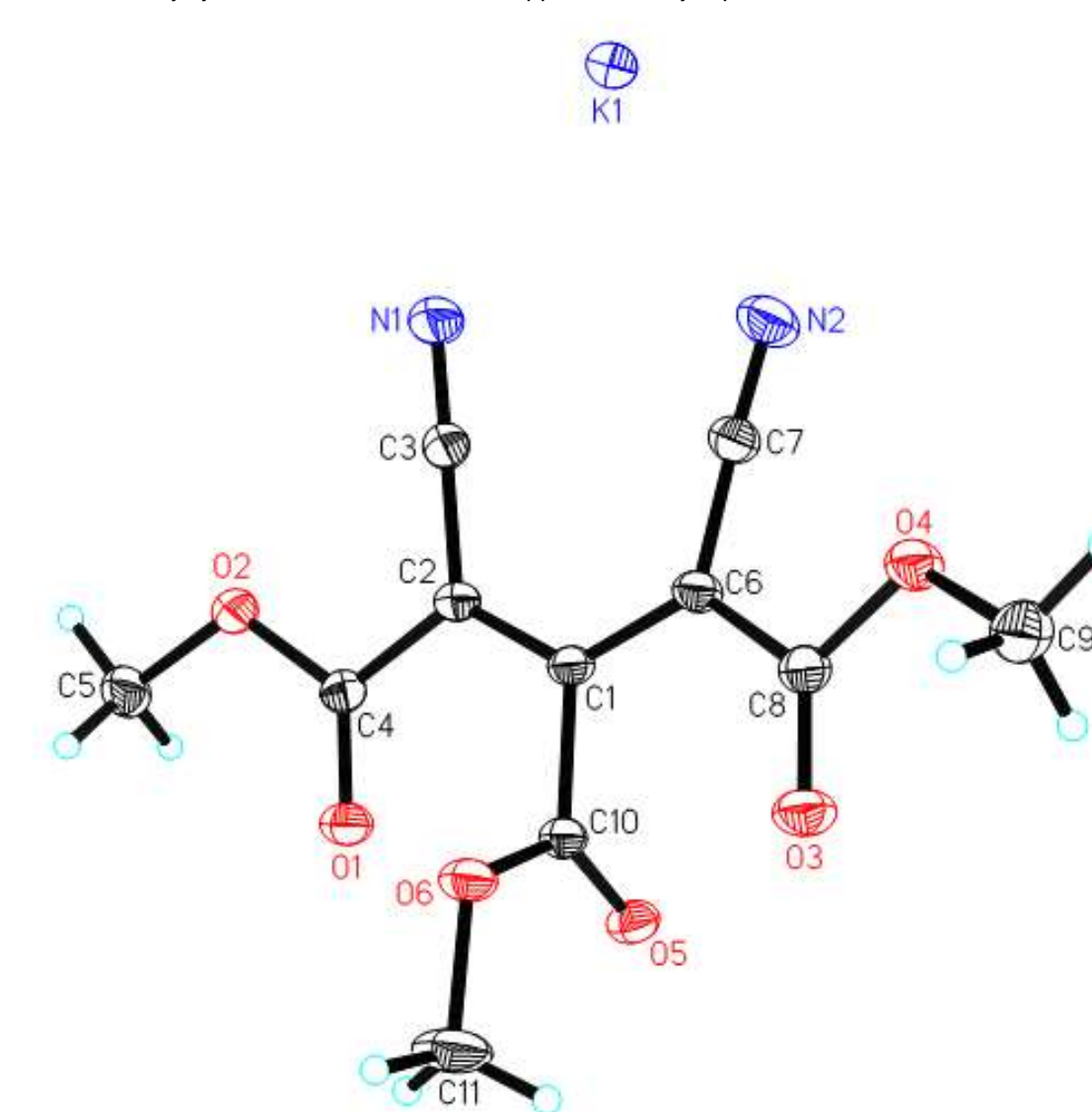
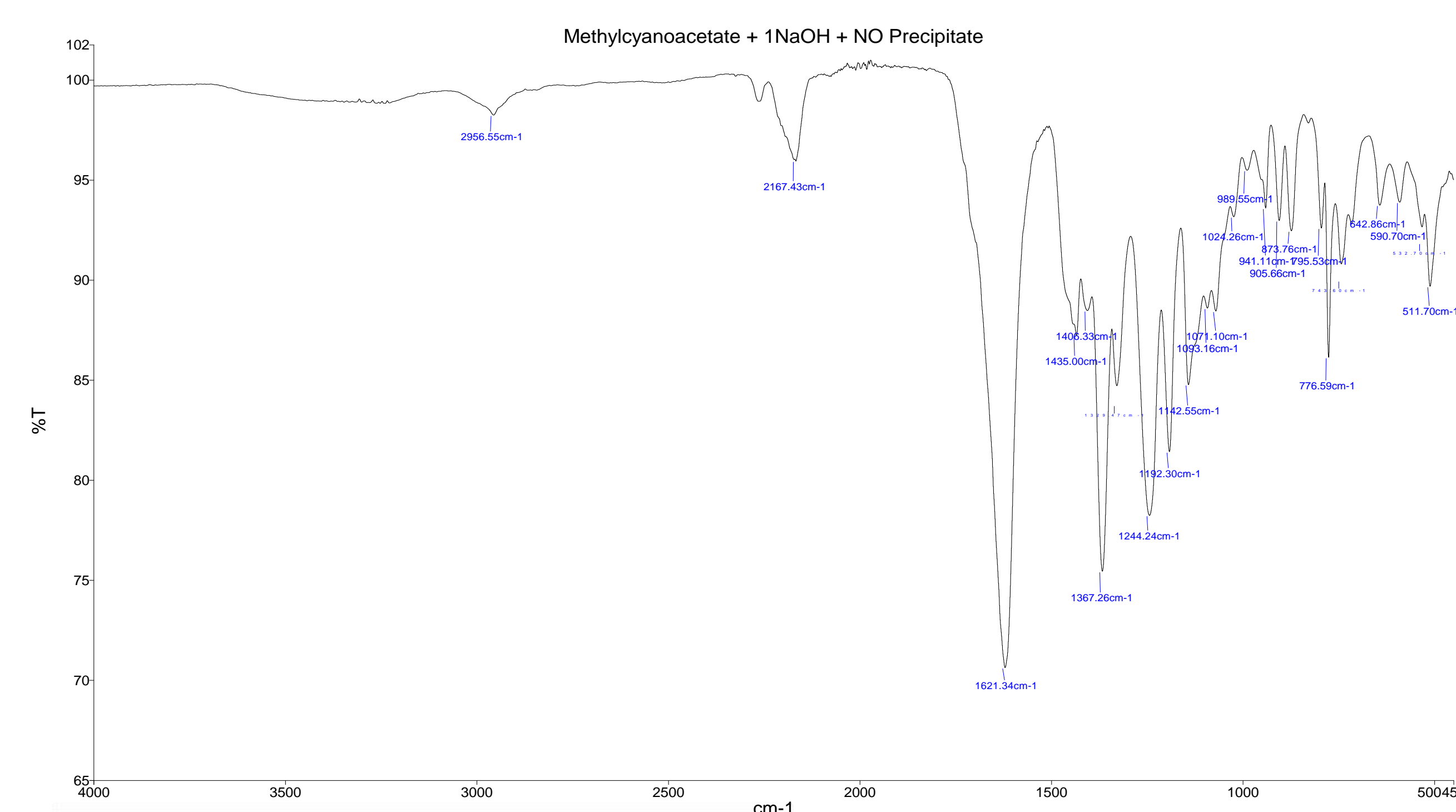
NO and its one electron reduction product NO⁻ (nitroxyl) play a number of physiological roles and are considered as a possible cure to cardiovascular diseases. It is also shown that the acid form of nitroxyl, HNO, is shown to act as a deterrent to alcoholism. Cyanamide is already used in Europe and Japan as a pro-drug for the in vivo generation of HNO. Therefore, there is considerable research interest in the synthesis and studies of NO and HNO. Donors capable of releasing either of the molecules under physiological conditions are receiving great attention. As part of our research effort towards the synthesis of new NO-donors and nitrogen-rich explosives, we have studied the nitrosylation of an active methylene-containing compound. Previous work in this lab has demonstrated that active methylene substrates such as diethylmalonate react with NO in the presence of a strong base forming diazeniumdiolate or sydnone-N-oxide salts. Diazenium-dioliates are a well-studied group of nitrogen-rich high-energy density materials and NO donor compounds. These salts contain one or more cis-N₂O₂⁻ groups. On the other hand, sydnone-N-oxides feature a trans-N₂O₂ grouping. The two types of compounds illustrate the versatility of NO reactivity. The compounds possess both explosive decomposition and NO-donor properties. Therefore, in this study we have extended the reactions of NO with another related substrate, namely, methyl cyanoacetate.

