

# SYNLETT Spotlight 165

## Dinitrogen Tetroxide: N<sub>2</sub>O<sub>4</sub>

Compiled by Morteza Shiri



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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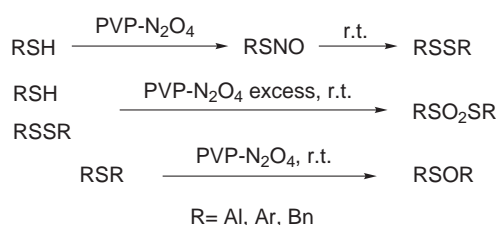
### Introduction

For over a century, dinitrogen tetroxide has found wide application in organic synthesis, such as nitration of aromatic compounds,<sup>1</sup> nitrosation of amines,<sup>2</sup> preparation of thionitrite<sup>3</sup> and sulfinyl nitrites,<sup>4</sup> oxidation of olefins<sup>5</sup> and dethioacetalization reactions.<sup>6</sup> This compound is commercially supplied at low price in a cylinder, and can be used directly or as liquid (bp 21 °C), collected by transfer distillation into an ice-cooled vessel. Apart from difficul-

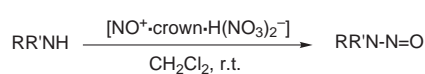
ties in handling the poisonous and corrosive dinitrogen tetroxide, the biggest disadvantage of utilizing gaseous N<sub>2</sub>O<sub>4</sub> in organic reactions is its high reactivity which usually causes undesired side reactions. In order to overcome the above mentioned limitations some reports are published on the use of N<sub>2</sub>O<sub>4</sub> complexes of organic,<sup>7</sup> polymeric<sup>8</sup> and inorganic compounds<sup>9</sup> as useful reagents in organic reactions.

### Abstract

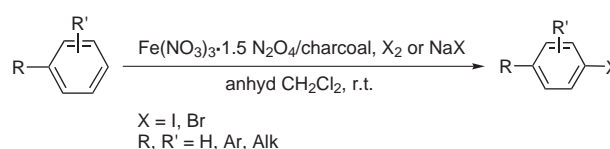
N<sub>2</sub>O<sub>4</sub> was supported on the cross-linked polyvinylpyrrolidone (PVP) by Iranpoor et al., which afforded a stable polymeric reagent. Thiols were converted to *S*-nitrosothiols (thionitrites) using this new nitrosating agent in *n*-hexane or CHCl<sub>3</sub> at 10 °C. With this reagent, thiols were also converted into their corresponding disulfides. Selective oxidation of sulfides to sulfoxides and disulfides to thiosulfonates can also be achieved by this reagent at room temperature. By using an excess of the reagent, the selective one-pot synthesis of thiosulfonates from thiols at room temperature was also performed.<sup>8a</sup>



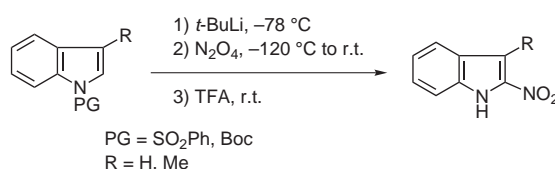
Zolfigol and co-workers reported a practical and efficient method for N-nitrosation of secondary amines using [NO<sup>+</sup>·Crown·H(NO<sub>3</sub>)<sub>2</sub>]<sup>+</sup>, an ionic complex of 18-crown-6 with N<sub>2</sub>O<sub>4</sub> gas. This complex, which is easily prepared and handled, is relatively stable and an efficient source for the delivery of nitrosonium ion (NO<sup>+</sup>) under mild and homogeneous conditions. 18-Crown-6 can be recycled and reused.<sup>7</sup>



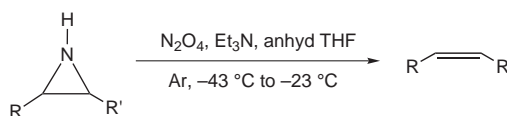
Firouzabadi et al. provided a simple method for the direct, regioselective iodination and bromination of benzene, naphthalene and other activated aromatic compounds using molecular iodine and bromine and their sodium salts in the presence of the stable Fe(NO<sub>3</sub>)<sub>3</sub>·1.5N<sub>2</sub>O<sub>4</sub>/charcoal system.<sup>9a</sup>



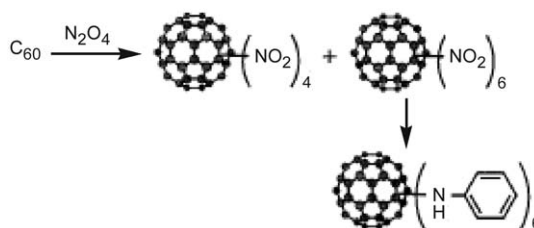
The C-2 lithiation of *N*-Boc- and *N*-(phenylsulfonyl)indoles, followed by reaction with dinitrogen tetroxide at low temperature affords the corresponding 2-nitroindoles in 63–78% yields. Deprotection of the *N*-Boc-2-nitroindoles with trifluoroacetic acid gives 2-nitroindole and 3-methyl-2-nitroindole in essentially quantitative yields.<sup>10</sup>



