

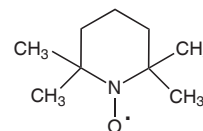
Free Radicals

Alfa Aesar offers an extensive range of free radicals for a variety of research and development purposes. Described below are the free radicals offered by Alfa Aesar and a technical product review with literature references.

A12733 TEMPO, free radical, 98+%

[2,2,6,6-Tetramethyl-1-piperidinyloxy, free radical]

[2564-83-2], C₉H₁₈NO, F.W. 156.25, m.p. 32-37°, b.p. 193° dec., f.p. 67°(152°F), Merck **14,9140**, Fieser **14,302 16,324 11,160 16,324 17,332 21,418**, UN1759, EINECS 219-888-8, RTECS TN8991900, BRN 1422418, MDL MFCD00009599



For brief features on TEMPO and related reagents, see: *Synlett*, 563 (2001); 1757 (2003); 657 (2006). For reviews on nitroxide radicals, see: *Synthesis*, 190, 401 (1971); *Chem. Rev.*, **78**, 37 (1978); *J. Sci. Ind. Res.*, **54**, 623 (1995).

In the presence of a catalytic amount of KBr, catalyzes the selective oxidation of primary and secondary alcohols to aldehydes and ketones by buffered NaOCl: *J. Org. Chem.*, **50**, 4888 (1985); **52**, 2559 (1987); *Org. Synth. Coll.*, **8**, 367 (1993). High yields of aldehydes can also be obtained under mild, phase-transfer conditions with Oxone®: *Org. Lett.*, **2**, 1173 (2000). In the presence of CuCl, aerobic oxidation of alcohols to aldehydes and ketones has been accomplished in the ionic liquid 1-n-Butyl-3-methylimidazolium hexafluorophosphate, L19086: *Org. Lett.*, **4**, 1507 (2002).

With NaOCl, α -amino or α -alkoxy alcohols have also been oxidized to the aldehydes: *Tetrahedron Lett.*, **33**, 5029 (1992). The use of I₂ as cooxidant is useful for sensitive substrates: *Org. Lett.*, **5**, 235 (2003).

The addition of quaternary salts to the reaction mixture permits further oxidation of aldehydes to acids. Selective oxidation of a primary OH to an aldehyde can be achieved in the presence of a secondary OH: *J. Org. Chem.*, **54**, 2970 (1989); *Tetrahedron Lett.*, **31**, 2177 (1990). The oxidation can also be performed using NCS under phase-transfer conditions: *J. Org. Chem.*, **61**, 7452 (1996), with Iodosobenzene diacetate, B24531: *J. Org. Chem.*, **62**, 6974 (1997), or Trichloroisocyanuric acid, B23906: *Org. Lett.*, **3**, 3041 (2001). For a review of the use of stable nitroxyl radicals for the oxidation of primary and secondary alcohols, see: *Synthesis*, 1153 (1996).

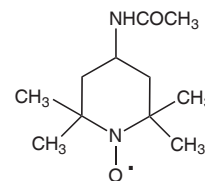
Compare also 4-Hydroxy-TEMPO, A12497, and 4-Acetamido-TEMPO, B23456.

Free Radicals

B23456 4-Acetamido-TEMPO, free radical, 98%

[4-Acetamido-2,2,6,6-tetramethyl-1-piperidinyloxy, free radical]

[14691-89-5], C₁₁H₂₁N₂O₂, F.W. 213.30, m.p. 143-145°, EINECS 423-840-3, BRN 3546225, MDL MFCD00043593

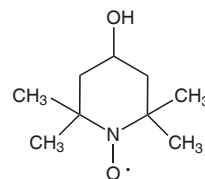


In the presence of an acid disproportionates to the oxoammonium salt, a highly selective reagent for alcohol oxidation. For a review of oxoammonium (nitrosonium) salts, see: *Heterocycles*, **27**, 509 (1988); for a brief feature on oxoammonium salts, see: *Synlett*, 1757 (2003). In combination with tosic acid, oxidizes alcohols to aldehydes and ketones: *J. Org. Chem.*, **56**, 6110 (1991). For oxidation of diols to α -dicarbonyl compounds, see: *J. Org. Chem.*, **59**, 6338 (1994). Review of the use of stable nitroxyl radicals for the oxidation of primary and secondary alcohols: *Synthesis*, 1153 (1996). Compare also 4-Hydroxy-TEMPO, A12497, and TEMPO A12733.

