Sodium Nitrite ($NaNO_2$): An Impressive and Efficient Nitrating/Nitrosating Reagent in Organic Synthesis

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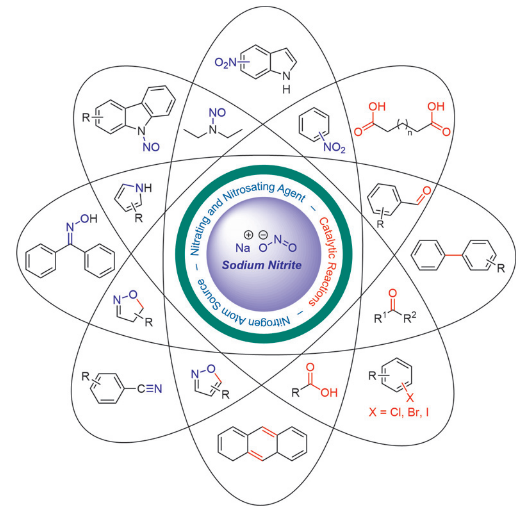

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Abstract This graphical review provides a concise overview of the key organic reactions reported in the literature that use sodium nitrite ($NaNO^2$) as a nitrating or nitrosating agent. It summarizes the diverse reactivity of this reagent with various substrates, leading to the functionalization and synthesis of a wide variety of useful organic molecules.

Key words sodium nitrite, nitrating, nitrosating, functionalization, synthesis, catalytic reactions

Sodium nitrite ($NaNO_2$) is a hygroscopic and crystalline inorganic salt that slowly oxidizes in air. It is highly soluble in water and slightly soluble in diethyl ether, methanol, and ethanol. Industrially, it is the most important salt produced from nitrous acid. It is obtained on large scale by the reaction between a mixture of nitrogen oxides and an alkaline solution of sodium hydroxide or sodium carbonate.[1a,b] Sodium nitrite finds extensive use in the chemical and pharmaceutical industries for the production of nitroso and isonitroso compounds, and is utilized in diazotization reactions (especially for dyes) and the synthesis of pharmaceutical products (e.g., caffeine) and agricultural pesticides (e.g., pyramin). In the food industry, sodium nitrite is used as a preservative for cured meat products. It contributes to flavor enhancement, prevents discoloration, and protects against the growth and toxin production of *Clostridium botulinum*.[1h–k]

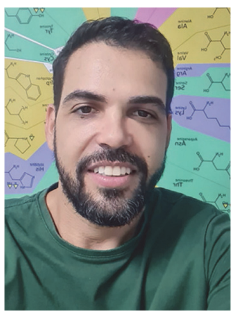
The applications of sodium nitrite in organic synthesis have been widely studied. $NaNO_2$, in mixtures with mineral or organic acids, results in the formation of unstable nitrous acid (HNO_2), a reactive species that readily participates in several reactions. Polyatomic species generated in situ, such as nitrosonium (NO^+) and nitronium (NO_2^+) ions, are capable of acting on several organic substrates.[1l] An important example is the reaction with primary aromatic amines to form aryl diazonium salts, which are widely used in modern organic synthesis. This reaction is exemplified by classic procedures such as those of Sandmeyer,[1e–g] Gomberg and Bachmann, and Balz and Schiemann, as well as the more robust methodologies developed by Heck and Matsuda.[1m,n]

The objective of this graphical review is to present methodologies that use sodium nitrite with different types of substrates for the synthesis of organic molecules, without involving the formation of aryl diazonium salt intermediates. $NaNO_2$, as a source of nitrite ions, has been used in various reactions as a nitrating and nitrosating agent. Examples include the direct nitration of arenes,[2] the nitrosation of secondary amines,[3] the synthesis of nitriles[6] and oximes,[7] the functionalization and formation of heterocycles,[8a] and catalytic reactions involving the cleavage and formation of C–C bonds.[9,10] Additionally, sodium nitrite plays a role in oxidation and halogenation reactions, acting as a catalyst or co-catalyst for the synthesis of organic compounds, specifically carbonyl and halogenated aromatic compounds.[4,5,11]

This graphical review explores pioneering studies and contemporary synthetic methodologies that encompass a variety of synthesized molecules, reaction yields, mechanistic aspects of reactions, and future prospects. All the figures are presented in color, highlighting the main reagents, and provide a logical and concise sequence of the key studies discussed.

Biosketches

Lamark Carlos I graduated in chemistry from the Federal University of Rio Grande do Norte in 2019. Currently, he is studying for an M.Sc. in pharmaceutical sciences at the same institute under the supervision of Prof. Dr. A. K. Jordão and Prof. Dr. E. G. Barbosa. His work involves the synthesis and antimalarial evaluation of new 1*H*-1,2,3-triazoles derived from melatonin and tryptamine.



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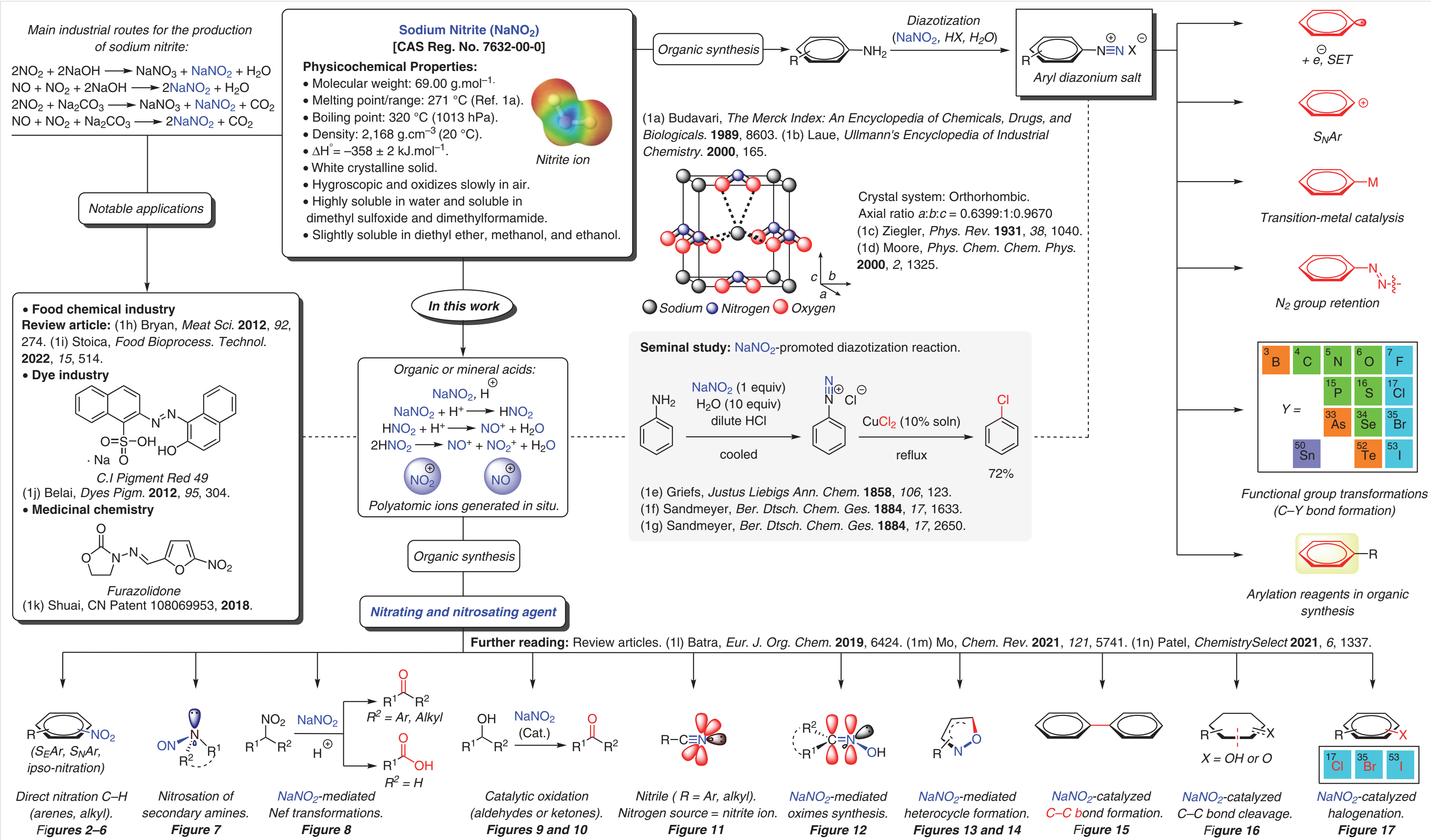

Figure 1 The use of $NaNO_2$ in organic synthesis[1a–n]

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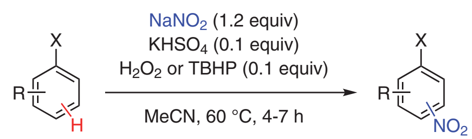
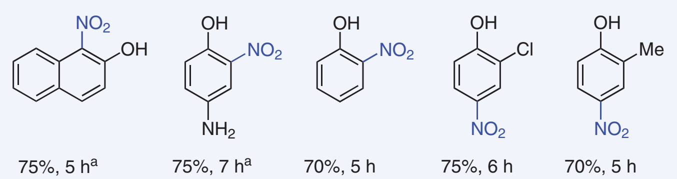
$NaNO_2$-Mediated (C–H) Direct Nitration. Notable Features:

- In situ generated nitrating species.
- Nitration via electrophilic and nucleophilic substitution reactions.
- Practical access to nitro compounds under mild reaction conditions.

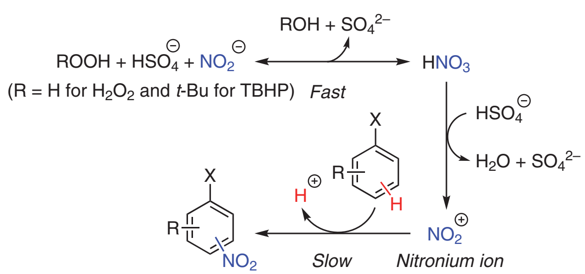
Direct nitration mediated by $NaNO_2$/hydroperoxides/$KHSO_4$.



Selected examples



(2a) Kamatala, *Chem. Data Collect.* **2019**, *21*, 100222. [a] TBHP (0.1 equiv).



Hydroperoxide-triggered mechanism for the nitration of aromatic compounds.

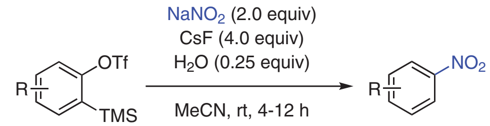
Further reading: $NaNO_2$-mediated synthesis of substituted nitrophenols. **Notable feature:** Distinct methodologies for direct nitration of aromatic compounds.

(2b) Zolfigol, *Molecules.* **2002**, *7*, 734.
(2c) Zolfigol, *Mendeleev Commun.* **2006**, *16*, 41.
(2d) Jereb, *Curr. Org. Chem.* **2013**, *17*, 1694.
(2e) Rajanna, *Int. J. Chem. Kinet.* **2017**, *49*, 209.
(2f) Rajanna, *Res. Chem. Intermed.* **2018**, *44*, 6023.

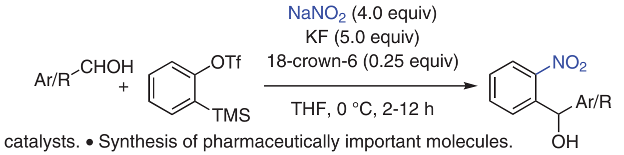
Other further reading:

(2g) Syvret, *J. Org. Chem.* **2002**, *67*, 4487.
(2h) Rajanna, *Synth. Commun.* **2018**, *48*, 59.
(2i) Terent'ev, *Chem. Eur. J.* **2019**, *25*, 5922.
(2j) Jia, *Org. Lett.* **2019**, *21*, 5030.
(2k) Ranjan, *J. Am. Chem. Soc.* **2023**, *145*, 2745.

Nucleophilic nitration of arynes by $NaNO_2$ and H_2O.

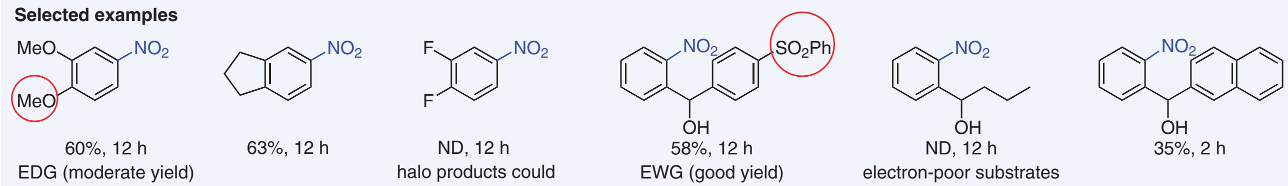


Multicomponent protocol to synthesize substituted (2-nitrophenyl)methanols.



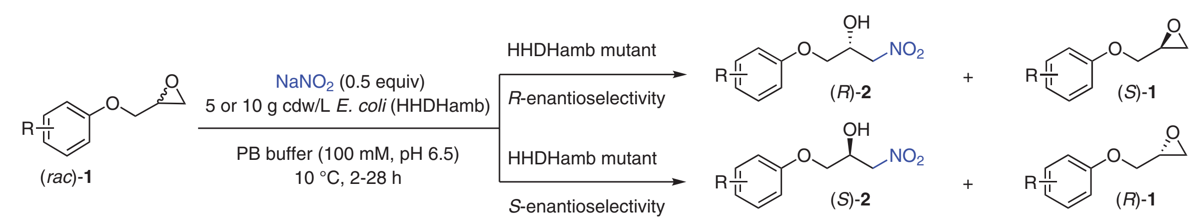
• Mild reaction conditions. • Free from transition-metal catalysts. • Synthesis of pharmaceutically important molecules.

