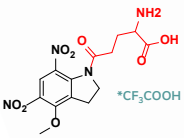
CAGED NEUROTRANSMITTERS

Femtonics Chemistry designs and develops new caged neurotransmitters for frontier neuroscience research. The two main products are a glutamate derivative and a GABA (gamma-amino-butyric acid) derivative. These dinitro-indoline-masked forms of glutamate and GABA release the bioactive forms of the two neurotransmitters more rapidly than other, commercially available versions of these compounds. They were developed to have high-quantum yield, requiring less irradiation for release, so their effective concentrations are lower than that of other caging scaffolds. DNI-Glu and iDMPO-DNI-GABA are compounds developed in-house, only available from Femtonics; in addition, iDMPO-DNI-GABA is the only commercially available caged GABA compound.

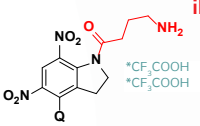


DNI-Glu*TFA

- **Name**: 4-methoxy-5,7-dinitroindolinyl-L-glutamate trifluoroacetate
- **Molecular formula**: $C_{16}H_{17}N_4O_{10}F_3$
- **MW**: 482.32 Da
- **Standard packaging size**: 6 mg
  (custom packaging available 14.5 mg or 20 mg)

DNI-Glu*TFA [1, 2, 3, 4, 5]

- Higher quantum yield (ca. 7 times, than MNI-Glu).
- Lower effective concentration (2-3 times), so less toxicity observed than MNI-Glu.
- Releases Glu more rapidly by the effect of two photon irradiation (720 nm) than MNI-Glu.
- Exists as trifluoroacetic acid salted form, ensuring good solubility, stability and low hygroscopicity of the product.



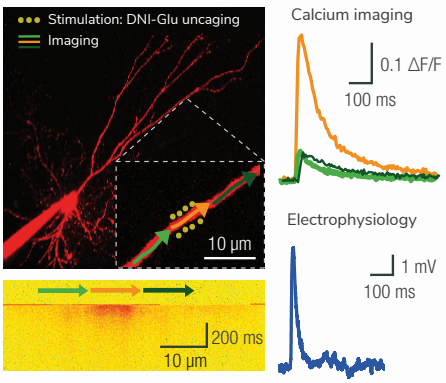
iDMPO-DNI-GABA*TFA

PATENTED

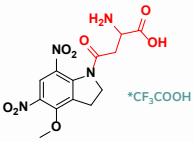
- **Name**: 4-aminoalkyl-5,7-dinitroindolinyl-GABA trifluoroacetate
- **Molecular formula**: $C_{21}H_{27}N_5O_{10}F_6$
- **MW**: 623.50 Da
- **Standard packaging size**: 19 mg
  (custom packaging available 6 mg -20 mg)

iDMPO-DNI-GABA*TFA [6, 7, 8, 9, 10]

- Rapidly and efficiently releases GABA (γ-aminobutyric acid) neurotransmitter, by the effect of one (360 nm) or two photon (720 nm) irradiation.
- GABA is the chief inhibitory neurotransmitter in the mammalian central nervous system. Its principal role is reducing neuronal excitability throughout the nervous system.
- Exists as trifluoroacetic acid salted form, ensuring good solubility, stability and low hygroscopicity of the product.
- Highly resistant to hydrolysis at neutral pH.
- High quantum yield.



DNI-Glu uncaging on a patch-clamped and Alexa-594 filled parvalbumin interneuron: the yellow spots show the locations of stimulation. Imaging was performed along the green, orange and blue lines. The right figures show the Glu-release induced Ca^{2+}-transients along the lines and the excitatory postsynaptic potential.

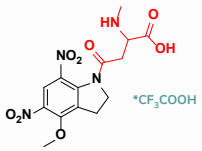


DNI-D-Asp*TFA

- **Name**: 4-methoxy-5,7-dinitroindolinyl-D-aspartate trifluoroacetate
- **Molecular formula**: $C_{15}H_{15}N_4O_{10}F_3$
- **MW**: 468.30 Da
- **Standard packaging size**: 6 mg
  (custom packaging available 14 mg or 20 mg)

DNI-D-Asp*TFA [11]

- Rapidly and efficiently releases D-Asp neurotransmitter, by the effect of one (360 nm) or two photon (720 nm) irradiation.
- Agonist at NMDA receptors and EAAT substrate.
- Exists as trifluoroacetic acid salted form, ensuring good solubility, stability and low hygroscopicity of the product.
- Highly resistant to hydrolysis at neutral pH.
- Higher quantum yield (ca. 7 times, than MNI-D-Asp).
- Releases D-Asp neurotransmitter more rapidly by the effect of two photon irradiation (720 nm) than MNI-D-Asp.