A12497 4-Hydroxy-TEMPO, free radical, 98+%

[4-Hydroxy-2,2,6,6-tetramethyl-1-piperidin-1-yloxy, free radical]

[2226-96-2], C₉H₁₈NO₂, F.W. 172.25, m.p. 69-72°, Fieser **9**,247, EINECS 218-760-9, RTECS TN8991000, BRN 1422990, MDL MFCD00006478

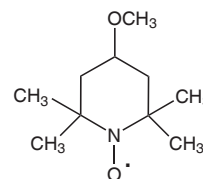


Reviews: Synthesis and reactions of stable nitroxyl radicals: *Synthesis*, 190, 401 (1971); Advances in the chemistry of nitroxide spin labels: *Chem. Rev.*, **78**, 37 (1978); Recent advances in the chemistry of nitroxides and their applications in spin labelling: *J. Sci. Ind. Res.*, **54**, 623 (1995). For a brief feature on derived oxoammonium salts, see: *Synlett*, 1757 (2003). Compare also 4-Acetamido-TEMPO, B23456, and TEMPO, A12733. Recommended as a stabilizer (antioxidant) for the protection of unsaturated fatty acids and their derivatives: *J. Am. Chem. Soc.*, **101**, 6748 (1979).

L15915 4-Methoxy-TEMPO, free radical, 98+%

[4-Methoxy-2,2,6,6-tetramethylpiperidinyloxy, free radical]

[95407-69-5], C₁₀H₂₀NO₂, F.W. 186.28, m.p. 39-41°, BRN 4740399, MDL MFCD00270334



Reviews: Synthesis and reactions of stable nitroxyl radicals: *Synthesis*, 190, 401 (1971); Advances in the chemistry of nitroxide spin labels: *Chem. Rev.*, **78**, 37 (1978); Recent advances in the chemistry of nitroxides and their applications in spin labelling: *J. Sci. Ind. Res.*, **54**, 623 (1995). The oxidation of alcohols to aldehydes has been effected catalytically, in the presence of a stoichiometric cooxidant such as ferricyanide: *J. Mol. Catal.*, **31**, 217 (1985), or with hypochlorite in a two-phase system: *J. Org. Chem.*, **52**, 2559 (1987). For a review of the use of stable nitroxyl radicals for the oxidation of primary and secondary alcohols, see: *Synthesis*, 1153 (1996). Compare also TEMPO, A12733 and 4-Acetamido-TEMPO, B23456.

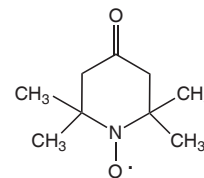
Free Radicals

L01084 4-Oxo-TEMPO, free radical, 96%

[4-Oxo-2,2,6,6-tetramethyl-1-piperidinyloxy, free radical]

[2896-70-0], C₉H₁₆NO₂, F.W. 170.23, m.p. 36-40°, EINECS 220-778-7, RTECS TN9200000, BRN 1818579, MDL MFCD00006187

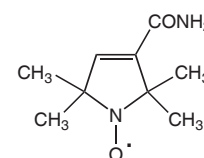
Reviews: Synthesis and reactions of stable nitroxyl radicals: *Synthesis*, 190, 401 (1971); Advances in the chemistry of nitroxide spin labels: *Chem. Rev.*, **78**, 37 (1978); Recent advances in the chemistry of nitroxides and their applications in spin labelling: *J. Sci. Ind. Res.*, **54**, 623 (1995).