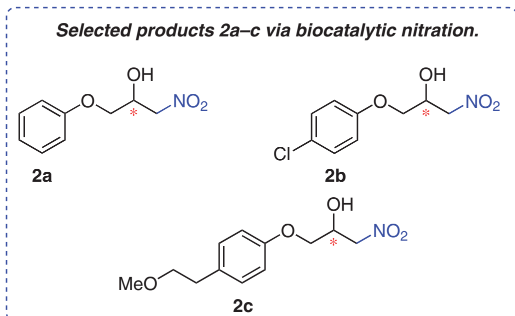
Selected examples



(2l) Mhaske, *Org. Lett.* **2016**, *18*, 3010.

Enantiocomplementary synthesis of β-adrenergic blocker precursors via biocatalytic nitration of phenyl glycidyl ethers.

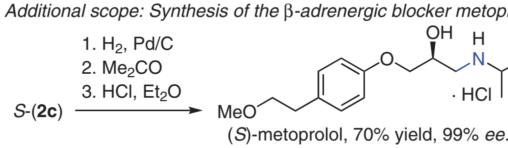


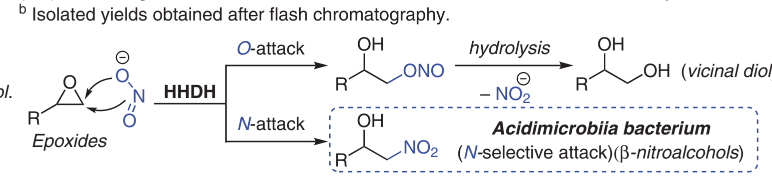


HHDHamb	Substrate	Product	Time (h)	*ee* 1 (%)[a]	*ee* 2 (%)[a]	Yield 2 (%)[b]
RM8	**1a**	*R*-(**2a**)	2	97	>99	41
SM7	**1a**	*S*-(**2a**)	21	85	95	42
RM8	**1b**	*R*-(**2b**)	8	96	>99	39
SM7	**1b**	*S*-(**2b**)	20	88	91	42
RM8	**1c**	*R*-(**2c**)	5	>99	99	40
SM7	**1c**	*S*-(**2c**)	28	91	96	41

(2m) Liu, *Bioorg. Chem.* **2023**, *138*, 106640. [a] The *ee* values were determined by chiral HPLC. [b] Isolated yields obtained after flash chromatography.

Additional scope: Synthesis of the β-adrenergic blocker metoprolol.

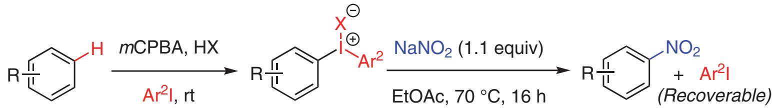




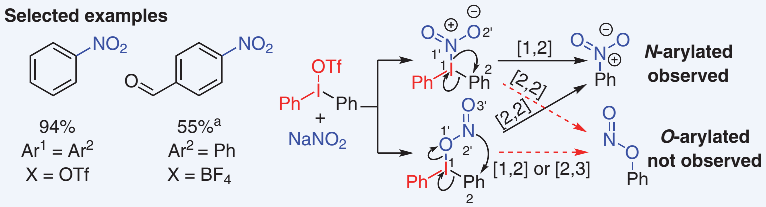
$NaNO_2$-mediated ring-opening reaction catalyzed by halohydrin dehalogenase (HHDH).
Further reading: (2n) Gao, *Enzyme Microb. Technol.* **2015**, *34*, 73.

Figure 2 Direct nitration (C–H) promoted by $NaNO_2$, part 1[2a–n]

One-pot C–H functionalization of arenes by diaryliodonium salts.

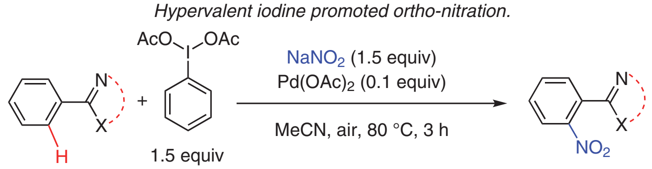


Selected examples

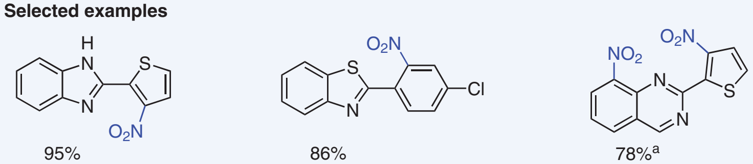


(2o) Olofsson, *Angew. Chem. Int. Ed.* **2016**, *55*, 8928. [a] NaOTf (1.0 equiv) was added.

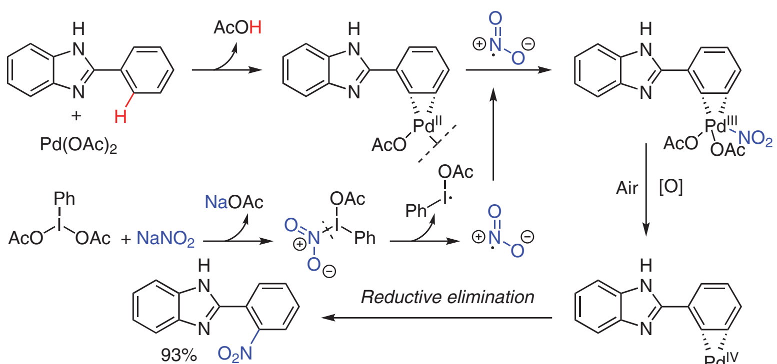
Hypervalent iodine promoted ortho-nitration.



Selected examples

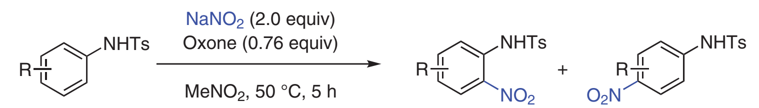


(2p) Das, *Org. Biomol. Chem.* **2020**, *18*, 941. [a] Reaction time of 9 h.

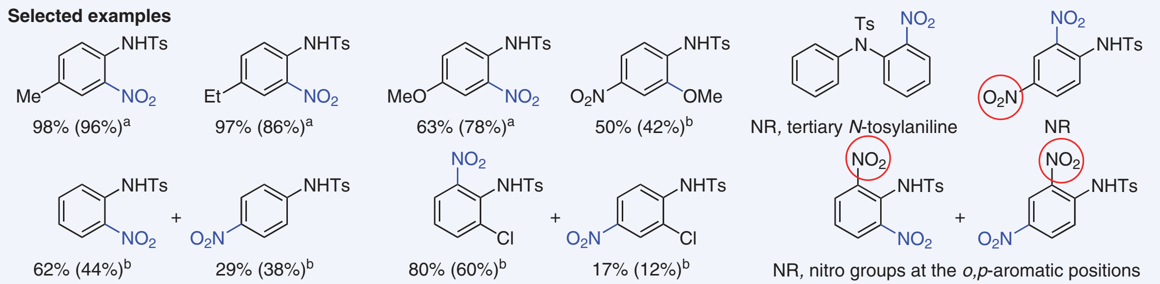


Further reading: (2q) Mo, *Synth Commun.* **2016**, *46*, 963.

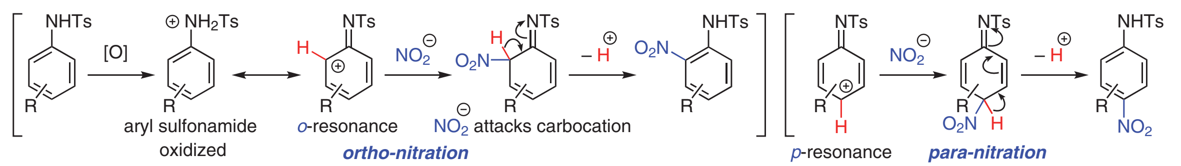
Direct oxidative nitration of aromatic sulfonamides.



Selected examples

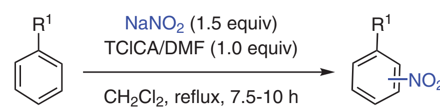


(2r) Liang, *Chem. Commun.* **2014**, *50*, 9936. [a] In CH_2Cl_2 at room temperature, 30 h. [b] In MeCN at 50 °C, 5 h.



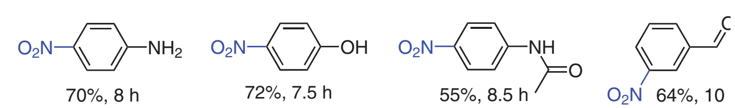
Further reading: Mild hypervalent iodine mediated oxidative nitration of *N*-aryl sulfonamides. (2s) Nachtsheim, *Chem. Commun.* **2014**, *50*, 10485.

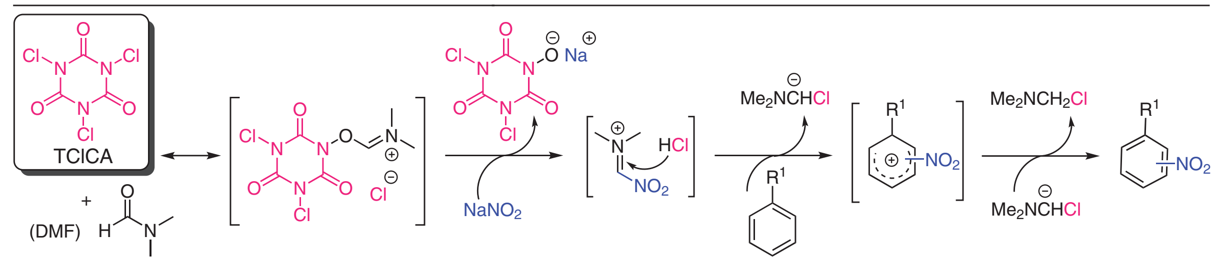
Nitration of aromatic compounds via trichloroisocyanuric acid/DMF/$NaNO_2$.



(2t) Rajanna, *Synth. Commun.* **2015**, *45*, 2251.

Selected examples - Yield, Time





Further reading: TCICA/$NaNO_2$-triggered nitration of aromatic compounds: (2u) Zolfigol, *Synlett.* **2003**, 191. (2v) Rajanna, *Int. J. Chem. Kinet.* **2019**, *51*, 445. (2w) Rajanna, *SN Appl. Sci.* **2019**, *1*, 1004. (2x) Kamatala, *Int. J. Chem. Kinet.* **2021**, *53*, 164.

Figure 3 Direct nitration (C–H) promoted by $NaNO_2$, part 2[2o–x]

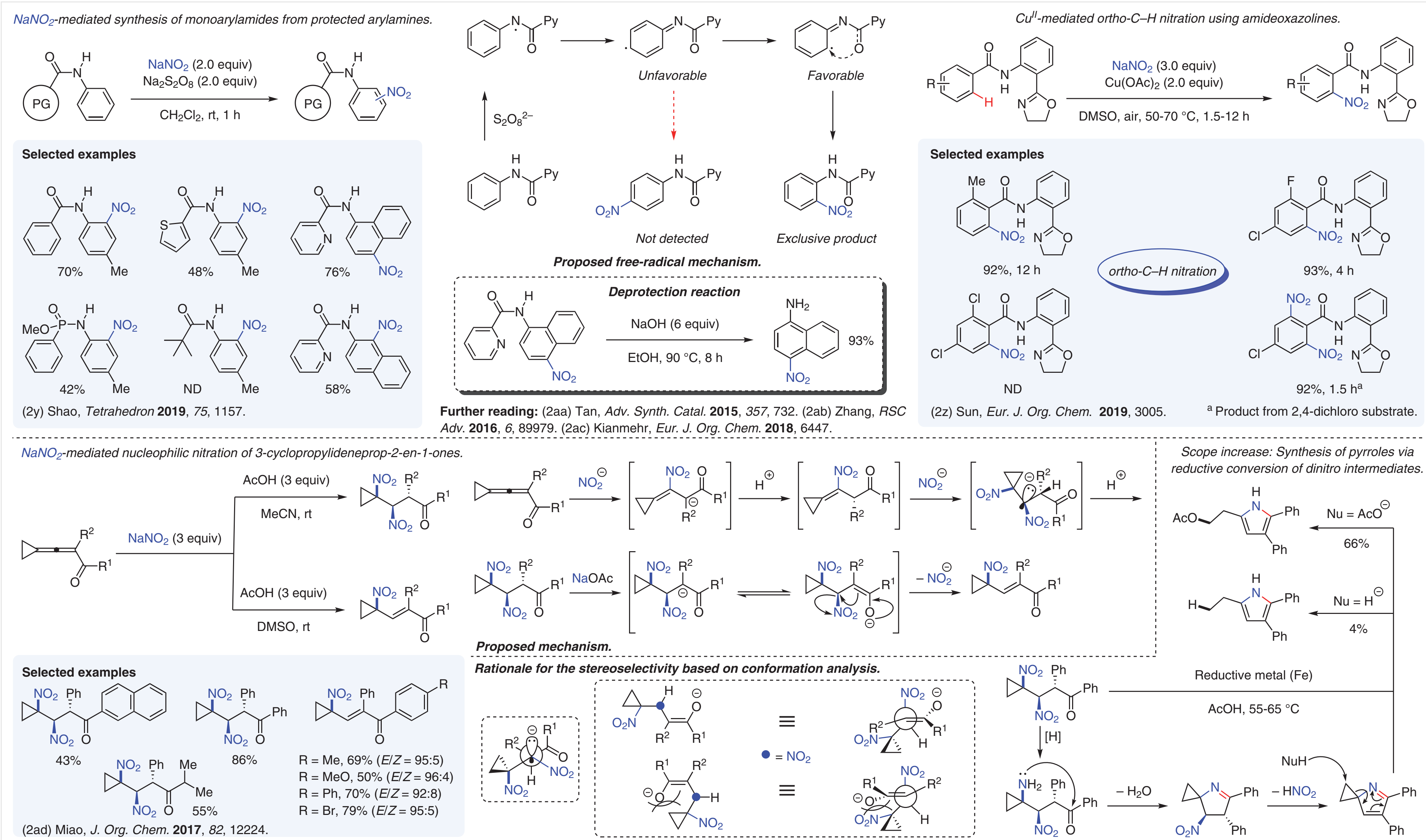
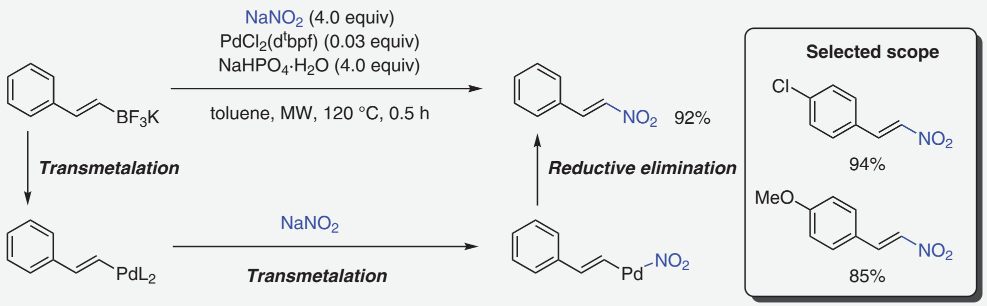


