

Phase transfer catalysed reaction of potassium superoxide with some nitroalkanes in the presence of α,β -unsaturated enones

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Superoxide ion, generated *in situ* by the phase transfer reaction of potassium superoxide and 18-crown-6 ether, brings about an easy Michael addition of nitroalkanes to α,β -unsaturated enones to afford 1,4-addition products.

Keywords: Superoxide ion, phase transfer catalyst, nitroalkanes, α,β -unsaturated enones, reactive oxygen species

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Superoxide anion radical (O_2^-), is a reactive oxygen species (ROS) and plays a key role in various life processes¹. From chemical viewpoint, it is multipotent reagent²⁻⁵ and is achieved using chemical or electrochemical method^{6,7}. The reactions leading to C–C bond formation are of tremendous importance in organic synthesis⁸. The versatile Michael addition is widely explored and has numerous applications in the elegant synthesis of useful products⁹⁻¹². Several catalysts have been employed and uncovered for the Michael reactions involving nitro compounds such as ethoxide¹³, diethylamine¹³, basic ion-exchange resins¹⁴, chiral Lewis acids¹⁵, chiral rubidium proline, proline and proline derivatives^{16,17}, chiral phase transfer catalysts¹⁸ and sugar derived crown ethers¹⁹.

In view of the above and as a part of the ongoing research on superoxide chemistry²⁰, herein is reported the results on the reaction of *in situ* generated superoxide ion and nitroalkanes in the presence of α,β -unsaturated enones. In the present course of reaction, O_2^- was generated *in situ* by the phase transfer reaction of KO_2 and 18-crown-6 ether in toluene at RT and was subsequently allowed to react with some Michael donors **1a-d** and acceptors **2a-d**. The results are given in **Table I**. As an outcome, Michael acceptor benzylideneacetone **2a** readily reacted with nitromethane **1a**, nitroethane **1b**, 2-

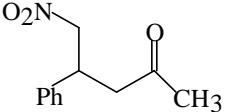
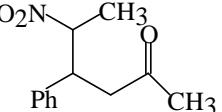
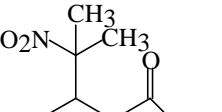
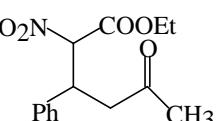
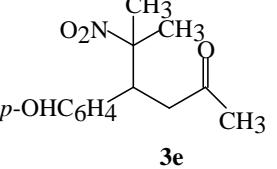
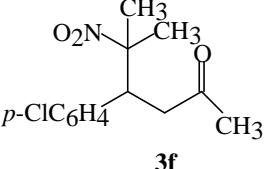
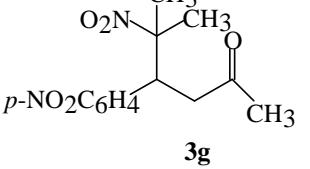
nitropropane **1c** and ethyl nitroacetate **1d** to give 5-nitro-4-phenylpentan-2-one **3a**, 5-nitro-4-phenylhexan-2-one **3b**, 5-methyl-5-nitro-4-phenylhexan-2-one **3c** and 2-nitro-5-oxo-3-phenylhexanoic acid ethyl ester **3d**, respectively in reasonably good yields (50-72%). The addition of Michael donor 2-nitropropane **1c** to various acceptors namely *p*-hydroxybenzylideneacetone **2b**, *p*-chlorobenzylideneacetone **2c** and *p*-nitro-benzylideneacetone **2d** afforded 4-(4-hydroxyphenyl)-5-methyl-5-nitrohexan-2-one **3e**, 4-(4-chlorophenyl)-5-methyl-5-nitrohexane-2-one **3f** and 5-methyl-5-nitro-4-(4-nitrophenyl)hexan-2-one **3g**, respectively in 71-77% yields (**Schemes I and II**).

A 4.0-fold molar excess of KO_2 and 2.0-fold molar excess of 18-crown-6 ether with respect to the substrate **2**, were employed for achieving the reaction. Progress of each reaction was monitored by TLC till its completion. The products were fully identified from their physical and spectral data which were in full agreement with the values described in literature²¹.

Based on product isolation and existing chemistry of superoxide ion, the following mechanism (**Scheme III**) may be envisaged for the observed products.

