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A novel synthesis of α-azidocinnamates, α-azido-α,β-unsaturated ketones and β-azidostyrenes mediated by cerium(IV) ammonium nitrate

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Abstract

Cerium(IV) ammonium nitrate mediated addition of azide to cinnamic esters, acids and α,β-unsaturated ketones, followed by reaction with sodium acetate afforded the α-azidocinnamates, β-azidostyrenes and α-azido-α,β-unsaturated ketones, respectively, in good yields. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: cerium(IV) ammonium nitrate; azides; radicals.

Cerium(IV) ammonium nitrate (CAN) has been widely used in carbon–carbon bond-forming reactions.[1–3] In addition, it has found important applications in carbon–hetero atom bond formation also.[4,5] As early as 1971, Trahanovsky and Robbins have reported the CAN-mediated addition of azide to styrenes.[6] Subsequent reports have involved the addition of azide radical to glycals[7] and other enol ethers[8] and also to α-methoxy acrylonitrile.[9] However, the oxidative addition of azide to α,β-unsaturated carbonyl compounds like cinnamic esters and acids is hitherto unknown; inexplicably, previous attempts have failed.[6,8] With the premise that the reaction can give rise to α-azido-β-nitrato compounds that can serve as precursors to biologically important α-amino-β-hydroxy acids or α-azidocinnamates that are useful in the synthesis of indoles, azirines[10] and isoquinolines,[11] we have undertaken an investigation of the reaction of azide with cinnamic acids and esters in the presence of CAN. Our preliminary results indicating the usefulness of the process are presented here. The reported procedure for the synthesis of α-azidocinnamates involves the condensation of aromatic aldehydes with ethyl azidoacetate in ethanolic sodium ethoxide.[12]

Our initial experiment involved the reaction of ethylcinnamate and sodium azide with CAN resulting in a 73% yield of the α-azido-β-nitrato ester **2** as a 1:1 mixture of *syn*- and *anti*-isomers (Scheme 1).

The crude product, on treatment with sodium acetate in dry acetone, afforded the α-azidocinnamate **3** in 68% yield (Scheme 2). The stereochemistry was assigned to be *Z* on the basis of the ^{1}H NMR spectrum.[12]

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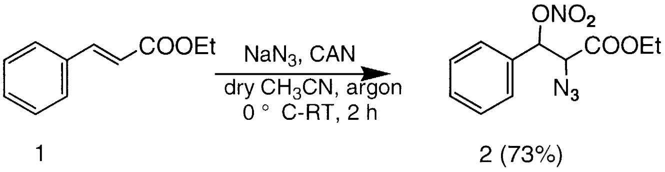
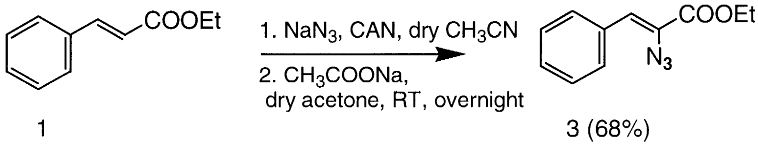


Scheme 1.

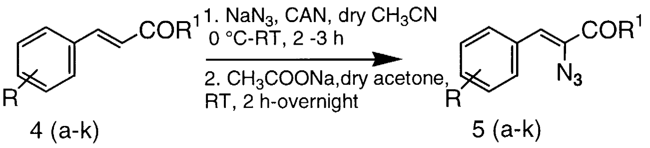


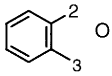
Scheme 2.

The reaction was found to be of general application to other substituted cinnamic esters and also α,β-unsaturated ketones (Table 1). Interestingly, when the experiment was conducted with cinnamic acid instead of the ester, the resulting product underwent concomitant elimination of nitrate and CO_2 to afford the β-azidostyrene as a 1:1 mixture of *E*- and *Z*-isomers. This reaction also appears to be general (Table 2).

Table 1

Synthesis of α-azidocinnamates and α-azido-α,β-unsaturated ketones



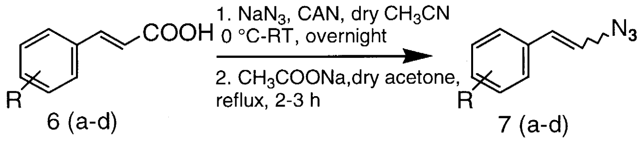
Entry	Substrate	R	R^1	Product	Yield (%)*
1	4a	4-Me	OMe	5a	74
2	4b	2-OMe	OEt	5b	60
3	4c	3-OMe	OEt	5c	64
4	4d	4-Cl	OEt	5d	67
5	4e		OEt	5e	64
6	4f	H	Me	5f	65
7	4g	4-Me	Me	5g	66
8	4h	4-Cl	Me	5h	60
9	4i	3-OMe	Me	5i	76
10	4j	H	Ph	5j	72
11	4k	4-Cl	Ph	5k	67

* Isolated yield

The present work constitutes a novel and expeditious process for the synthesis of α-azidocinnamates, α-azido-α,β-unsaturated ketones and β-azidostyrenes. In view of the experimental simplicity, the process described is likely to emerge as the method of choice for the synthesis of these compounds of proven versatility in heterocyclic synthesis.[10,11] Further work is in progress.

Typical experimental procedure: To a deoxygenated solution of cinnamic ester **1** (176 mg, 1 mmol) and

Table 2
Synthesis of β-azidostyrenes



Entry	Substrate	R	Product	Yield (%)[a,b]
1	6a	H	7a	61
2	6b	4-Me	7b	65
3	6c	3-OMe	7c	64
4	6d	4-Cl	7d	39

(a) Isolated yield; (b) 1:1 mixture of E and Z isomers

NaN_3 (98 mg, 1.5 mmol) in dry acetonitrile, a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent (10 mL) was added dropwise at 0°C and stirred well. On completion of the reaction it was worked up using CH_2Cl_2–water, dried and concentrated. The crude residue, on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) followed by usual work up and purification by silica gel column chromatography using hexane:ethyl acetate mixture (98:2) as eluent, afforded **3** (161 mg, 68%) as a pale yellow viscous liquid.

Compound **3**:[12] IR (film): 3069, 2119, 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.79 (m, 2H, ArH), 7.33 (m, 3H, ArH), 6.88 (s, 1H, olefinic), 4.35 (q, J=7.1 Hz, 2H, CH_2), 1.39 (t, J=7.1 Hz, 3H, CH_3).

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