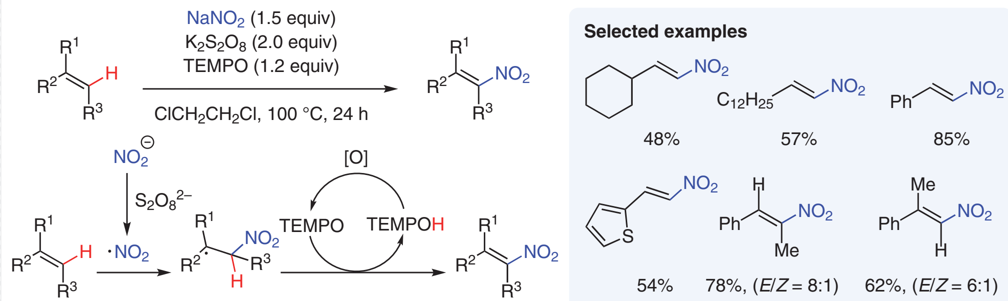
Figure 4 Direct nitration (C–H) promoted by $NaNO_2$, part 3[2y–ad]

Seminal Study: $NaNO_2$-mediated nitration of potassium styryltrifluoroborates via cross-coupling.



(2ae) Saito, *Tetrahedron Lett.* **2005**, *46*, 4715. (2af) Al-Masum, *Tetrahedron Lett.* **2013**, *54*, 1141.

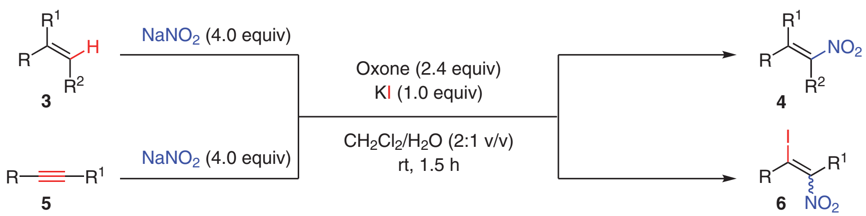
$K_2S_2O_8$-mediated nitration of alkenes with $NaNO_2$ and TEMPO: Stereoselective synthesis of (E)-nitroalkenes.



(2ah) Zhao, *Tetrahedron Lett.* **2016**, *57*, 80.

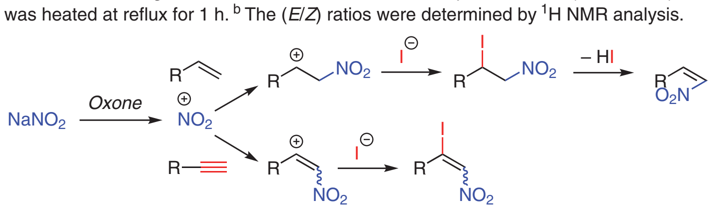
Proposed mechanism for the nitration.

Oxone/KI-mediated nitration of alkenes and alkynes: Synthesis of nitro- and β-iodonitro-substituted alkenes.

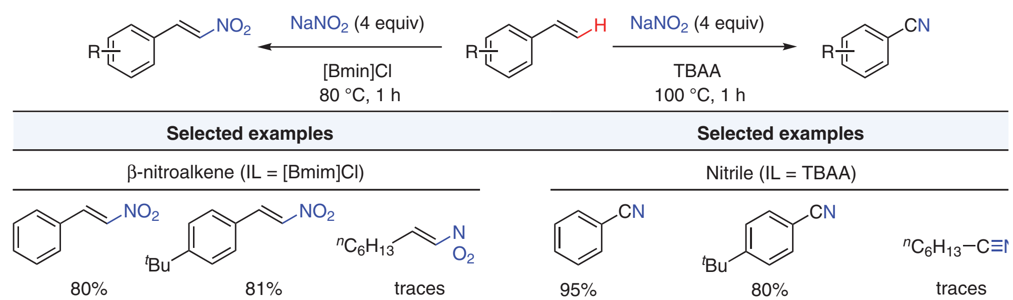


Substrate	R	R^1	R^2	Product	Yield (%)	(E/Z)[b]
3a	4-BrC_6H_4	H	H	**4a**	88	-
3b[a]	3-ClC_6H_4	H	H	**4b**	87	-
3c[a]	C_6H_5	H	H	**4c**	75	-
3d[a]	4-($ClCH_2$)C_6H_4	H	H	**4d**	73	-
5a	C_6H_5	H	–	**6a**	62	5.6:1
5b	C_6H_5	Me	–	**6b**	53	4.7:1
5c	4-BrC_6H_4	H	–	**6c**	63	6.7:1
5d	4-MeC_6H_4	H	–	**6d**	70	4.8:1

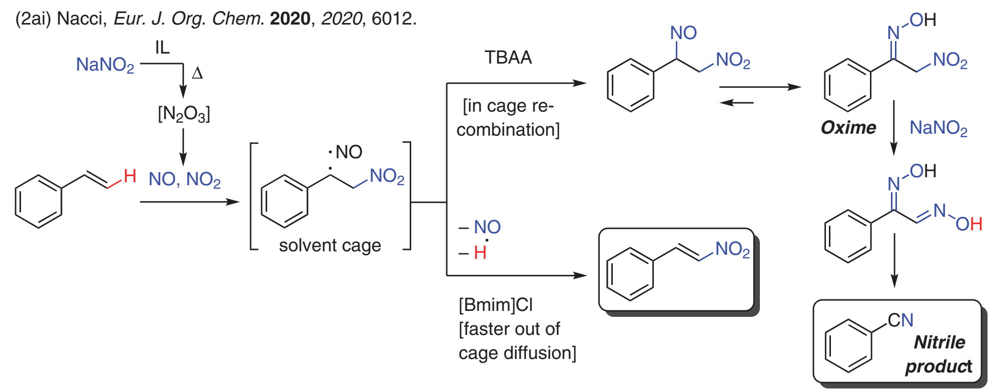
(2ag) Kuhakarn, *Eur. J. Org. Chem.* **2014**, 7433. [a] After 1.5 h, aqueous NaOH (10 M, 1 mL) was added, and the mixture was heated at reflux for 1 h. [b] The (*E*/*Z*) ratios were determined by ^{1}H NMR analysis.



Proposed ionic nitration of alkenes and alkynes.



(2ai) Nacci, *Eur. J. Org. Chem.* **2020**, *2020*, 6012.



Plausible mechanism for the nitration of styrenes in ionic liquids. ***Beckmann rearrangement***

Further reading: $NaNO_2$-mediated direct nitration of alkenes and alkynes. (2aj) Bonetti, *J. Org. Chem.* **1968**, *33*, 237. (2ak) Hwu, *J. Chem. Soc., Chem. Commun.* **1994**, 1425. (2al) Hwu, *Organometallics* **1996**, *15*, 499. (2am) Buevich, *Tetrahedron Le* **2008**, *49*, 2132. (2an) Motornov, *J. Org. Chem.* **2017**, *82*, 5274.

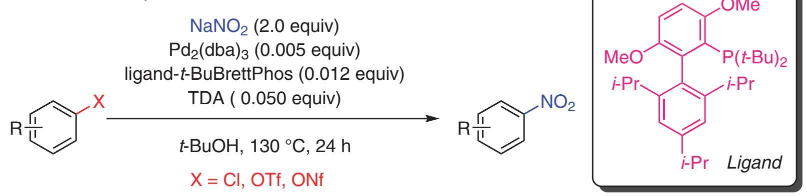
Figure 5 Direct nitration (C–H) promoted by $NaNO_2$, part 4[2ae–an]

$NaNO_2$-Mediated *ipso*-Nitration of Boronic Acids, Aryl Halides, Aryl Triflates and Nonaflates.

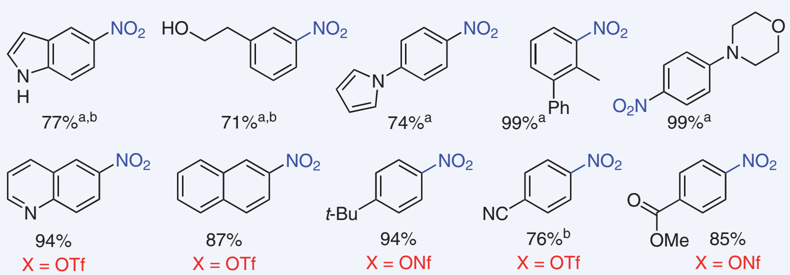
Notable Features:

- Chemo and homoselective *ipso*-nitration.
- Broad range of synthesized compounds.
- Mild reaction conditions.

Preparation of nitro aromatic compounds via ipso-nitration of aryl chlorides, triflates and nonaflates.

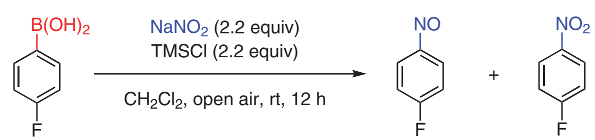


Selected examples

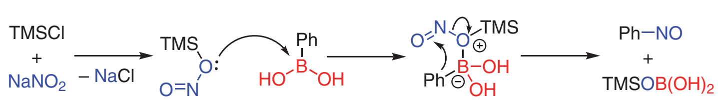


(2ao) Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 12898. [a] X = Aryl halide. [b] $Pd_2(dba)_3$ (0.025 equiv), ligand (0.06 equiv).

Ipso-nitrosation/nitration of aryl boronic acids using $NaNO_2$ and TMSCl.

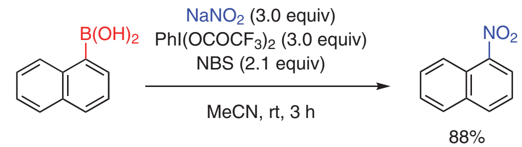


(2ap) Prakash, *Tetrahedron Lett.* **2014**, *55*, 1975.



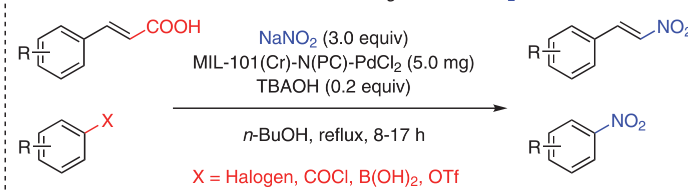
Proposed mechanism for ipso-nitrosation.

Futher reading: (2au) Feldman, *J. Am. Chem. Soc.* **1979**, *101*, 4768. (2av) Fu, *Chem. Eur. J.* **2011**, *17*, 5652. (2aw) Bora, *Appl. Organomet. Chem.* **2019**, *33*, 4951.

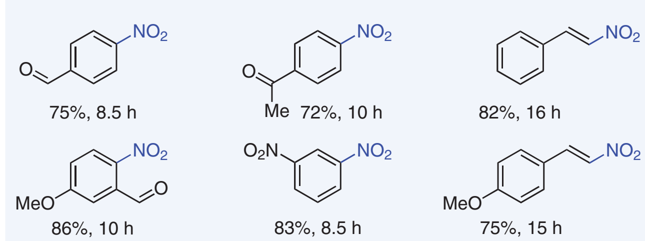


(2aq) Goswami, *Org. Biomol. Chem.* **2015**, *13*, 4828.