This report demonstrates the use of KO_2 /18-crown-6 combination for an efficient addition of nitroalkanes to α,β -unsaturated enones under significantly mild

Table I — Reaction of KO_2 /18-crown-6 with nitroalkanes in the presence of α,β -unsaturated enones

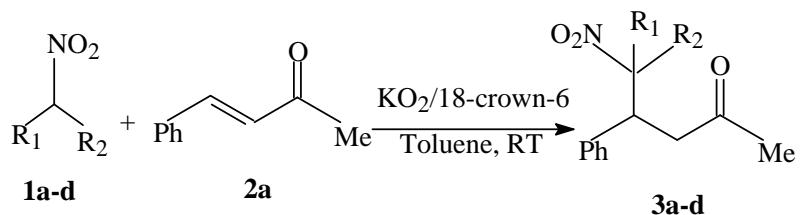
Reactants		Product	Yield (%)
CH_3NO_2	$\text{Ph}-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		50
1a	2a	3a	
$\text{CH}_3\text{CH}_2\text{NO}_2$	$\text{Ph}-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		70
1b	2a	3b	
$\text{CH}_3-\text{CH}(\text{NO}_2)-\text{CH}_3$	$\text{Ph}-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		72
1c	2a	3c	
$\text{CH}_3-\text{CH}(\text{NO}_2)-\text{CH}_2-\text{COOEt}$	$\text{Ph}-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		61
1d	2a	3d	
$\text{CH}_3-\text{CH}(\text{NO}_2)-\text{CH}_3$	$p\text{-OHC}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		71
1c	2b	3e	
$\text{CH}_3-\text{CH}(\text{NO}_2)-\text{CH}_3$	$p\text{-ClC}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		72
1c	2c	3f	
$\text{CH}_3-\text{CH}(\text{NO}_2)-\text{CH}_3$	$p\text{-NO}_2\text{C}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{CH}_3$		77
1c	2d	3g	

conditions at RT and offers an alternative way of carbon-carbon bond formation.

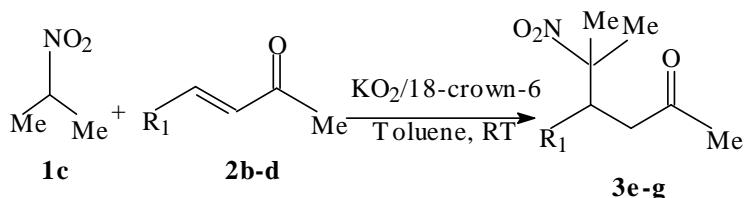
Experimental Section

Potassium superoxide and 18-crown-6 were procured from Aldrich, USA and were used as

received. The substrate nitromethane **1a**, nitroethane **1b**, 2-nitropropane **1c** and ethyl nitroacetate **1d** were purchased from Aldrich, USA whereas benzylideneacetone **2a**, *p*-hydroxybenzylideneacetone **2b**, *p*-chlorobenzylideneacetone **2c** and *p*-nitrobenzyl-



Scheme I



Scheme II

ideneacetone **2d** were prepared according to literature procedure²². The other reagents and solvents were of AR grade and were used after necessary purification. ¹H and ¹³C NMR spectra were run on a JEOL AL300 FT-NMR spectrometer. The chemical shift are reported in ppm downfield to TMS ($\delta=0$).

General procedure for the reaction of *in situ* generated superoxide ion with nitroalkanes in the presence of α,β -unsaturated enones

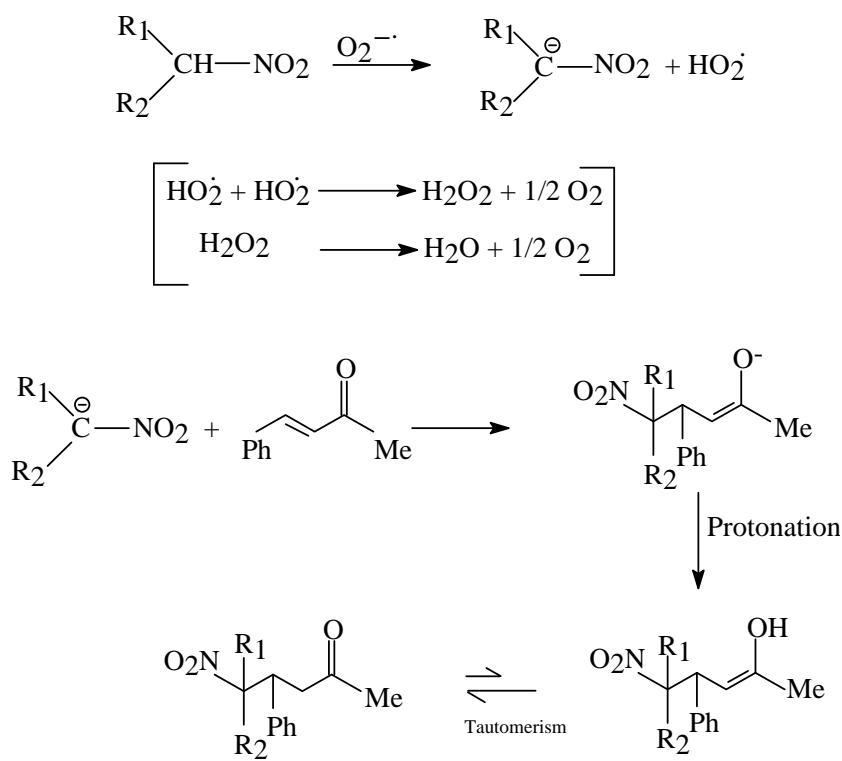
Sodium dried toluene (80 mL) was placed into a three-necked round bottom flask fitted with a dropping funnel, an inlet nitrogen bubbler, a magnetic stirrer and a Liebig condenser guarded with calcium chloride tube. Potassium superoxide (0.68 g, 0.0096 mole) and 18-crown-6 ether (1.27 g, 0.0048 mole) were weighed under nitrogen atmosphere using atmosbag and were transferred into the flask. To the stirred reaction mixture, were added