A17381 Carbamoyl-2,2,5,5-tetramethyl-3-pyrrolin-1-yloxy, free radical, 99%

[2,2,5,5-Tetramethyl-3-pyrrolin-1-oxyl-3-carboxamide]

[3229-73-0], C₉H₁₅N₂O₂, F.W. 183.23, m.p. 198-200°, EINECS 221-765-9, BRN 4138020, MDL MFCD00005341

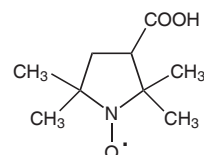


L15068 3-Carboxy-PROXYL, free radical, 98%

[3-Carboxy-2,2,5,5-tetramethyl-1-pyrrolidinyloxy, free radical]

[2154-68-9], C₉H₁₆NO₃, F.W. 186.23, m.p. ca 200° dec., EINECS 218-448-2, BRN 4136411, MDL MFCD00003167

Reviews: Synthesis and reactions of stable nitroxyl radicals: *Synthesis*, 190, 401 (1971); Advances in the chemistry of nitroxide spin labels: *Chem. Rev.*, **78**, 37 (1978); Recent advances in the chemistry of nitroxides and their applications in spin labelling: *J. Sci. Ind. Res.*, **54**, 623 (1995).

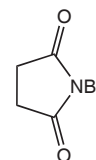


Free Radicals

A15922 N-Bromosuccinimide, 99%

[NBS]

[128-08-5], C₄H₄BrNO₂, F.W. 177.99, m.p. 175-180° dec., d. 2.098, Merck **14**,1438, Fieser **1**,78 **12**,79 **13**,49 **14**,57 **15**,50 **16**,49 **18**,65 **19**,50 **20**,58 **21**,72, UN3261, EINECS 204-877-2, BRN 113916, MDL MFCD00005510

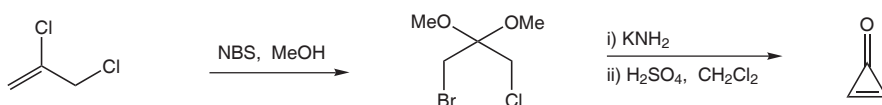


Source of free-radical or positive bromine. For examples of radical benzylic bromination (Wohl-Ziegler), see: *Org. Synth. Coll.*, **4**, 921 (1963); **5**, 145, 329, 825 (1973). The use of the ozone depleting solvent CCl₄ has been avoided by the use of the ionic liquid 1-n-Butyl-3-methylimidazolium hexafluorophosphate, L19086: *Synlett*, 702 (2003). Cleavage of carbohydrate benzyl ethers: *J. Org. Chem.*, **55**, 378 (1990), and of benzyl esters: *Synlett*, 219 (1994), occur under mild conditions; the benzyl group is converted to benzaldehyde. For allylic bromination, see e.g.: *Org. Synth. Coll.*, **4**, 108 (1963); **9**, 112, 191 (1998) review: *Chem. Rev.*, **43**, 271 (1948).

For free-radical α -bromination of a Boc glycine ester, see: *Org. Synth. Coll.*, **9**, 526 (1998). Both aliphatic and aromatic aldehydes are converted to acyl bromides under free-radical conditions: *Tetrahedron Lett.*, 3809 (1979); *Synlett*, 347 (1990); *Tetrahedron Lett.*, **31**, 7237 (1990).

In acetonitrile, NBS is a mild and regiospecific nuclear brominating agent for activated aromatics such as methoxybenzenes and naphthalenes: *J. Org. Chem.*, **60**, 5328 (1995). Deactivated aromatics, e.g. nitroarenes and benzotrifluorides, can be *m*-brominated under mild conditions in good yield with NBS in TFA, in the presence of H₂SO₄: *Synlett*, 1245 (1999). In the presence of a phosphine or phosphite, converts alcohols to alkyl bromides with inversion: *Tetrahedron Lett.*, 3937 (1973). For a review of this and related reactions, see: *Org. React.*, **29**, 1 (1983).