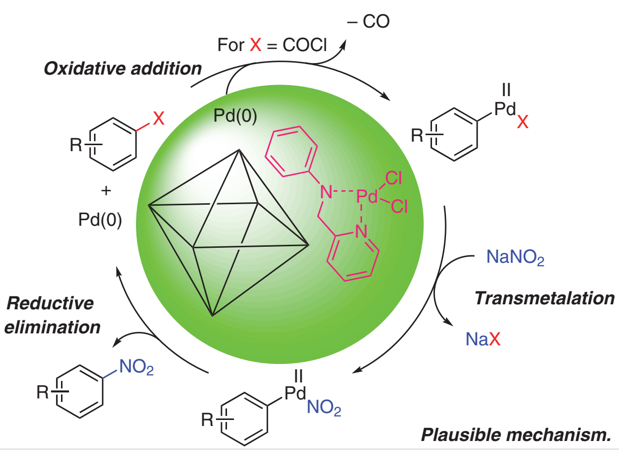
Selective nitration using MOFs/$NaNO_2$.



Selected examples

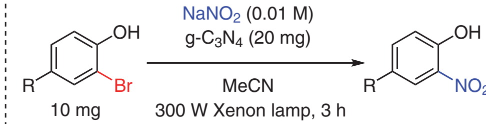


(2ar) Sepehrmansourie, *Mol. Catal.* **2022**, *531*, 112639.

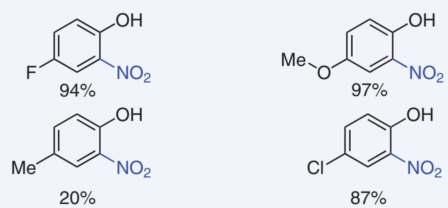


Plausible mechanism.

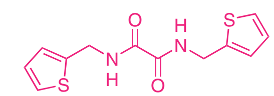
Photocatalytic ipso-nitration.



Selected examples

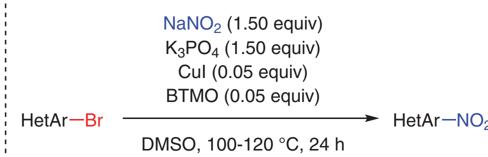


(2as) Liang, *Sustainable Chem. Pharm.* **2023**, *33*, 101077.

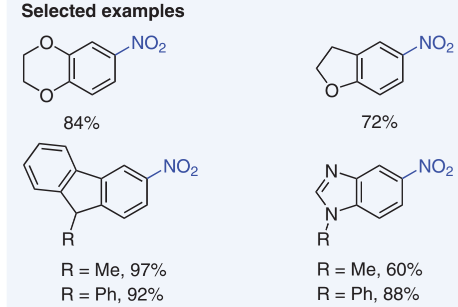


BTMO

Ligand for Cu-catalyzed ipso-nitration.



Selected examples



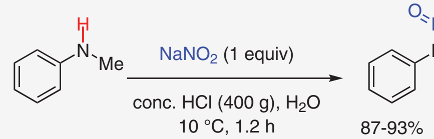
(2at) Ma, *J. Org. Chem.* **2024**, *89*, 6626.

Figure 6 Direct *ipso*-nitration (C–H) promoted by $NaNO_2$, part 5[2ao–aw]

Nitrosamines. Notables Features:

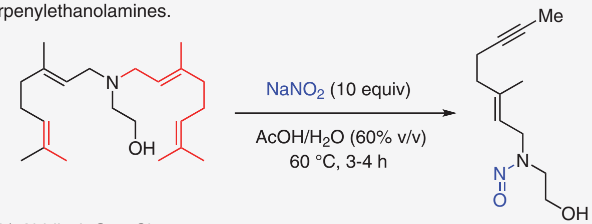
- $NaNO_2$-mediated nitrosation of secondary amines.
- Nitrosonium ions, $NO^{\oplus}$, generated in situ.

Seminal study: Sodium nitrite mediated synthesis of *N*-nitrosamines.



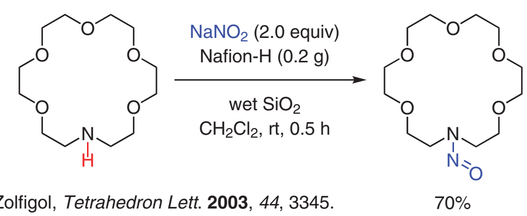
(3a) Hartman, *Org. Synth.* **1933**, *13*, 8.

Seminal study: Sodium nitrite mediated nitrosative dealkylation of tertiary terpenylethanolamines.

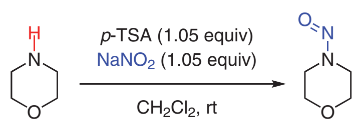


(3b) Abidi, *J. Org. Chem.* **1986**, *51*, 2687.

Further reading: $NaNO_2$-mediated Abidi transformation (review article).
(3c) Zard, *J. Chem. Soc., Chem. Commun.* **2002**, 1555.

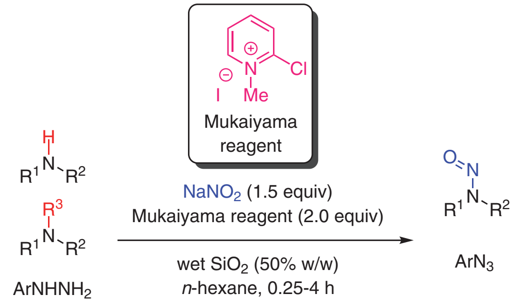


(3d) Zolfigol, *Tetrahedron Lett.* **2003**, *44*, 3345.

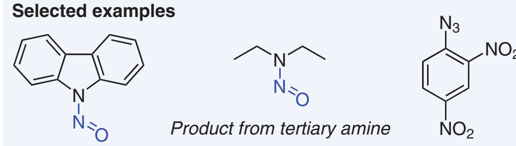


(3e) Borikar, *Synth. Commun.* **2010**, *40*, 654.

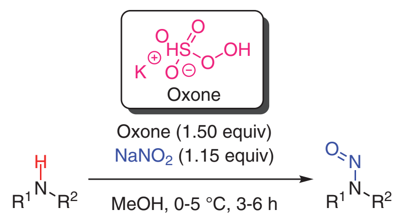
Futher reading:
(3l) Smith, *J. Am. Chem. Soc.* **1967**, *89*, 1147.
(3m) Hecht, *J. Org. Chem.* **1978**, *43*, 72.
(3n) Nakajima, *Tetrahedron Lett.* **1984**, *25*, 2619.
(3o) Giumanini, *Tetrahedron* **1990**, *46*, 4303.
(3p) Chehardoli, *J. Chem. Sci.* **2009**, *121*, 441.



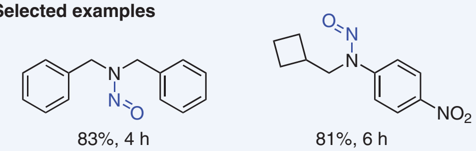
Selected examples



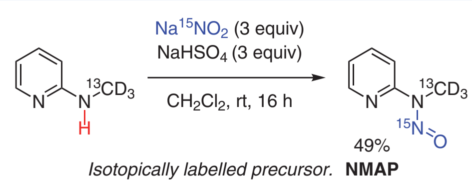
(3f) Azadi, *Tetrahedron Lett.* **2015**, *56*, 5613.



Selected examples

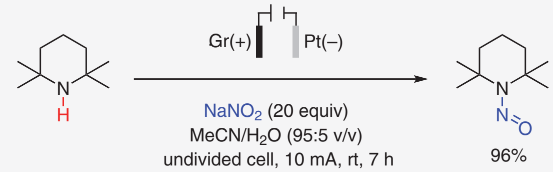


(3g) Banerjee, *Synth. Commun.* **2019**, *49*, 2270.

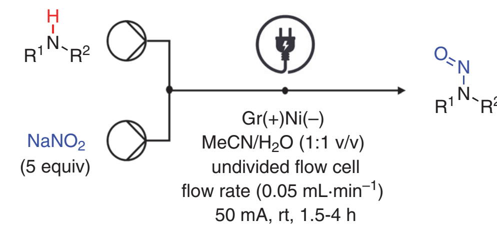


(3h) Derdau, *J. Labelled Compd. Radiopharm.* **2023**, *66*, 41.

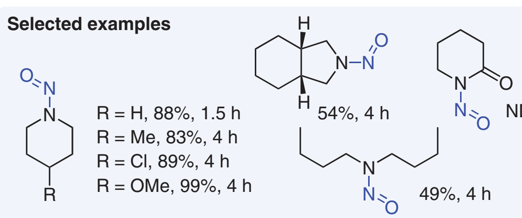
Seminal study: An electrochemical flow method mediated by sodium nitrite.



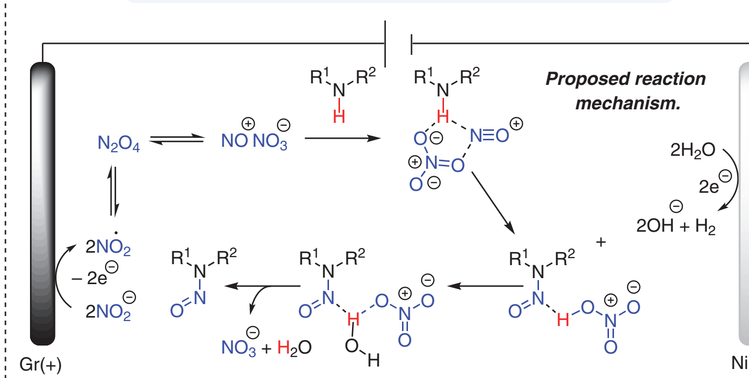
(3i) Masui, *Chem. Pharm. Bull.* **1988**, *36*, 459.



Selected examples



(3j) Ali, *Chem. Eur. J.* **2023**, *29*, e202300957.

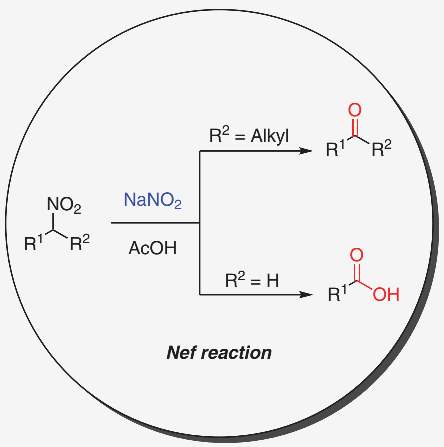


Futher Reading: A review article using electrochemical methods.
(3k) Ali, *Chem. Methods* **2024**, *4*, e20230005.

Figure 7 $NaNO_2$-mediated nitrosation of secondary amines[3a–p]

$NaNO_2$-Mediated Nef Transformations.

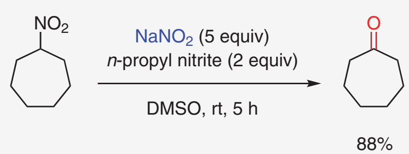
Seminal study: Acid hydrolysis of primary and secondary nitroalkane salts into aldehydes or ketones.



(4a) Nef, *Justus Liebigs Ann. Chem.* **1894**, *280*, 263.

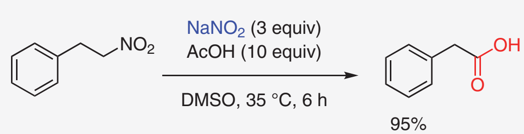
Use of sodium nitrite in the Nef reaction:

Seminal study: Synthesis of ketones and carboxylic acids from nitro compounds mediated by $NaNO_2$/alkyl nitrites.

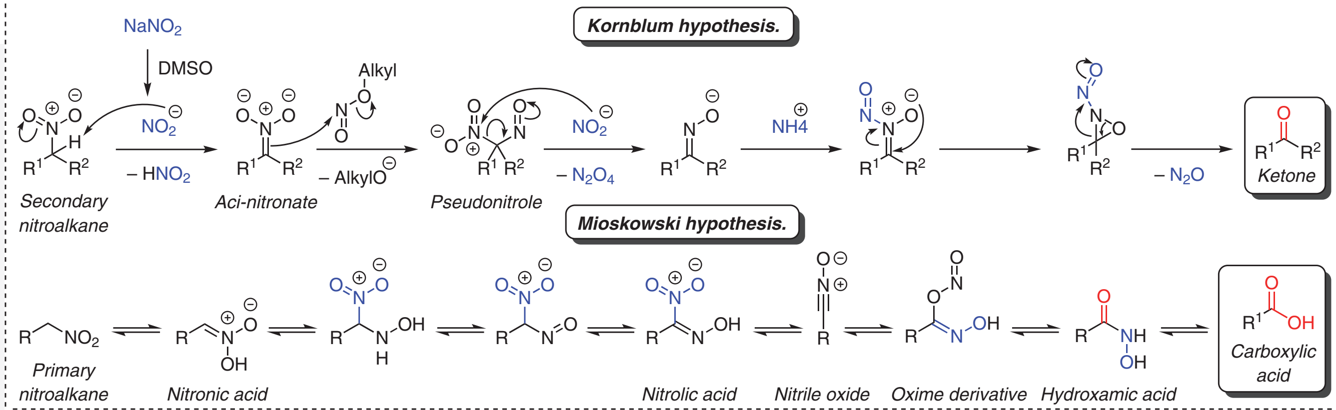


(4b) Kornblum, *J. Am. Chem. Soc.* **1956**, *78*, 1497. (4c) Kornblum, *J. Org. Chem.* **1973**, *38*, 1418.

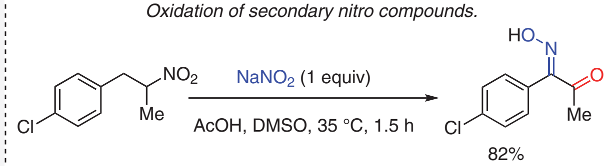
Seminal study: Conversion of primary nitro compounds into carboxylic acids in the presence of $NaNO_2$/AcOH.



