

## Phase transfer catalysed reaction of potassium superoxide with some nitroalkanes in the presence of $\alpha,\beta$ -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  $\alpha,\beta$ -unsaturated enones to afford 1,4-addition products.

**Keywords:** Superoxide ion, phase transfer catalyst, nitroalkanes,  $\alpha,\beta$ -unsaturated enones, reactive oxygen species

**IPC:** Int.Cl.<sup>8</sup> C07C

Superoxide anion radical ( $O_2^{\cdot-}$ ), is a reactive oxygen species (ROS) and plays a key role in various life processes<sup>1</sup>. From chemical viewpoint, it is multipotent reagent<sup>2-5</sup> and is achieved using chemical or electrochemical method<sup>6,7</sup>. The reactions leading to C–C bond formation are of tremendous importance in organic synthesis<sup>8</sup>. The versatile Michael addition is widely explored and has numerous applications in the elegant synthesis of useful products<sup>9-12</sup>. Several catalysts have been employed and uncovered for the Michael reactions involving nitro compounds such as ethoxide<sup>13</sup>, diethylamine<sup>13</sup>, basic ion-exchange resins<sup>14</sup>, chiral Lewis acids<sup>15</sup>, chiral rubidium proline, proline and proline derivatives<sup>16,17</sup>, chiral phase transfer catalysts<sup>18</sup> and sugar derived crown ethers<sup>19</sup>.

In view of the above and as a part of the ongoing research on superoxide chemistry<sup>20</sup>, herein is reported the results on the reaction of *in situ* generated superoxide ion and nitroalkanes in the presence of  $\alpha,\beta$ -unsaturated enones. In the present course of reaction,  $O_2^{\cdot-}$  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-

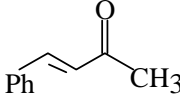
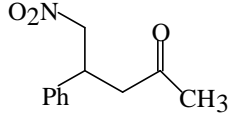
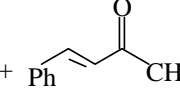
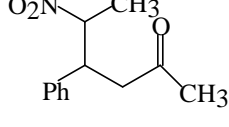
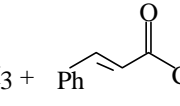
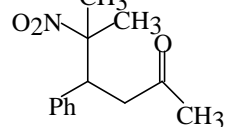
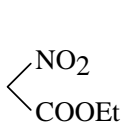
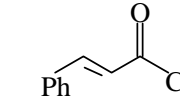
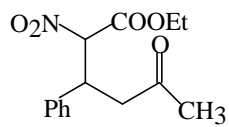
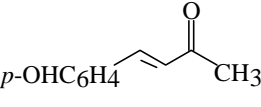
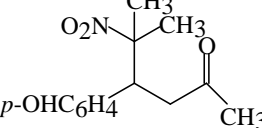
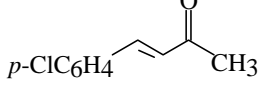
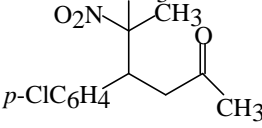
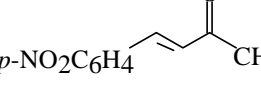
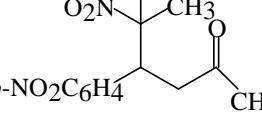
nitropropane **1c** and ethyl nitroacetate **1d** to give 5-nitro-4-phenylpentan-2-one **3a**, 5-nitro-4-phenylhexan-2-one **3b**, 5-methyl-5-nitro-4-phenylhexan-2-one **3c** and 2-nitro-5-oxo-3-phenylhexanoic acid ethyl ester **3d**, respectively in reasonably good yields (50-72%). The addition of Michael 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-nitrohexan-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 literature<sup>21</sup>.

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  $\alpha,\beta$ -unsaturated enones under significantly mild

**Table I** — Reaction of  $\text{KO}_2$ /18-crown-6 with nitroalkanes in the presence of  $\alpha,\beta$ -unsaturated enones

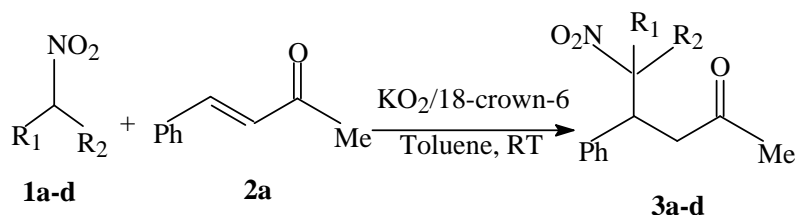
Reactants		Product	Yield (%)
$\text{CH}_3\text{NO}_2$			50
<b>1a</b>	<b>2a</b>	<b>3a</b>	
$\text{CH}_3\text{CH}_2\text{NO}_2$			70
<b>1b</b>	<b>2a</b>	<b>3b</b>	
$\text{CH}_3\text{CH}(\text{NO}_2)\text{CH}_3$			72
<b>1c</b>	<b>2a</b>	<b>3c</b>	
			61
<b>1d</b>	<b>2a</b>	<b>3d</b>	
$\text{CH}_3\text{CH}(\text{NO}_2)\text{CH}_3$			71
<b>1c</b>	<b>2b</b>	<b>3e</b>	
$\text{CH}_3\text{CH}(\text{NO}_2)\text{CH}_3$			72
<b>1c</b>	<b>2c</b>	<b>3f</b>	
$\text{CH}_3\text{CH}(\text{NO}_2)\text{CH}_3$			77
<b>1c</b>	<b>2d</b>	<b>3g</b>	