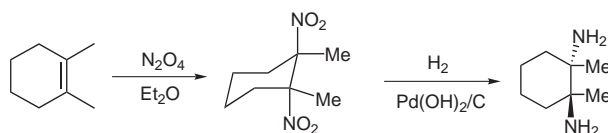
Various aziridines were reacted with dinitrogen tetroxide in the presence of Et<sub>3</sub>N in anhyd THF to give the corresponding ethylenes in good to excellent yields.<sup>11</sup>



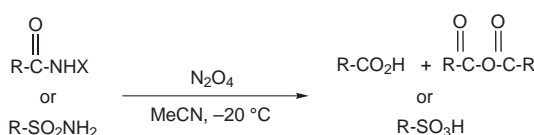
[60]Fullerene was selectively and efficiently nitrated with dinitrogen tetroxide to yield monodisperse hexanitro[60]fullerene. The use of this compound as reactive precursor in the synthesis of organo-amino derivatives of C<sub>60</sub> was also demonstrated. The allylic *tert*-nitro moieties in hexanitro[60]fullerenes were found to be excellent leaving groups in nucleophilic substitutions by amino nucleophiles, such as anilines, leading to the formation of hexaanilino[60]fullerenes.<sup>12</sup>



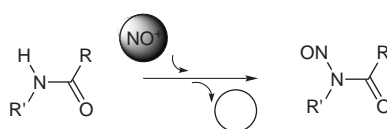
Reaction of N<sub>2</sub>O<sub>4</sub> with 1,2-dimethylcyclohexene led to the corresponding dinitro compound with high *trans* stereoselectivity (>30:1). Catalytic hydrogenation of 1,2-dimethyl-1,2-dinitrocyclohexene with Pd(OH)<sub>2</sub> on carbon afforded a quantitative yield of (*d,l*)-1,2-diamino-1,2-dimethylcyclohexane, which was resolved to pure enantiomers with mandelic acid. This approach constitutes a simple and potentially general route to interesting new chiral auxiliaries.<sup>13</sup>



Carboxamides and sulfonamides were reacted with dinitrogen tetroxide to give the corresponding acids, while such as *N*-bromoamides and hydroxamic acids were also converted to the corresponding acids together with their anhydrides.<sup>14</sup>



A novel class of stable, mild and size-shape-selective nitrosating agents for secondary amides was introduced by Zyryanov et al. These are based on reversible entrapment and release of reactive nitrosonium species by calix[4]arenes. The NO<sup>+</sup> encapsulation controls the reaction selectivity.<sup>15</sup>



## References and Notes

- (1) Squadrito, G. L.; Fronczek, F. R.; Watkins, S. F.; Church, D. F.; Pryor, W. A. *J. Org. Chem.* **1990**, *55*, 4322.
- (2) Boyer, J. H.; Pillai, T. P. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1661.
- (3) Oae, S.; Shinhama, K.; Kim, Y. H. *J. Chem. Soc., Chem. Commun.* **1977**, 407.
- (4) Oae, S.; Shinhama, K.; Kim, Y. H. *Tetrahedron Lett.* **1979**, *35*, 3307.
- (5) Giamalva, D. H.; Kenion, G. B.; Church, D. F.; Pryor, W. A. *J. Am. Chem. Soc.* **1987**, *109*, 7059.
- (6) Mehta, G.; Uma, R. *Tetrahedron Lett.* **1996**, *37*, 1897.
- (7) Zolfigol, M. A.; Zebarjadian, M. H.; Chehardoli, G.; Keypour, H.; Salehzadeh, S.; Shamsipur, M. *J. Org. Chem.* **2001**, *66*, 3619.
- (8) (a) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Tetrahedron* **2002**, *58*, 5179. (b) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Synthesis* **2003**, 1591.
- (9) (a) Firouzabadi, H.; Iranpoor, N.; Shiri, M. *Tetrahedron Lett.* **2003**, *44*, 8781. (b) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Synlett* **2004**, 347. (c) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006**, *181*, 473. (d) Iranpoor, N.; Firouzabadi, H.; Heydari, R.; Shiri, M. *Synth. Commun.* **2005**, *35*, 263. (e) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Synth. Commun.* **2005**, *35*, 1517. (f) Iranpoor, N.; Firouzabadi, H.; Pourali, A. *Synth. Commun.* **2005**, *35*, 1527. (g) Iranpoor, N.; Firouzabadi, H.; Heydari, R. *Synth. Commun.* **2003**, *33*, 703.
- (10) Jiang, J.; Gribble, G. W. *Tetrahedron Lett.* **2002**, *43*, 4115.
- (11) Lee, K.; Kim, Y. H. *Synth. Commun.* **1999**, *29*, 1241.
- (12) Anantharaj, V.; Bhonsle, J.; Canteenwala, T.; Chiang, L. Y. *J. Chem. Soc., Perkin Trans. 1* **1999**, 31.
- (13) Zhang, W.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 1711.
- (14) Kim, Y. H.; Kim, K.; Park, Y. J. *Tetrahedron Lett.* **1990**, *31*, 3893.
- (15) (a) Zyryanov, G. V.; Rudkevich, D. M. *Org. Lett.* **2003**, *5*, 1253. (b) Zyryanov, G. V.; Rudkevich, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 4264.