(4d) Mioskowski, *J. Org. Chem.* **1997**, *62*, 234.

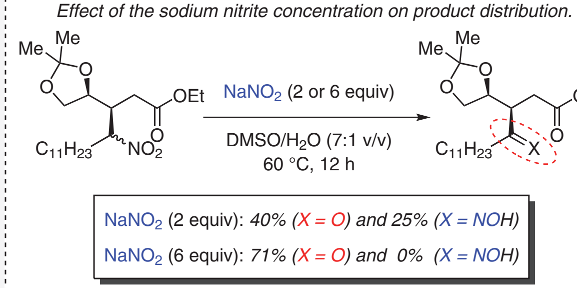


Oxidation of secondary nitro compounds.



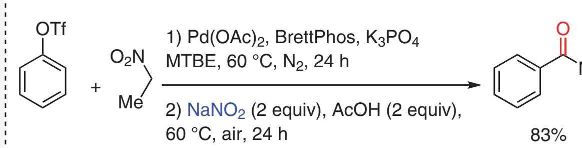
(4e) Ran, *Tetrahedron. Lett.* **2003**, *44*, 8061.

Effect of the sodium nitrite concentration on product distribution.



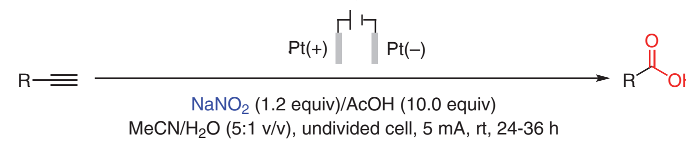
(4f) Patrocinio Pereira, *Tetrahedron Lett.* **2009**, *50*, 6389.

Access to ketones through Pd-catalyzed cross-coupling of phenol derivatives with nitroalkanes.

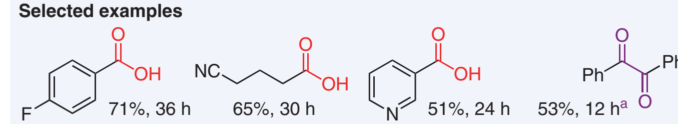


(4g) Yu, *Eur. J. Org. Chem.* **2022**, e202200731.

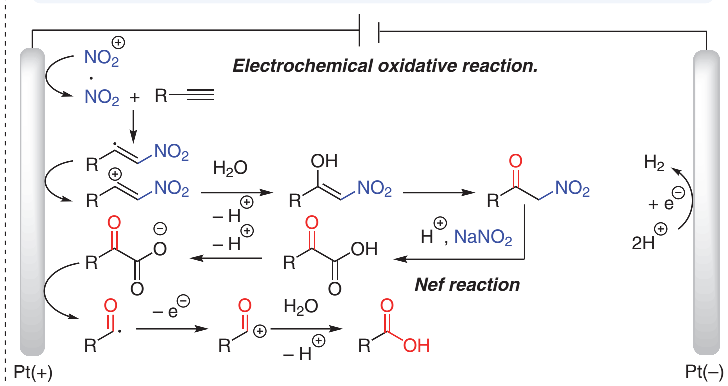
Electrochemical oxidative cleavage of alkynes to carboxylic acids.



Selected examples



(4h) Huang, *Org. Lett.* **2023**, *25*, 293. [b] Product from internal alkyne.



Further reading: A review article on new perspectives on the Nef reaction and $NaNO_2$-mediated methodologies. (4i) Petrini, *Adv. Synth. Catal.* **2015**, *357*, 2371.

Figure 8 $NaNO_2$-mediated Nef reactions[4a–i]

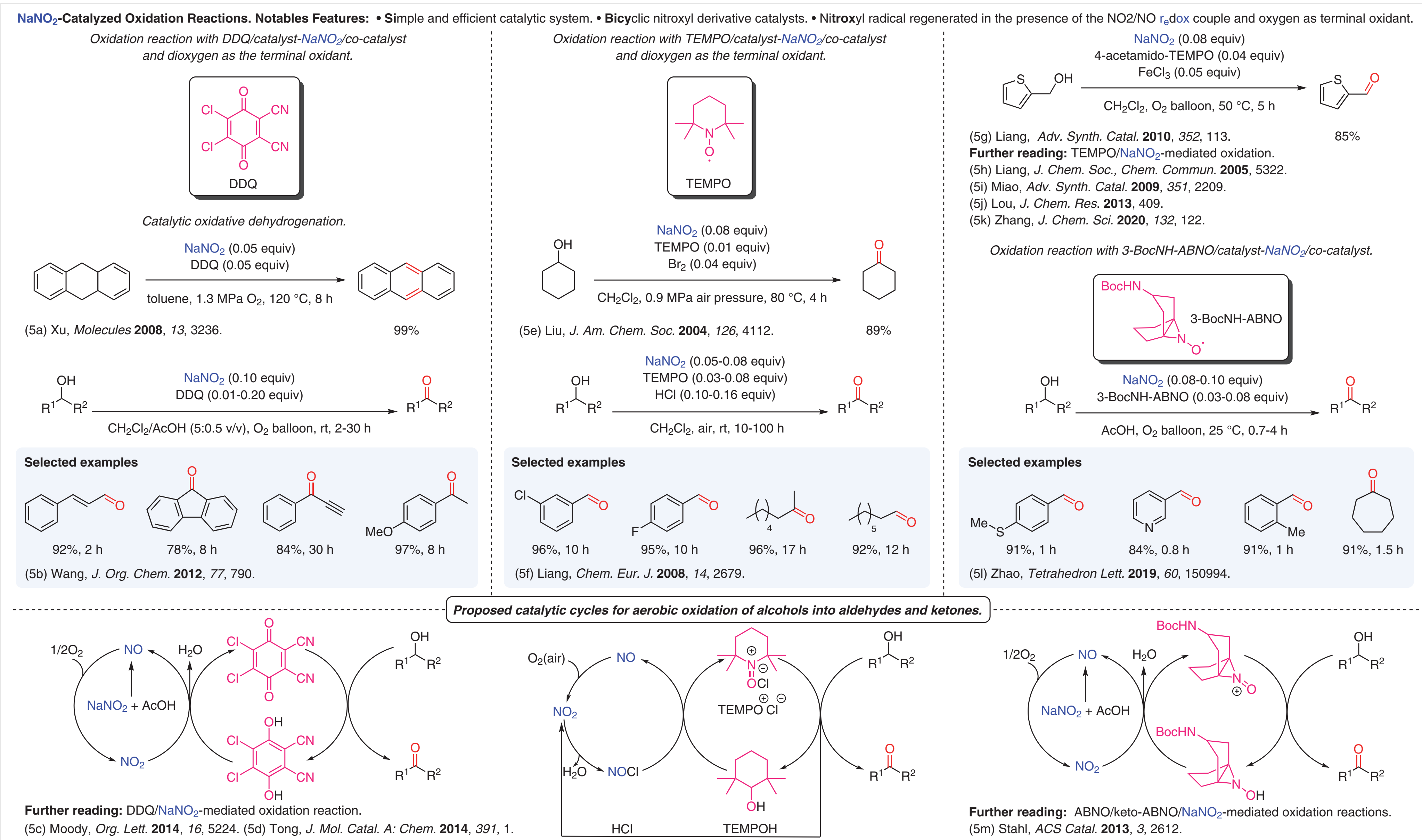
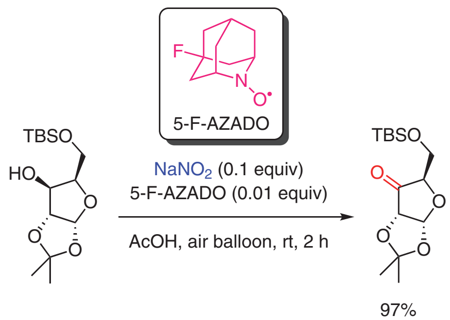
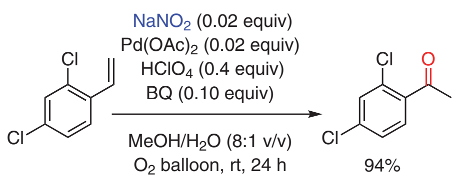


Figure 9 $NaNO_2$-mediated oxidation reactions, part 1[5a–m]

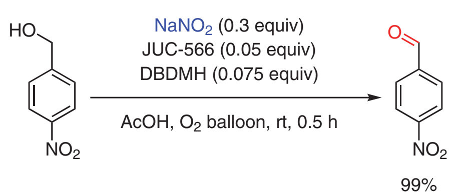


(5n) Iwabuchi, *J. Am. Chem. Soc.* **2011**, *133*, 6497.
Further reading: Mechanistic studies.
(5o) Iwabuchi, *J. Org. Chem.* **2014**, *79*, 10256.
Chemoselective oxidation of α-hydroxy acids to α-keto acids catalyzed by AZADO/NaNO$_2$:
(5p) Shibuya, *Org. Lett.* **2016**, *18*, 4230.

Wacker oxidation of styrene derivatives into ketones.

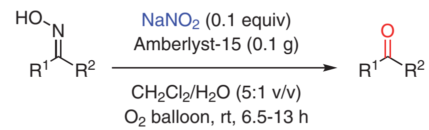


(5q) Ding, *Org. Biomol. Chem.* **2013**, *11*, 2947.
Further reading: Wacker oxidation.
(5r) Grubbs, *J. Am. Chem. Soc.* **2014**, *136*, 890.
(5s) Wan, *Org. Biomol. Chem.* **2022**, *20*, 7814.

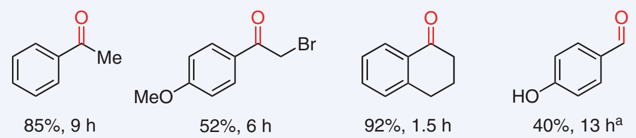


(5t) Chen, *Angew. Chem. Int. Ed.* **2021**, *60*, 22230.
Other further reading:
(5u) Bosch, *J. Org. Chem.* **1994**, *59*, 2529.
(5v) Liang, *Angew. Chem. Int. Ed.* **2005**, *44*, 5520.
(5w) Xu, *Adv. Synth. Catal.* **2009**, *351*, 558.
(5x) Liu, *Org. Lett.* **2021**, *23*, 4057.

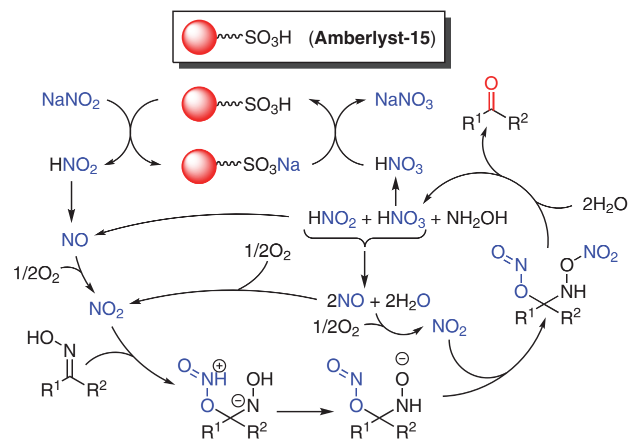
NaNO$_2$-catalyzed aerobic oxidative deoximation.



Selected examples

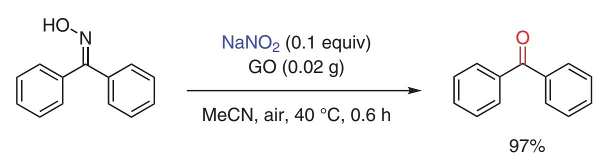


(5y) Ding, *J. Org. Chem.* **2011**, *76*, 4665. [a] Incomplete conversion.

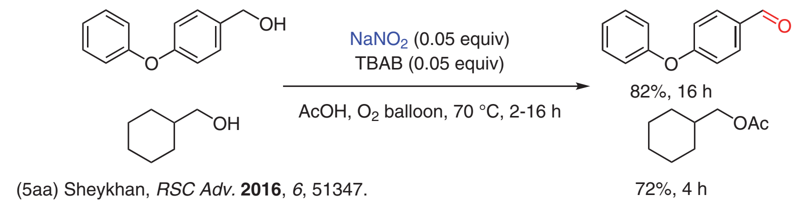


Plausible mechanism for aerobic oxidative deoximation catalyzed by NaNO$_2$.

A deoximation method for the deprotection of ketones and aldehydes using a graphene oxide (GO)/sodium nitrite based catalytic system.

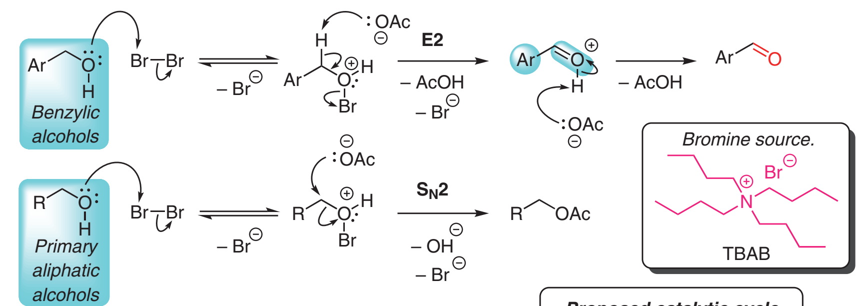


(5z) Tong, *Adv. Synth. Catal.* **2019**, *361*, 3137.