Alkenes undergo *trans*-addition reactions with NBS in combination with a nucleophile. For examples, see: *Org. Synth. Coll.*, **6**, 184, 560 (1988). With alcohols, bromohydrin ethers are formed. For use in the synthesis of cyclopropenone, see: *Org. Synth. Coll.*, **6**, 361 (1988):



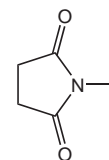
In the presence of DBU in MeOH, amides rearrange to amines in good yields, providing a mild and efficient alternative to the classical Hofmann halogen/caustic alkali conditions: *J. Org. Chem.*, **62**, 7495 (1997). Examples of the use of NBS as a mild, selective oxidizing agent: Sulfides to sulfoxides: *J. Org. Chem.*, **37**, 3976 (1968). Oximes to nitrile oxides: *J. Org. Chem.*, **37**, 436 (1968). Secondary alcohol in the presence of primary: *Tetrahedron Lett.*, 2745 (1979). (In DMSO): Alkynes to α -diketones: *Can. J. Chem.*, **49**, 1099 (1979).

(Free radical): Aldehydes to acyl bromides or amides: *Tetrahedron Lett.*, **31**, 7237 (1990). Benzyl silyl ethers to aldehydes: *Synlett*, 345 (1990). Aldehydes to esters: *Synlett*, 347 (1990). For use as a mild catalyst in acetalization reactions, see Triethyl orthoformate, A13587. For a brief feature on uses in synthesis, see: *Synlett*, 498 (2006). See also 1,3-Dibromo-5,5-dimethylhydantoin, A15510.

Free Radicals

A14320 N-Iodosuccinimide, 97+%

[516-12-1], C₄H₄INO₂, F.W. 224.99, m.p. ca 196° dec., d. 2.245, Merck **14,5045**, Fieser **1,510 10,216 12,258 15,178 16,185 18,193 19,177 21,234**, EINECS 208-221-6, RTECS WN2817000, BRN 113917, MDL MFCD00005512



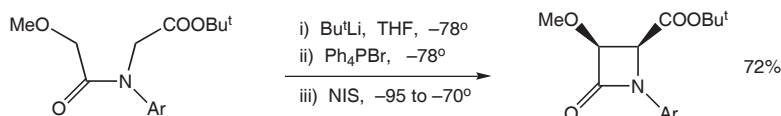
Source of positive iodine. Iodinates methoxy benzenes and naphthalenes in acetonitrile, e.g. anisole gives 95% yield of 4-iodoanisole: *Tetrahedron Lett.*, **37**, 4081 (1996). In combination with TFA and TFA anhydride, iodinate 2,4-diethoxypyrimidines or N-alkyluracils specifically to their 5-iodo-derivatives: *Synth. Commun.*, **18**, 855 (1988). With triflic acid, the "superelectrophile" iodine(I) triflate is formed. This species will iodinate even deactivated aromatics, e.g. nitrobenzene to the *m*-iodo derivative: *J. Org. Chem.*, **58**, 3194 (1993).

Alone or with a catalytic amount of triflic acid, is a powerful coupling agent in oligosaccharide synthesis, particularly for thioglycosyl donors; see, e.g.: *Tetrahedron Lett.*, **34**, 8523 (1993). For reviews, see: *Chem. Rev.*, **93**, 1503 (1993); *Contemp. Org. Synth.*, **3**, 173 (1996).

In the presence of triphenylphosphine or triphenyl phosphite, converts alcohols to iodides stereoselectively with inversion: *Tetrahedron Lett.*, 3937 (1973). See also: *Carbohydr. Res.*, **24**, 45 (1972).

In combination with the phase-transfer catalyst, Tetra-*n*-butylammonium iodide, **A15484**, oxidizes alcohols to carbonyl compounds in high yield under neutral conditions: *Synthesis*, 394 (1981). Glycols are cleaved to carbonyl compounds; the rate of reaction is increased by u.v. irradiation: *J. Org. Chem.*, **46**, 1927 (1981). Similarly, α -hydroxyacids are oxidatively decarboxylated to ketones: *J. Org. Chem.*, **47**, 3006 (1982).