Results

The reaction of NO with the anion of methyl cyanoacetate generated with a variety of bases yields a poorly characterized crude product. As shown below, we expected the formation of two diazeniumdiolate and two sydnone products.



The reaction proceeds similarly with a variety of bases, namely, ammonium, lithium, sodium and potassium hydroxides. The UV-Vis spectra for the products in aqueous media exhibit an intense peak at ca. 275 nm indicating the presence of one or two -N₂O₂⁻ groups. The spectra change over 2 h and eventually show stable peaks at 270 and 370 nm revealing slow decomposition. The IR spectra contain prominent peaks at ca. 2200 and 1600 cm⁻¹ indicating the presence of the nitrile and carboxylate groups, respectively. The potassium salt is characterized by X-ray data.

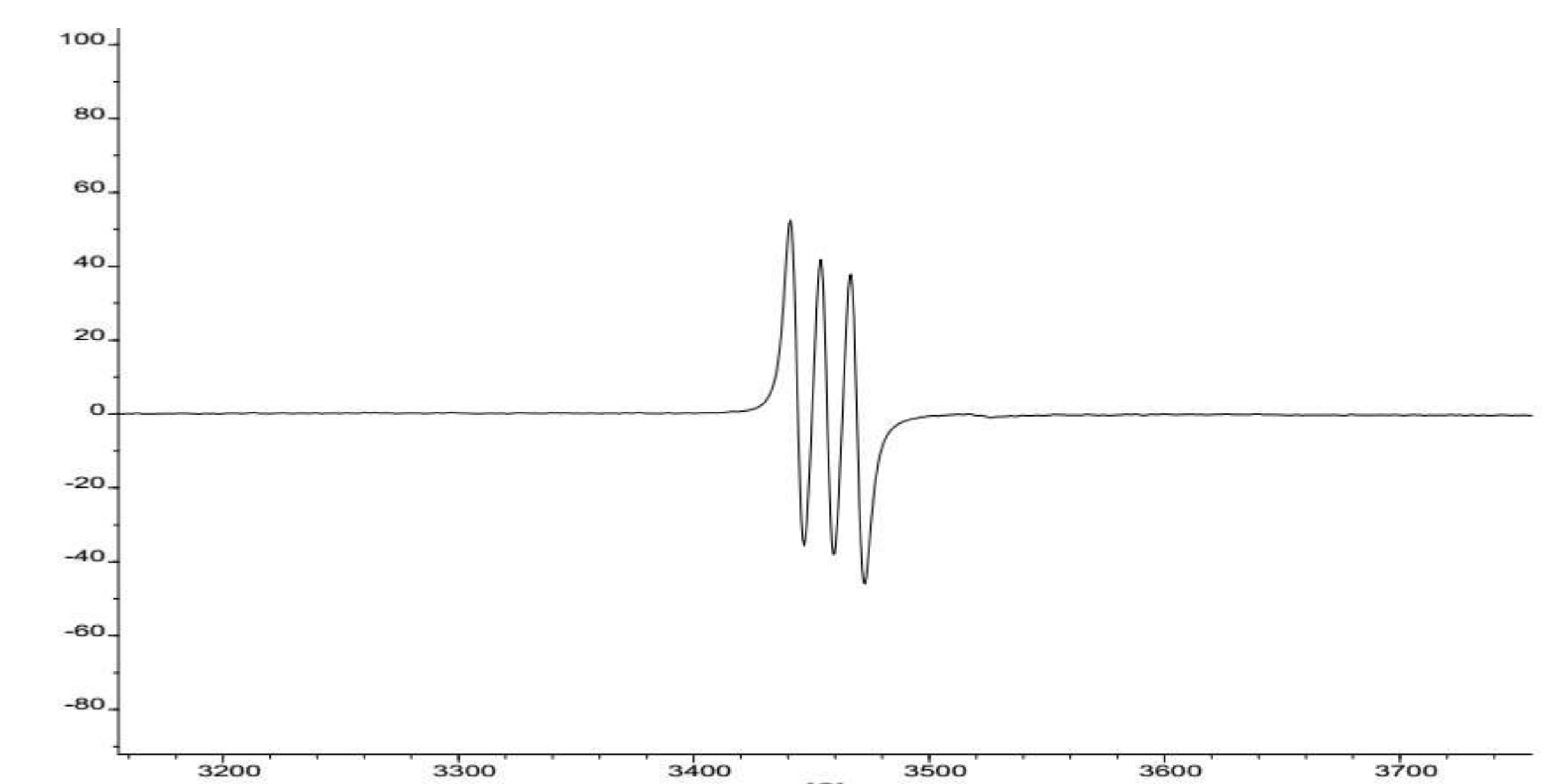
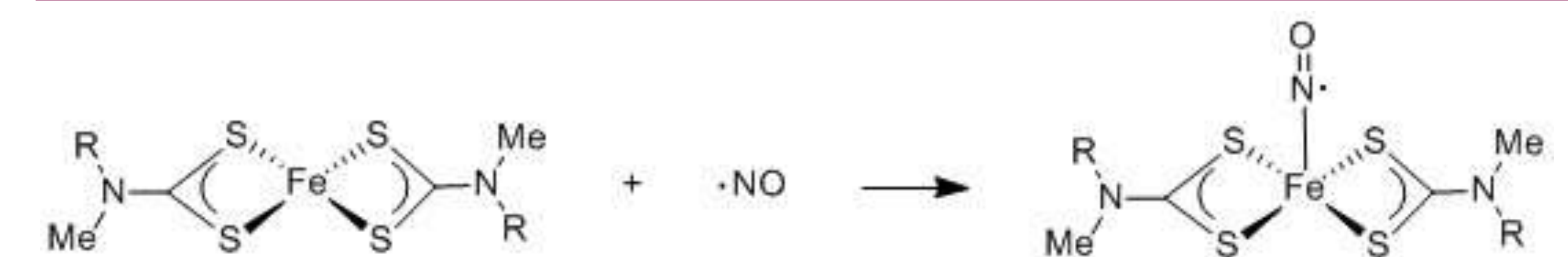


Selected Bond Distances (Å)

- C1 – C2 1.3935(12)
- C1 – C6 1.3957(12)
- C2 – C3 1.4237(12)
- C6 – C7 1.4173(12)

Discussion

Methyl cyanoacetate reacts with NO in the presence of ammonium hydroxide and alkali hydroxides forming highly reactive diazeniumdiolate products. The crude products isolated are poorly characterized but a final product formed after the complete decomposition of the potassium derivative is satisfactorily characterized as potassium trimethyl 1,3-dinitrilopropenyl-1,2,3-tricarboxylate. The release of NO from the crude products at pH 7.4 and room temperature in aqueous media is verified by the trapping of the free radical with the well-known trapping reagent Fe(MGD)₂. EPR spectral data measured for the NO adduct of Fe(MGD)₂ exhibits the expected three-line pattern.



EPR spectrum measured for the crude product obtained from the reaction with KOH in the presence of Fe(MGD)₂.

Conclusions

NO-Donor products are prepared from the reaction of NO with methyl cyanoacetate under basic conditions. The products are highly unstable and quickly release NO to form trimerized stable product. A similar but less acidic substrates, perhaps, containing a less electron-withdrawing group in place of -CN may produce sufficiently stable NO donor products.

Acknowledgement

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