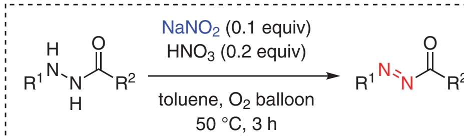


(5aa) Sheykhan, *RSC Adv.* **2016**, *6*, 51347.

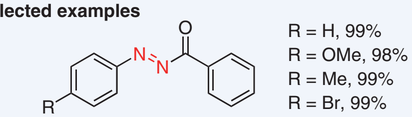
(1) $NO_2^- + 2AcOH \rightarrow NO^+ + H_2O + 2AcO^-$ (2) $NO^+ + O_2 + H_2O \rightarrow NO_2^+ + H_2O_2$
(3) $NO_2^+ + 2Br^- \rightarrow NO_2^- + Br_2$ *Recycle into step* (1).



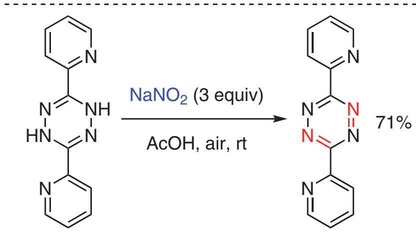
Proposed catalytic cycle for the aerobic oxidation.



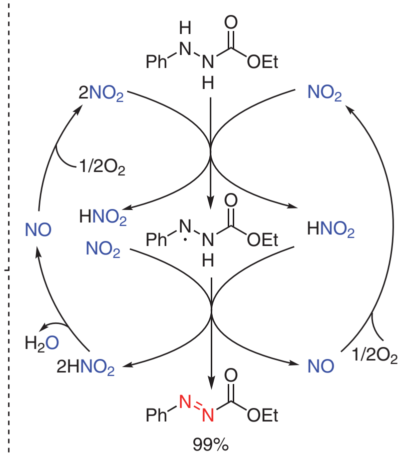
Selected examples



(5ab) Kim, *J. Org. Chem. Front.* **2020**, *7*, 834.



(5ac) Méndez, *Angew. Chem. Int. Ed.* **2023**, *62*, 11186.



Synthesis of azo compounds catalyzed by NaNO$_2$.

Figure 10 NaNO$_2$-mediated oxidation reactions, part 2[5n–ac]

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

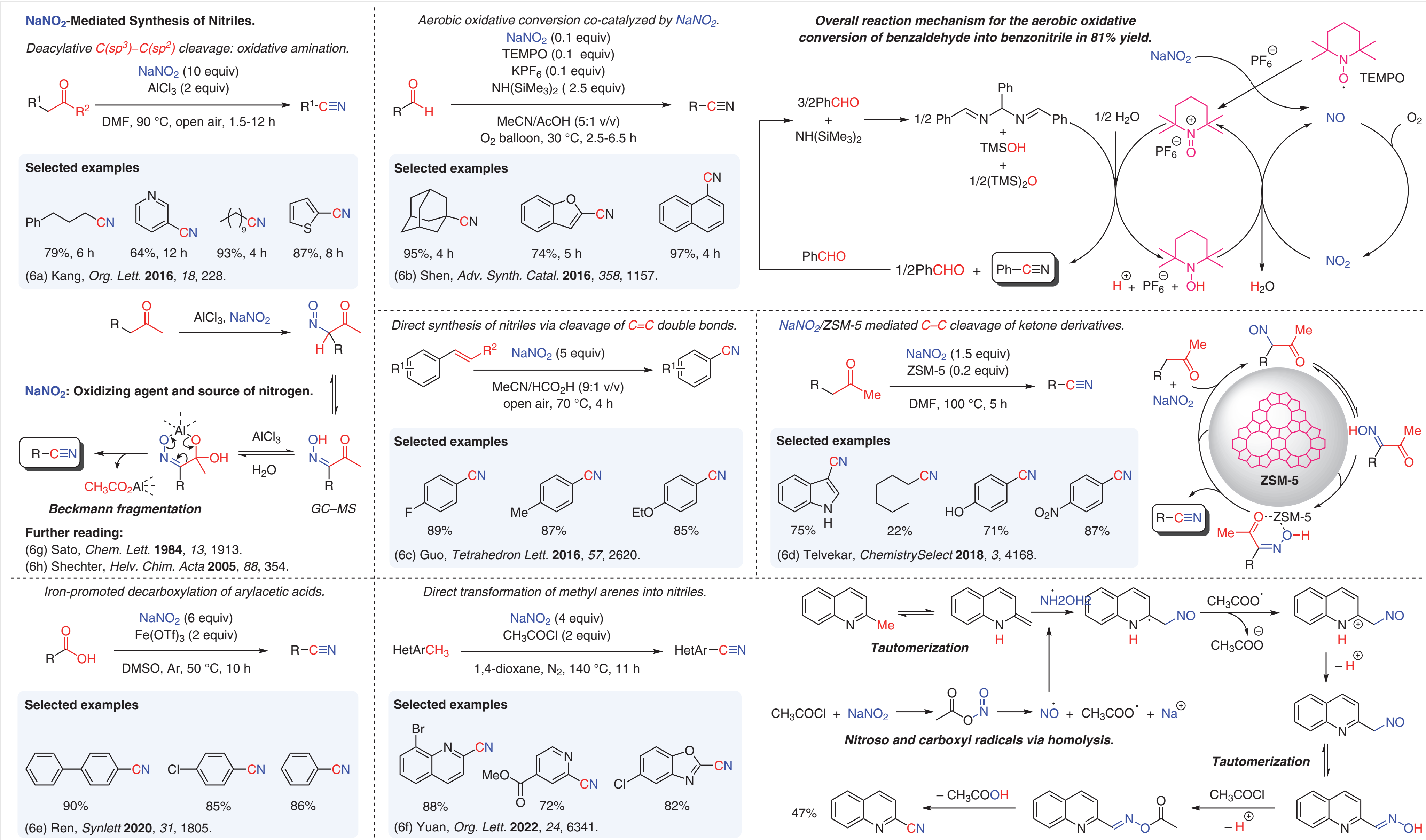


Figure 11 $NaNO_2$-mediated synthesis of nitriles[6a–h]

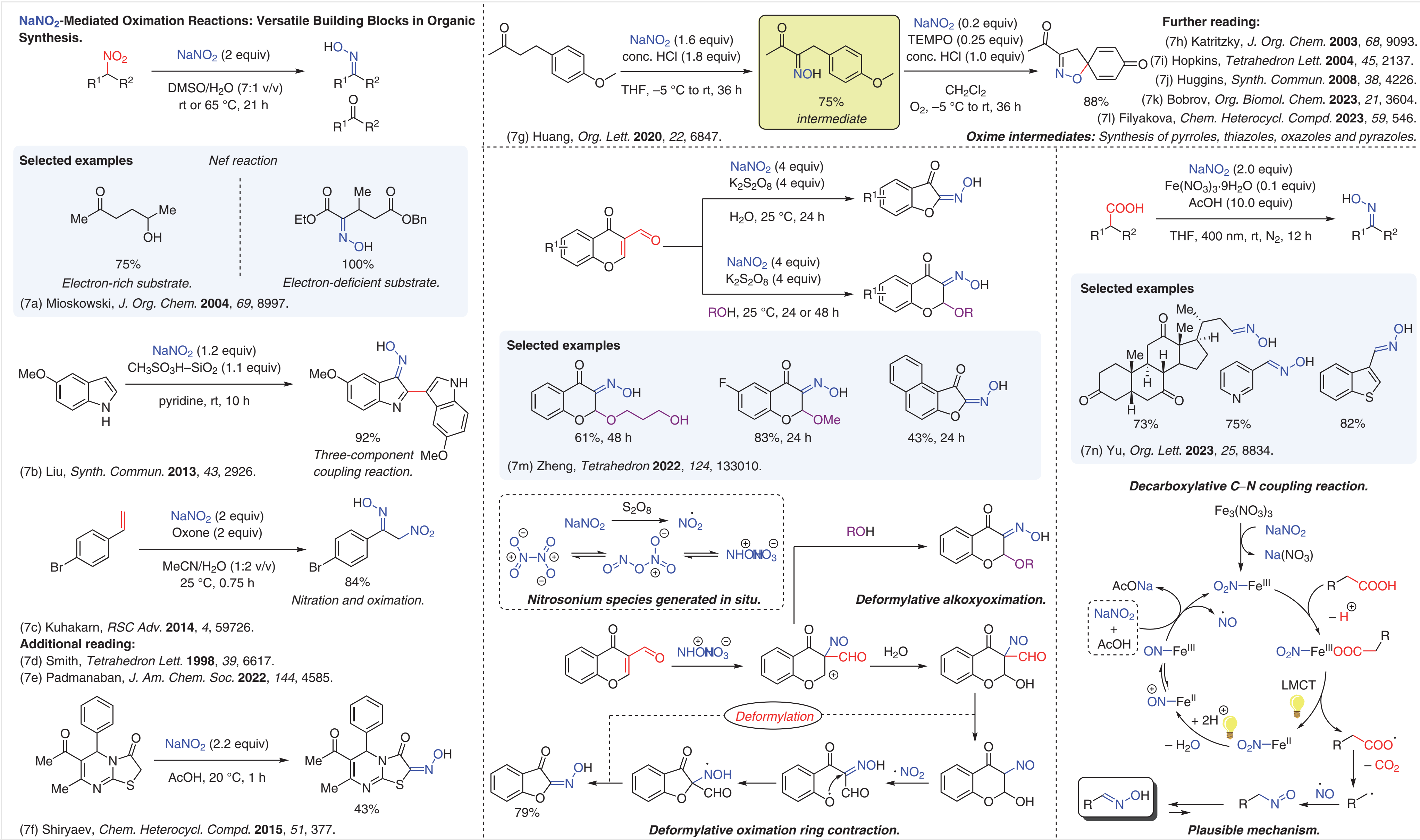


Figure 12 $NaNO_2$-mediated oximation reactions[7a–n]