With K₂CO₃ in MeOH, aldehydes can be oxidized directly to methyl esters: *J. Org. Chem.*, **54**, 1213 (1989). Oxidative coupling of dianions of acyclic tertiary amides gives a stereoselective preparation of β -lactams: *J. Org. Chem.*, **57**, 1864 (1992):



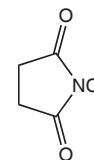
Has been used in the construction of disulfide bridges in cystine peptides, from cysteine in a DMF-dichloromethane solvent: *J. Org. Chem.*, **58**, 3003 (1993). For a brief feature on uses of the reagent in synthesis, see: *Synlett*, 960 (2006).

Free Radicals

A10310 N-Chlorosuccinimide, 98%

[NCS]

[128-09-6], $C_4H_4ClNO_2$, F.W. 133.53, m.p. 146-150°, d. 1.65, Merck **14,2164**, Fieser **1,139**
13,79 14,87 15,86 16,84 18,101 19,95 20,108 21,131, UN1759, EINECS 204-878-8, RTECS
UY1013500, BRN 113915, MDL MFCD00005511



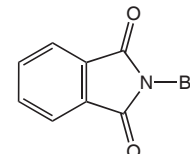
Source of positive chlorine in chlorination and oxidation reactions. Methyl ketones may be monochlorinated via their Li enolates: *J. Org. Chem.*, **49**, 1286 (1984). For the α -chlorination of acid chlorides formed *in situ*, see: *Tetrahedron Lett.*, 3235 (1974). For chlorination of deactivated anilines, see: *Synthesis*, 669 (1985).

In the presence of triphenylphosphine or triphenyl phosphite, converts alcohols to alkyl chlorides stereospecifically with inversion: *Tetrahedron Lett.*, 3937 (1973). For a review, see: *Org. React.*, **29**, 1 (1983). Amides have been prepared by treatment of a carboxylic acid with NCS/ PPH_3 followed by an amine: *Synth. Commun.*, **25**, 959 (1995). With dimethyl sulfide, forms the Corey-Kim reagent, a mild, selective oxidant for alcohols. For a review, see: *Synthesis*, 857 (1990); for tabulated examples, see: *Org. Synth. Coll.*, **6**, 220 (1988).

Primary alcohols are oxidized cleanly to aldehydes using NCS and a catalytic amount of TEMPO, **A12733**, under phase-transfer conditions: *J. Org. Chem.*, **61**, 7452 (1996). NCS in ether is a convenient alternative to hypochlorite for the conversion of amines to N-chloroamines, for use, e.g. in the Hofmann-Loeffler reaction, see: *Chem. Ber.*, **88**, 883 (1955).

A11601 N-Bromophthalimide, 98+%

[2439-85-2], $C_8H_4BrNO_2$, F.W. 226.03, m.p. 204-208°, EINECS 219-467-9, BRN 131211,
MDL MFCD00005888

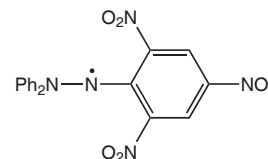


Brominating agent comparable to N-Bromosuccinimide, **A15922**.

44150 2,2-Diphenyl-1-picrylhydrazyl, free radical, 95%

[DPPH]

[1898-66-4], $C_{18}H_{12}N_5O_6$, F.W. 394.32, Powder, Merck **14,3330**, UN2811, EINECS 217-
591-8, MDL MFCD00007231, Note: Store cold,



Free Radicals

H27530 Oxynitrox[®] S100, free radical, 99+% (Avge MW ca 2250)

[Poly[[6-[1,1,3,3-tetramethylbutyl)amino]1,3,5-triazin-2,4-diy]][(2,2,6,6-tetramethyl-1-oxy-4-piperidiny)-imino]-1,6-hexa, PIPO]
91993-31-6]

Other Products

Selected Alfa Aesar products with applications in free radical chemistry. Most are referred to in the text of this publication.

| | |
|--------|---|
| A15510 | 1,3-Dibromo-5,5-dimethylhydantoin |
| L19086 | 1-n-Butyl-3-methylimidazolium hexafluorophosphate |
| B24531 | Iodosobenzene diacetate |
| A15484 | Tetra-n-butylammonium iodide |
| B23906 | Trichloroisocyanuric acid |
| A13587 | Triethyl orthoformate |

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