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

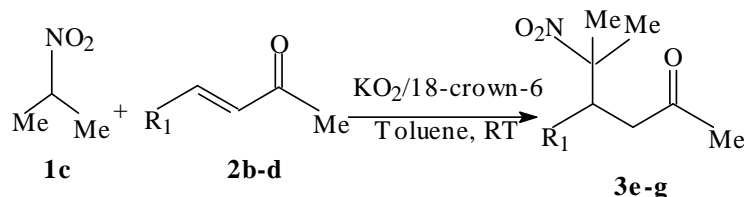
### Experimental Section

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-

**1a** : R<sub>1</sub> = R<sub>2</sub> = H**1b** : R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>3</sub>**1c** : R<sub>1</sub> = R<sub>2</sub> = CH<sub>3</sub>**1d** : R<sub>1</sub> = H, R<sub>2</sub> = COOEt**3a** : R<sub>1</sub> = R<sub>2</sub> = H**3b** : R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>3</sub>**3c** : R<sub>1</sub> = R<sub>2</sub> = CH<sub>3</sub>**3d** : R<sub>1</sub> = H, R<sub>2</sub> = COOEt

Scheme I

**2b** : R<sub>1</sub> = *p*-HOC<sub>6</sub>H<sub>4</sub>**2c** : R<sub>1</sub> = *p*-ClC<sub>6</sub>H<sub>4</sub>**2d** : R<sub>1</sub> = *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>**3e** : R<sub>1</sub> = *p*-HOC<sub>6</sub>H<sub>4</sub>**3f** : R<sub>1</sub> = *p*-ClC<sub>6</sub>H<sub>4</sub>**3g** : R<sub>1</sub> = *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>

Scheme II

ideneacetone **2d** were prepared according to literature procedure<sup>22</sup>. The other reagents and solvents were of AR grade and were used after necessary purification. <sup>1</sup>H and <sup>13</sup>C NMR spectra were run on a JEOL AL300 FT-NMR spectrometer. The chemical shift are reported in ppm downfield to TMS (δ=0).

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

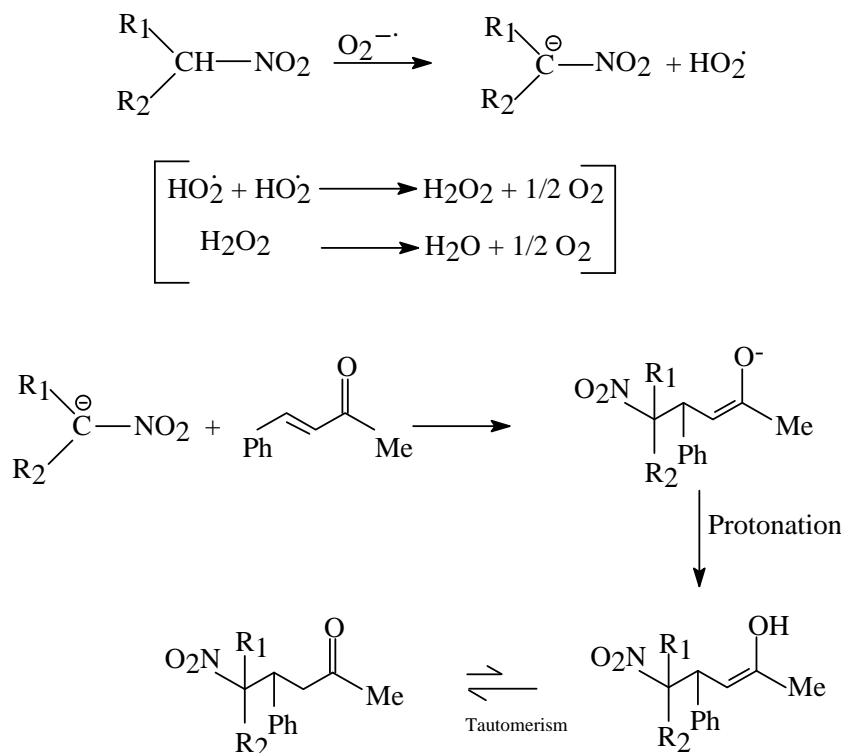
Sodium dried toluene (80 mL) was placed into a three-necked round bottom flask fitted with a dropping funnel, an inlet nitrogen bubbler, a magnetic stirrer and a Liebig condenser guarded with calcium chloride tube. Potassium superoxide (0.68 g, 0.0096 mole) and 18-crown-6 ether (1.27 g, 0.0048 mole) 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<sub>2</sub>SO<sub>4</sub> (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:** <sup>1</sup>H 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); <sup>13</sup>C 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:** <sup>1</sup>H 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); <sup>13</sup>C 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,**

Scheme III

205.0.