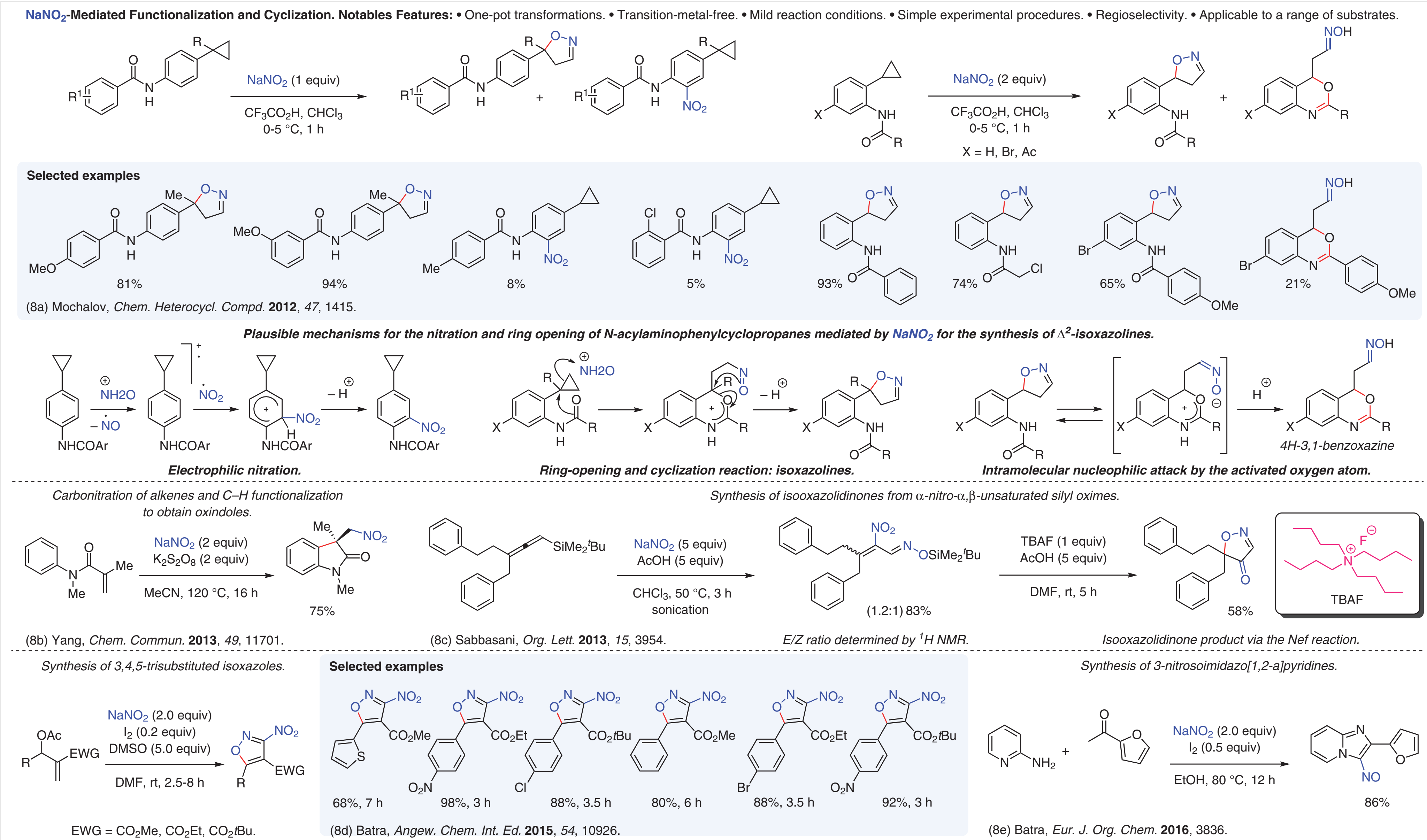
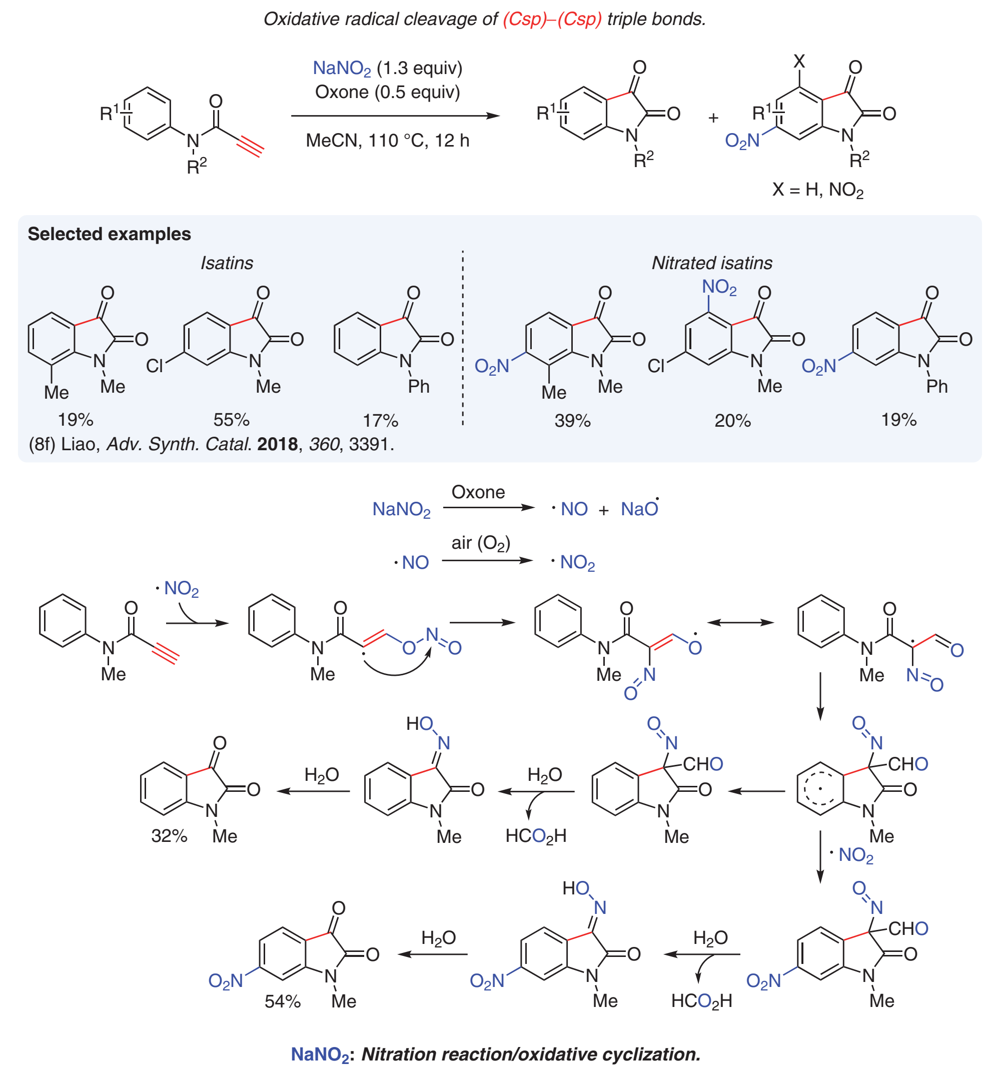
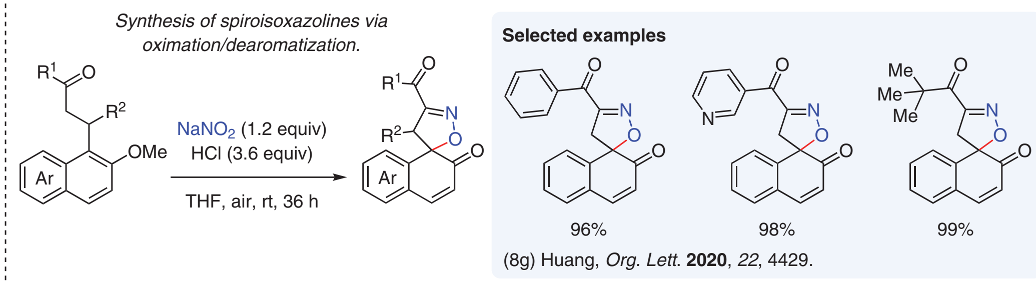
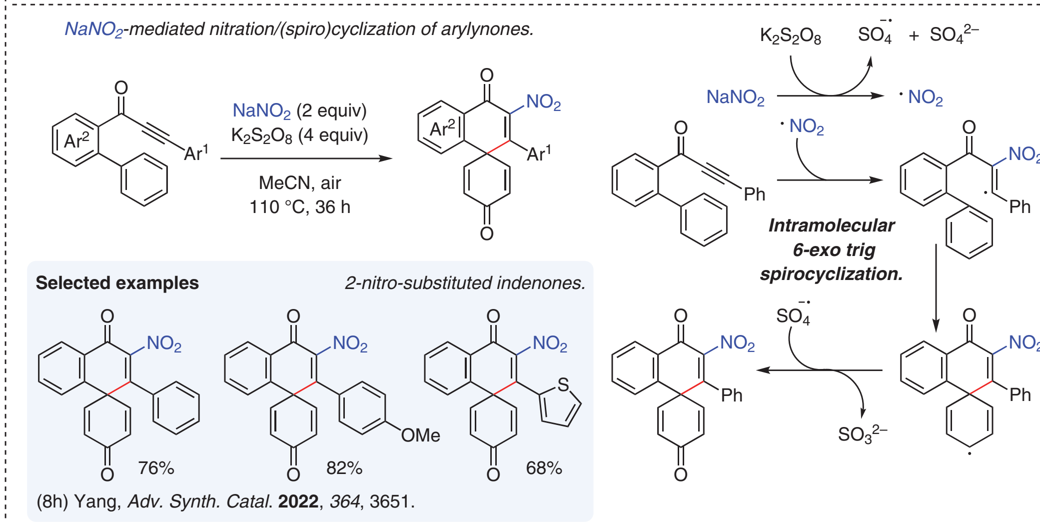


Figure 13 $NaNO_2$-mediated heterocycle formation, part 1[8a–e]



Further reading:
(8j) Tan, *Tetrahedron Lett.* **2008**, *49*, 4424.
(8k) Robina, *Org. Lett.* **2009**, *11*, 4778.
(8l) Saikia, *Asian J. Org. Chem.* **2016**, *5*, 528.
(8m) Ila, *J. Org. Chem.* **2016**, *81*, 5606.
(8n) Patil, *Org. Lett.* **2022**, *24*, 5840.
Copper-mediated nitrosation: 2-Nitrosophenolato complexes and their use in the synthesis of heterocycles:
(8o) McKillop, *J. Org. Chem.* **1976**, *41*, 1079.
(8p) Baxendale, *Molecules* **2019**, *24*, 4154.





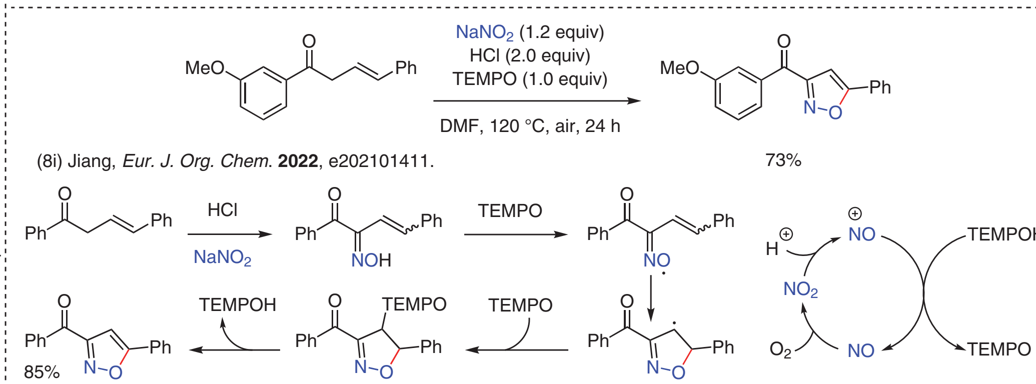
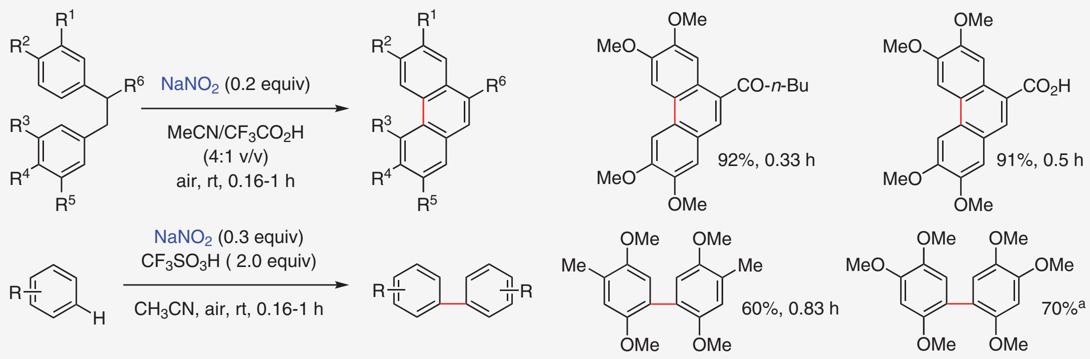


Figure 14 $NaNO_2$-mediated heterocycle formation, part 2[8f–p]

Coupling Reactions and C–C Bond Formation Catalyzed/Mediated by $NaNO_2$.

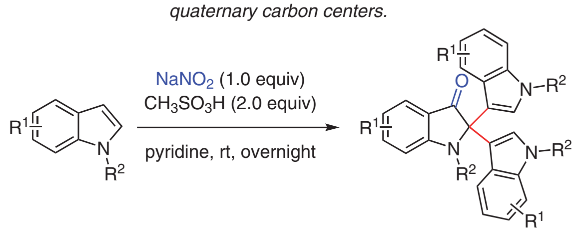
Seminal Study: $NaNO_2$-catalyzed oxidative coupling for construction of the phenanthrene ring using O_2 as the terminal oxidant.



(9a) Wang, *Adv. Synth. Catal.* **2012**, *354*, 383. [a] CF_3CO_2H/MeCN (1:9 v/v), 0.16 h.

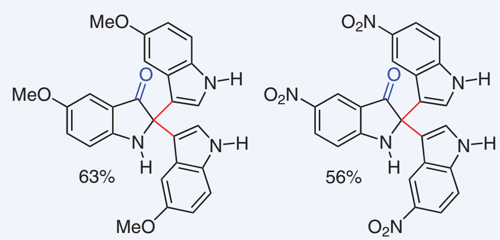
Synthesis of methoxybiaryls.

Oxidative trimerization of indoles using $NaNO_2$ to construct quaternary carbon centers.

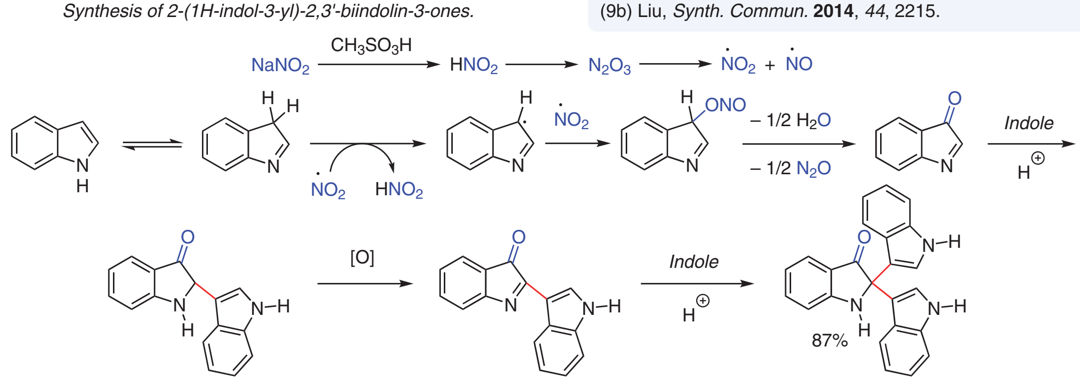


Synthesis of 2-(1H-indol-3-yl)-2,3'-biindolin-3-ones.

Selected examples

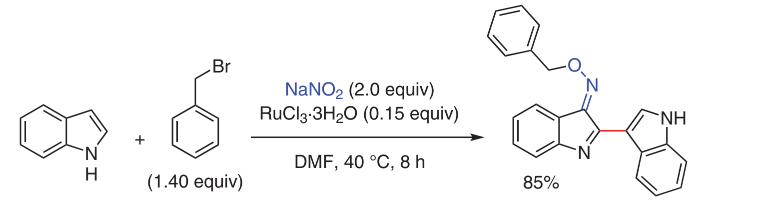


(9b) Liu, *Synth. Commun.* **2014**, *44*, 2215.



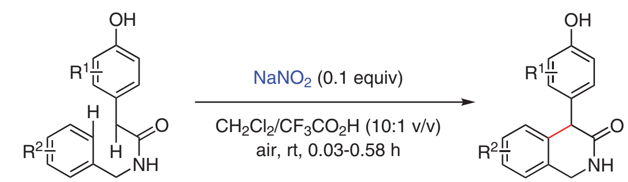
Plausible mechanism for the $NaNO_2$-promoted oxidative trimerization of indoles.

