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An efficient synthesis of conjugated nitro-olefins using ceric ammonium nitrate

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Abstract—An efficient method for the synthesis of conjugated nitro-olefins from α,β-unsaturated acids under extremely mild conditions using ceric ammonium nitrate (CAN) at room temperature in acetonitrile in moderate to good yields is described.

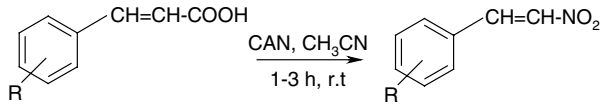
1. Introduction

The nitro group is a powerful electron-withdrawing substituent and this property dominates the chemistry of all molecules containing this functional group. Nitroalkenes are powerful dienophiles in the Diels–Alder reaction.[1] The versatility of the nitro group makes possible its transformations into many compounds with diverse functionalities. Removal of a nitro group leading to the formation of carbonyl compounds in the classical Nef reaction is well known.[1] Significant biological activities[2] have been reported for some nitro-olefins.

Several methods are reported in the literature for the synthesis of nitro-olefins. All these center on the classical Henry reaction, involving the condensation of aldehydes/ketones with nitroalkanes and subsequent dehydration of the β-nitro alcohols. A variety of reagents have been used for dehydration[3] such as phthalic anhydride,[4] dicyclohexylcarbodiimide,[5] methanesulfonyl chloride,[6] pivaloyl chloride,[7] etc.

Synthesis of nitro-alkenes has also been achieved by direct condensation of aldehydes/ketones with nitroalkanes using heterogeneous catalysts such as Envirocat EPZG[8] and GEBC.[9]

Ceric ammonium nitrate (CAN) has been employed as a mild oxidizing agent in organic synthesis.[10–12] Peterson et al.[10] reported the formation of ring-substituted products using N_2O_4 as the nitrating agent in the presence of CAN, however, the reaction was handicapped by low yields. To further explore the usage, herein, we report a novel method for the synthesis of nitro-alkenes from α,β-unsaturated aromatic acids using CAN in acetonitrile at room temperature (Scheme 1).



Scheme 1.

In a typical experimental procedure, a mixture of CAN and ferulic acid (entry 2) in acetonitrile was stirred for 2 h at room temperature and the product was obtained in 80% yield. In a similar fashion, various nitro-olefins were synthesized and their isolated yields are tabulated in Table 1. Substitution on the phenyl ring, especially with electron-donating groups, improved the yields.

The present letter deals with the formation of the *ipso*-substituted product exclusively, in moderate to good yields at ambient temperatures. We suggest that the change in reaction solvent to acetonitrile is responsible for the exclusive formation of the *ipso*-product, without the formation of the ring-substituted product.

2. General experimental procedure

Acid (0.515 mmol) and CAN (1 mmol, 2 equiv) were stirred in acetonitrile (10 ml) at room temperature for 1 h. The reaction was monitored by TLC. After

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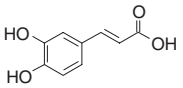
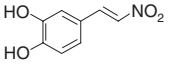
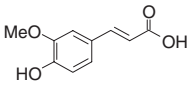
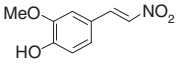
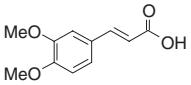
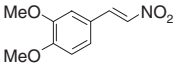
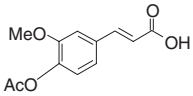
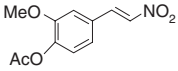
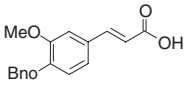
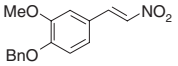
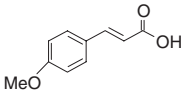
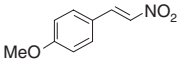
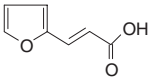
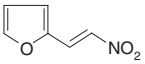
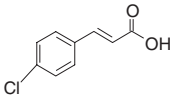
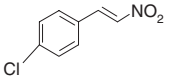
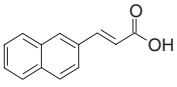
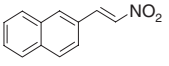
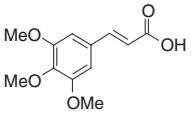
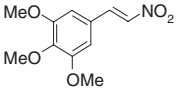
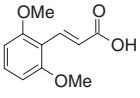
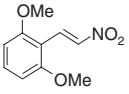
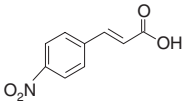
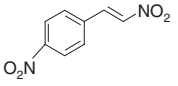
Table 1. Conversion of α,β-unsaturated acids in to conjugated nitro-olefins

S. No.	Substrate	Product	Time (h)	Yields (%)
1			1	75
2			2	80
3			1.5	70
4			3	60
5			3	65
6			2.5	70
7			1.5	75
8			5	40
9			5	40
10			1.5	75
11			1.5	75
12			5	30

completion of the reaction, the acetonitrile was removed under vacuum and the residue dissolved in EtOAc, the solution washed with water then dried over anhydrous Na_2SO_4. The crude product was subjected to column chromatography over silica gel and eluted with 20% EtOAc in hexane to obtain the pure compound. All the products were characterized by IR, ^{1}H NMR, and mass spectroscopic methods and also by comparison with the reported values.

2.1. 2,6-Dimethoxy-β-nitrostyrene

^{1}H NMR ($CDCl_3$, 200 MHz): 3.82 (s, 3H, OMe), 3.98 (s, 3H, OMe), 6.92–7.10 (m, 3H), 7.90 (d, 1H, $J = 12$ Hz, olefinic), 8.18 (d, 1H, $J = 12$ Hz, olefinic). ^{13}C NMR ($CDCl_3$, 75 MHz): 55.8, 56.0, 112.4, 116.3, 119.1, 119.1, 135.1, 138.6, 153.6, and 153.9. Mass: *m/z*: 209 (100). Anal. Calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.26. Found: C, 57.38: H, 5.24.

2.2. 3-Methoxy-4-acetoxy-β-nitrostyrene

^{1}H NMR ($CDCl_3$, 200 MHz): 2.36 (s, 3H, $COCH_3$), 3.96 (s, 3H, OMe), 7.12–7.18 (m, 3H), 7.54 (d, 1H, $J = 12$ Hz, olefinic), 7.98 (d, 1H, $J = 12$ Hz, olefinic). Mass: *m/z*: 237 (100).

2.3. 3-Methoxy-4-benzyloxy-β-nitrostyrene

^{1}H NMR ($CDCl_3$, 200 MHz): 3.80 (s, 3H, OMe), 5.20 (s, 2H, OCH_2), 6.30 (d, 1H, $J = 12$ Hz, olefinic), 6.99 (s, 1H), 7.40–7.60 (m, 6H), 7.70 (d, 1H), 8.20 (d, 1H, $J = 12$ Hz, olefinic); ^{13}C NMR ($CDCl_3$, 75 MHz): 153.6, 150.5, 139.8, 136.5, 131.5, 129.2, 128.5,

127.2, 124.3, 114.5, 111.5, 71.0, 56.5. Mass: m/z: 285 (100).

In conclusion, we have developed a simple, novel, efficient and mild methodology for the conversion of aryl α,β-unsaturated acids into conjugated nitro-olefins using ceric ammonium nitrate at room temperature. It is anticipated that this method will find wide applications in the synthesis of bioactive nitro-alkenes.

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