**5-Methyl-5-nitro-4-phenylhexan-2-one, 3c:**  $^1\text{H}$  NMR:  $\delta$  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);  $^{13}\text{C}$  NMR:  $\delta$  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:**  $^1\text{H}$  NMR:  $\delta$  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);  $^{13}\text{C}$  NMR:  $\delta$  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:**  $^1\text{H}$  NMR:  $\delta$  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);  $^{13}\text{C}$  NMR:  $\delta$  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-nitrohexan-2-one, 3f:**  $^1\text{H}$  NMR:  $\delta$  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);  $^{13}\text{C}$  NMR:  $\delta$  22.6, 25.5, 30.2, 43.8, 48.0, 90.8, 128.7, 130.4, 133.8, 136.0, 204.8.

**3g:**  $^1\text{H}$  NMR:  $\delta$  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);  $^{13}\text{C}$  NMR:  $\delta$  23.0, 25.0, 30.2, 43.8, 48.2, 90.2, 123.6, 130.0, 145.4, 147.4, 204.2.

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### References

- 1 Fridovich I, *Science*, 201, **1978**, 875.
- 2 (a) Afanas'ev I B, *Superoxide Ion Chemistry and Biological Implications*, (CRC Press, Boca Roton, Florida), Vol I, **1989**; (b) *ibid*, Vol II, **1991**.
- 3 Sawyer D T & Valentine J S, *Acc Chem Res*, 14, **1981**, 393.
- 4 Frimer A A, in *Chemistry of Enones*, Part 2, edited by Patai S, (Wiley Interscience, Chichester, England), **1989**, p.781.
- 5 Frimer A A, in *The Chemistry of Peroxides*, edited by Patai S, (Wiley Interscience, Chichester, England), **1983**, p.429.
- 6 Sawyer D T & Roberts (Jr.) J L, *J Electroanal Chem*, 12, **1966**, 90.
- 7 Valentine J S & Curtis A B, *J Am Chem Soc*, 97, **1975**, 224.
- 8 Trost B M, *Comprehensive Organic Synthesis*, (Pergamon Press, Oxford), **1991**, p. 133.
- 9 Perlmutter P, *Conjugate Addition Reactions in Organic Synthesis*, (Pergamon Press, Oxford), **1992**.

- 10 Ono N, *The Nitro Group in Organic Synthesis*, (Wiley-VCH, New York), **2001**.
- 11 Larock R C, *Comprehensive Organic Transformations*, (VCH, New York), **1989**, p.411.
- 12 (a) Pinnick H W, *Org React*, 38, **1990**, 655; (b) Tamura R, Kaminura A O & Ono N, *Synthesis*, **1991**, 423; (c) Mukayama T & Hoshino T, *J Am Chem Soc*, 82, **1960**, 5339.
- 13 Baer H H & Urbas L, in *The Chemistry of the Nitro and Nitroso Group*, Part 2, edited by Feuer H, (Interscience Publisher, New York), **1970**.
- 14 (a) Bergmann E D & Corett R, *J Org Chem*, 21, **1956**, 107; (b) *ibid*, 23, **1958**, 1507.
- 15 Funabashi K, Saida Y, Kanai M, Arai T, Sasai H & Shibasaki M, *Tetrahedron Lett*, 39, **1998**, 7557.
- 16 Hanessian S & Pham V, *Org Lett*, 2, **2000**, 2975.
- 17 List B, Pojarliev P & Martin H J, *Org Lett*, 3, **2001**, 2423.
- 18 Banfi S, Cinquini M & Colonna S, *Bull Chem Soc Jpn*, 54, **1981**, 1841.
- 19 Bako P, Bajor Z & Toke L, *J Chem Soc Perkin Trans*, 1, **1999**, 3651.
- 20 (a) Singh S, Verma M & Singh K N, *Synth Commun*, 34, **2004**, 4471; (b) Singh K N & Kumar R, *Indian J Chem*, 44B, **2005**, 381; (c) Shukla A K, Verma M & Singh K N, *Indian J Chem*, 43B, **2004**, 1748.
- 21 Holland N, Hazell R G & Jorgensen K A, *J Org Chem*, 67, **2002**, 8331.
- 22 Vogel's Textbook of Practical Organic Chemistry, 4<sup>th</sup> Edn. (ELBS, Longman, England), p.794.