nitroalkane (0.0048 mole) and α,β -unsaturated enone (0.0024 mole) successively. Nitrogen was bubbled continuously and reaction mixture was stirred magnetically for 6-10 hr at RT until the starting material was consumed as indicated by TLC. The solvent was removed using a rotary evaporator and the residue was treated with brine solution and then extracted with diethyl ether. The combined ether extract was dried over Na_2SO_4 (anhyd.), filtered and concentrated to furnish a residue which was passed through column to get pure addition product **3**.

5-Nitro-4-phenylpentan-2-one, 3a: ¹H NMR: δ 2.1 (s, 3H), 2.9 (d, 2H), 4.0 (q, 1H) 4.6 (dd, 1H), 4.7 (dd, 1H), 7.1-7.4 (m, 5H); ¹³C NMR: δ 30.4, 38.8, 46.0, 79.5, 127.2, 127.6, 129.0, 138.8, 205.5.

5-Nitro-4-phenylhexan-2-one, 3b: ¹H NMR: δ 1.3 (d, 3H), 2.0 (s, 3H), 2.8 (dd, 1H), 3.0 (dd, 1H), 3.7 (td, 1H), 4.8 (dq, 1H), 7.1-7.4 (m, 5H); ¹³C NMR: δ 17.8,

30.5, 45.3, 46.1, 87.0, 127.8, 128.0, 129.0, 138.0,

5-Methyl-5-nitro-4-(4-nitrophenyl)hexan-2-one,

205.0.

5-Methyl-5-nitro-4-phenylhexan-2-one, 3c: ^1H NMR: δ 1.5 (s, 3H), 1.6 (s, 3H), 2.0 (s, 3H) 2.7 (dd, 1H), 3.0 (dd, 1H), 4.0 (dd, 1H) 7.2-7.4 (m, 5H); ^{13}C NMR: δ 22.7, 25.8, 30.2, 44.0, 48.8, 91.0, 128.0, 128.5, 129.2, 137.6, 205.2.

2-Nitro-5-oxo-3-phenylhexanoic acid ethyl ester, 3d: ^1H NMR: δ 1.0 (t, 3H), 2.1 (s, 3H), 2.9 (d, 2H), 3.9 (m, 1H), 4.1 (q, 2H), 5.5 (d, 1H) 7.2-7.3 (m, 5H); ^{13}C NMR: δ 13.6, 30.0, 41.0, 45.0, 62.8, 91.0, 127.8, 128.3, 128.8, 136.8, 163.0, 204.7.

4-(4-Hydroxyphenyl)-5-methyl-5-nitrohexan-2-one, 3e: ^1H NMR: δ 1.5 (s, 3H), 1.6 (s, 3H), 2.0 (s, 3H), 2.6 (dd, 1H), 3.0 (dd, 1H), 3.8 (dd, 1H), 5.6 (s, 1H), 6.7 (d, 2H), 7.0 (d, 2H); ^{13}C NMR: δ 22.0, 25.2, 30.0, 44.0, 48.0, 91.3, 115.0, 127.5, 130.0, 156.4, 207.6.

4-(4-Chlorophenyl)-5-methyl-5-nitrohexane-2-one, 3f: ^1H NMR: δ 1.4 (s, 3H), 1.5 (s, 3H), 2.0 (s, 3H) 2.7 (dd, 1H), 3.0 (dd, 1H), 3.9 (dd, 1H), 7.1 (d, 2H), 7.3 (d, 2H); ^{13}C NMR: δ 22.6, 25.5, 30.2, 43.8, 48.0, 90.8, 128.7, 130.4, 133.8, 136.0, 204.8.

3g: ^1H NMR: δ 1.5 (s, 3H), 1.6 (s, 3H), 2.0 (s, 3H), 2.9 (dd, 1H), 3.1 (dd, 1H), 4.0 (dd, 1H), 7.4 (d, 2H), 8.2 (d, 2H); ^{13}C NMR: δ 23.0, 25.0, 30.2, 43.8, 48.2, 90.2, 123.6, 130.0, 145.4, 147.4, 204.2.

Acknowledgement

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