Additional study: *$NaNO_2$/ruthenium-catalyzed synthesis of (E)-2,3'-bi(3H-indol)-3-one O-alkyl oximes.*

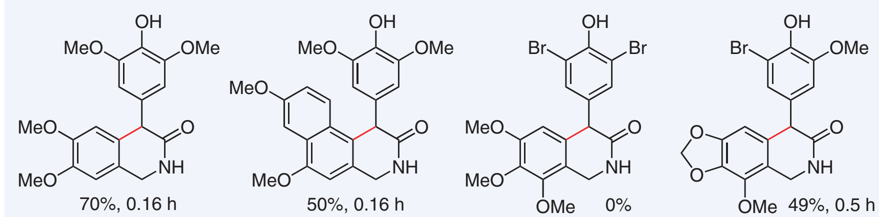


(9c) Qu, *Synth. Commun.* **2015**, *45*, 993. *C–C, C=N, and C–O bonds formed in one pot.*

Construction of the 4-aryldihydroisoquinolinone moiety via direct oxidative Csp^2–Csp^3 coupling.

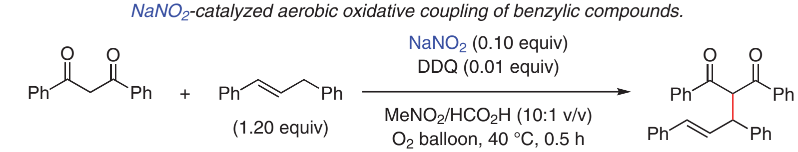


Selected examples

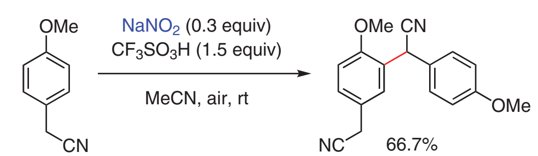


(9d) Wang, *Adv. Synth. Catal.* **2014**, *356*, 977.

$NaNO_2$-catalyzed aerobic oxidative coupling of benzylic compounds.



(9e) Yan, *Tetrahedron Lett.* **2015**, *56*, 1641. 98%



(9f) Wang, *Curr. Org. Synth.* **2018**, *15*, 989. **Further reading:** (9g) Basavaiah, *RSC Adv.* **2014**, *4*, 23966.

Figure 15 $NaNO_2$-catalyzed/mediated C–C bond formation[9a–g]

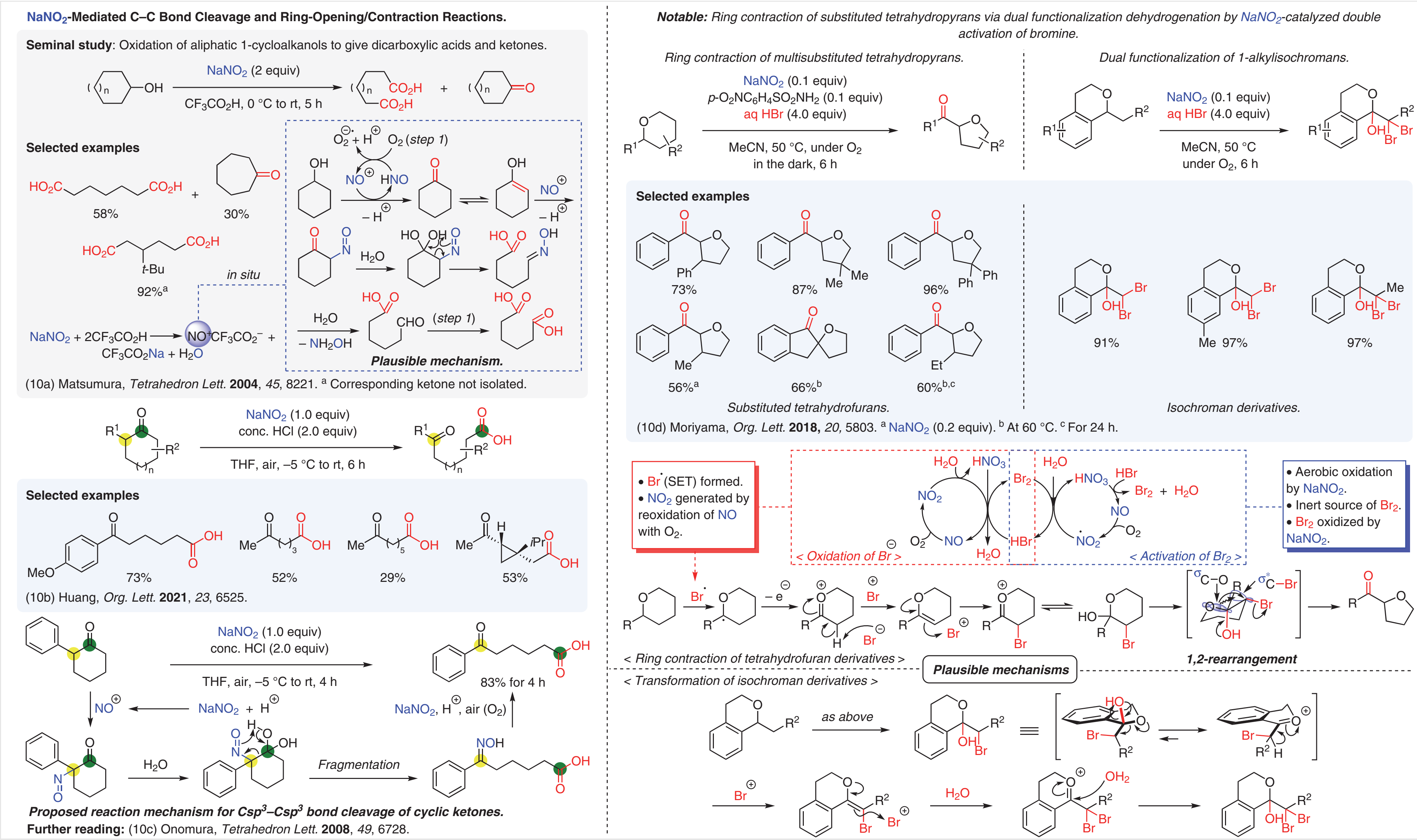
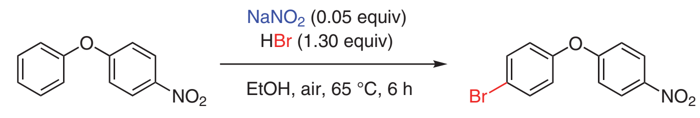


Figure 16 NaNO$_2$-mediated ring-opening/contraction reactions[10a–d]

$NaNO_2$-Catalyzed Aerobic Halogenation of Organic Compounds.

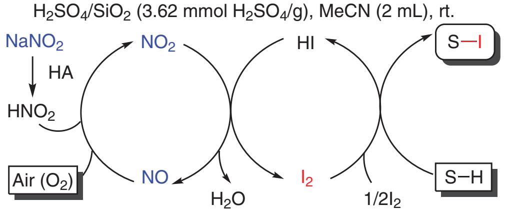


(11a) Zhang, *Adv. Synth. Catal.* **2006**, *348*, 862.

Aerobic oxidative iodination activated by $NaNO_2$.

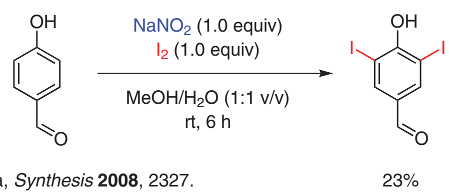
Substrate	Acid (mmol)	Time (h)	Product	Yield (%)
*t*Bu–C6H4–OH	0.25	12	*o*-I	85
C6H5–NHAc	1.0	24	*p*-I	97
*t*Bu–C6H4–Me	1.0	24	*o*-I	95

Reaction conditions: substrate (1 equiv), I_2 (0.5 equiv), $NaNO_2$ (0.03 equiv), 50% H_2SO_4/SiO_2 (3.62 mmol H_2SO_4/g), MeCN (2 mL), rt.

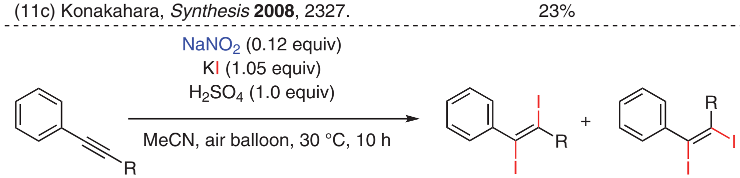


- Effective and selective.
- Saving 100% of iodine atoms.
- H_2SO_4/SiO_2 used for the activation of the catalyst and iodination.

(11b) Iskra, *Tetrahedron Lett.* **2008**, *49*, 893.



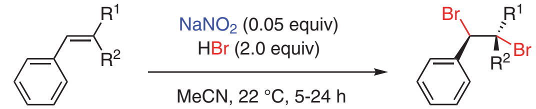
(11c) Konakahara, *Synthesis* **2008**, 2327.



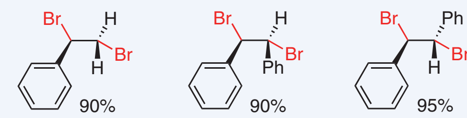
Stereospecific anti-addition forming (E)-1,2-diiodophenylethene.

Selected examples - Yield (%)		
R = H	100	0
R = Me	87	13

(11d) Stavber, *Adv. Synth. Catal.* **2008**, *350*, 2921.

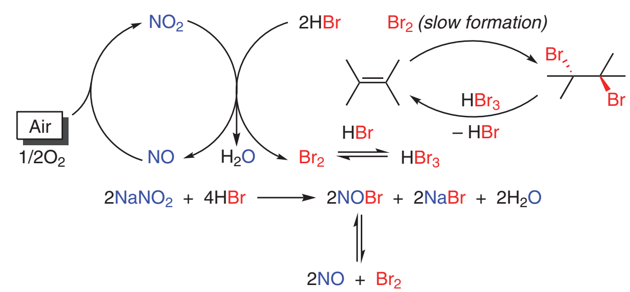


Selected examples



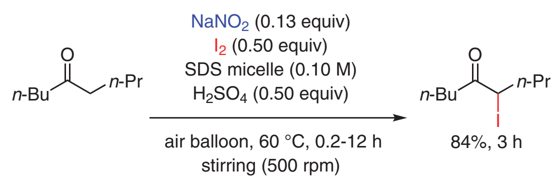
(11e) Iskra, *Green Chem.* **2009**, *11*, 120.

$NaNO_2$-catalyzed aerobic dibromination of alkenes.



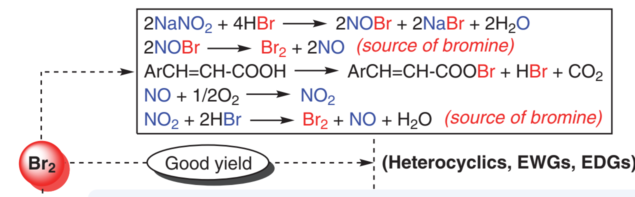
Plausible mechanism for the selective trans-dibromination of alkenes.

Iodination of ketones catalyzed by $NaNO_2$ in a micelle-based aqueous system.

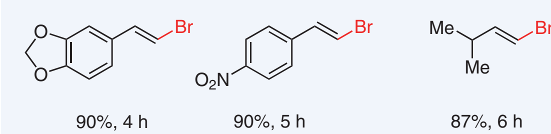


(11f) Stavber, *Green Chem.* **2009**, *11*, 1262.

Bromodecarboxylation of α,β-unsaturated carboxylic acids.

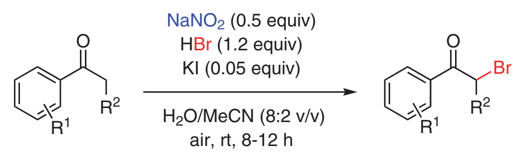


Selected examples

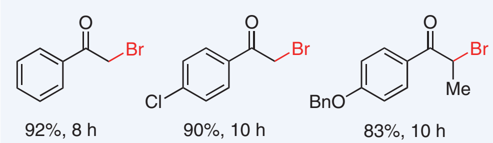


(11g) Telvekar, *Tetrahedron Lett.* **2011**, *52*, 2394.

Catalytic system for α-monobromination of ketones.

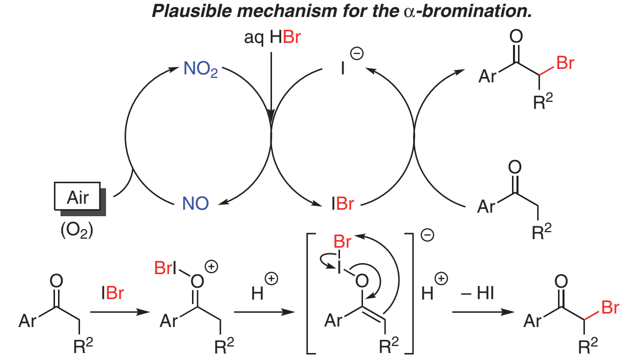


Selected examples



(11h) Akamanchi, *Tetrahedron Lett.* **2016**, *57*, 4918.

Plausible mechanism for the α-bromination.



Further reading: (11i) Zhang, *Synlett* **2011**, 2265. (11j) Lu, *Org. Lett.* **2018**, *20*, 5264.

Figure 17 $NaNO_2$-mediated halogenation reactions[11a–j]

Conflict of Interest

The authors declare no conflict of interest.

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