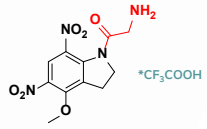


DNI-NMDA*TFA

- **Name**: 4-methoxy-5,7-dinitroindolinyl-N-methyl-D-aspartate trifluoroacetate
- **Molecular formula**: $C_{16}H_{17}N_4O_{10}F_3$
- **MW**: 482.32 Da
- **Standard packaging size**: 6 mg
  (custom packaging available 14 mg or 20 mg)

DNI-NMDA*TFA [12, 13]

- Rapidly and efficiently releases NMDA (N-methyl-D-Asp) neurotransmitter (selective NMDAR agonist), by the effect of one (360 nm) or two photon (720 nm) irradiation.
- Exists as trifluoroacetic acid salted form, ensuring good solubility, stability and low hygroscopicity of the product.
- Highly resistant to hydrolysis at neutral pH.
- Higher quantum yield (ca. 7 times, than MNI-NMDA).
- Releases NMDA neurotransmitter more rapidly by the effect of two photon irradiation (720 nm) than MNI-NMDA.



DNI-Gly*TFA

- **Name**: 2-amino-1-(4-methoxy-5,7-dinitroindolin-1-yl) ethan-1-one trifluoroacetate
- **Molecular formula**: $C_{13}H_{13}N_4O_8F_3$
- **MW**: 410.24 Da
- **Standard packaging size**: 12,5 mg
  (custom packaging available 6 mg -20 mg)

DNI-Gly*TFA [14]

- Rapidly and efficiently releases Gly (Glycine) neurotransmitter, by the effect of one (360 nm) or two photon (720 nm) irradiation.
- Glycine is an inhibitory neurotransmitter on GlyR in the CNS, especially in the spinal cord, brainstem, and retina, via ionotropic receptors, causing an Inhibitory postsynaptic potential (IPSP).
- Exists as trifluoroacetic acid salted form, ensuring good solubility, stability and low hygroscopicity of the product.
- Highly resistant to hydrolysis at neutral pH.
- High quantum yield.

References:

1. Pálfi, D. et al. High efficiency two-photon uncaging coupled by the correction of spontaneous hydrolysis. *Org. Biomol. Chem.* (2018).
2. Marko, A. et al. Electrical behaviour of dendritic spines as revealed by voltage imaging. *Nature Communications* (2015).
3. Wolfgang, G. et al. Local Postsynaptic Voltage-Gated Sodium Channel Activation in Dendritic Spines of Olfactory Bulb Granule Cells. *Neuron* (2015).
4. Tønnesen, J. et al. Spine neck plasticity regulates compartmentalization of synapses. *Nature Neuroscience* (2014).
5. Chiovini, B. et al. Dendritic spikes induce ripples in parvalbumin interneurons during hippocampal sharp waves. *Neuron* (2014).
6. Chiovini, B. et al. Theoretical Design, Synthesis, and In Vitro Neurobiological Applications of a Highly Efficient Two-Photon Caged GABA Validated on an Epileptic Case. *ACS Omega* (2021).
7. Watanabe, M. et al. GABA and GABA receptors in the central nervous system and other organs. *Int. Rev. Cytol.* (2002).
8. Trigo, F. F. et al. Presynaptic miniature GABAergic currents in developing interneurons. *Neuron* (2010).
9. Trigo, F. F. et al. Laser photolysis of DPNI-GABA, a tool for investigating the properties and distribution of GABA receptors and for silencing neurons in situ. *J.Neurosci.Meths.* (2009).
10. Nunez-Parra, A. et al. Disruption of centrifugal inhibition to olfactory bulb granule cells impairs olfactory discrimination. *PLoS One* (2013).
11. Huang, Y. H. et al. Synthesis and characterization of 4-methoxy-7-nitroindolinyl-D-aspartate, a caged compound for selective activation of glutamate transporters and N-MthD.-aspartate receptors in brain tissue. *Biochemistry* (2005) .
12. Palma-Cerda, F. et al. New caged neurotransmitter analogs selective for glutamate receptor sub-types based on methoxynitroindoline and nitrophenyleth-oxycarbonyl caging groups. *Neuropharmacology* (2012).
13. Zhang, R. W. et al. Stereotyped initiation of retinal waves by bipolar cells via presynaptic NMDA autoreceptors. *Nat. Commun.* (2016) .
14. Lynch, J. W. Molecular structure and function of the glycine receptor chloride channel. *Physiological Reviews* (2004).

THINKING AHEAD
FEMTONICS
MICROSCOPY
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