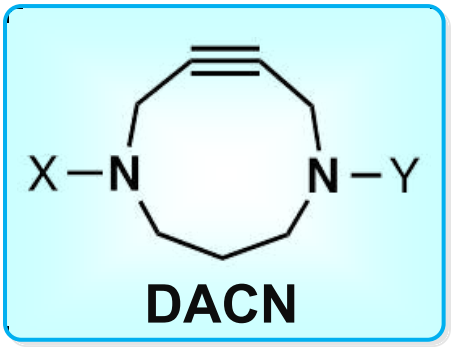
Catalyst Free Click Reagent

Highly Functionalized Alkyne

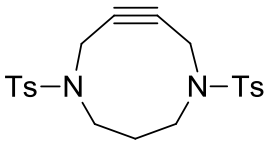
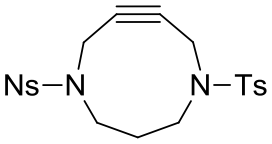
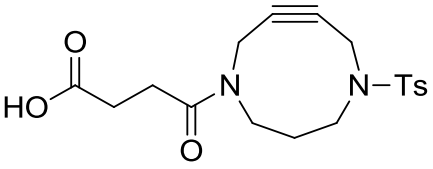
Kanto Reagents

Our company newly launched a highly functionalized alkyne "4,8-diazacyclononyne (**DACN**)" developed by Prof. Katsuhiko Tomooka and Dr. Kazunobu Igawa of Institute for Materials Chemistry and Engineering (IMCE), Kyushu University.[1)] The DACN has high reactivity toward Huisgen reaction with azide along with high bioorthogonality despite its high thermal stability. Furthermore, DACN has high functional diversity with introduction of function units to the endocyclic nitrogen atoms.



- Catalyst Free
- High Click Reactivity
- High Thermal Stability
- High Bioorthogonality
- High Functional Diversity

Product List

Product	Product No.	Package
N,*N*′-bis(*p*-toluenesulfonyl)-4,8-diazacyclononyne *N*Ts, *N*Ts-DACN CAS ：1797508-57-6 FW ：432.56 	05628-68	100 mg
	05628-65	25 mg
N-*o*-nitrobenzenesulfonyl-*N*′-*p*-toluenesulfonyl-4,8-diazacyclononyne *N*Ns, *N*Ts-DACN CAS ：1797508-58-7 FW ：463.53 	28197-68	100 mg
	28197-65	25 mg
N-succinoyl-*N*′-*p*-toluenesulfonyl-4,8-diazacyclononyne *N*Su, *N*Ts-DACN CAS ：— FW ：378.44 	37104-68	100 mg
	37104-65	25 mg

※Ts = *p*-toluenesulfonyl、Ns = *o*-nitrobenzenesulfonyl、Su = succinoyl

Advantages of DACN

1. High Click Reactivity

DACN has higher click reactivity toward azides than that of cyclooctyne derivative (OCT).[2)]

2. High Thermal Stability

Reported strained cyclic alkynes (e.g. DIFO[3)], DIBAC[4)]) occasionally show thermal decomposition in experimental operations and during storage.[5)] In sharp contrast, DACN is thermally stable compared with reported bent cycloalkynes. For example, no significant decomposition and/or oligomerization were observed by heating in 80 °C toluene for 2 weeks, at least.

Our company supplies DACN as crystaline form.

3. High Bioorthogonality

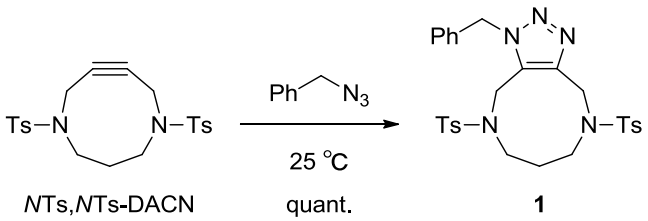
Side reactions with bio-thiols become problem in biological applications of strained cyclic alkynes.[6)] In sharp contrast, DACN shows high reaction specificity toward Huisgen reaction. No addition product was obtained in the presence of *p*-toluenethiol at room temperature, although reaction with equimolar amount of benzyl azide provides click reaction product quantitatively.

4. High Functional Diversity

A variety of functional units such as biological ligand, fluorescent tag, biotin tag, PEG chain, etc. can be introduced to endocyclic nitrogen and/or a terminal of succinic acid moiety of DACNs.

Reaction Example

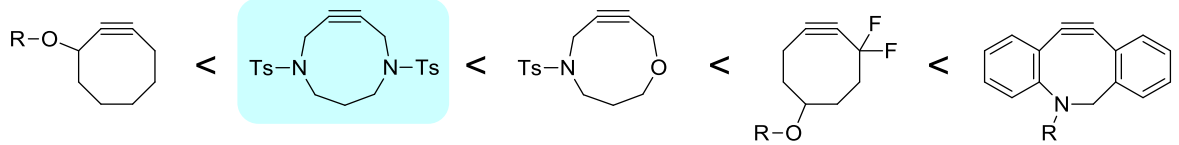
*N*Ts, *N*Ts-DACN reacts with equimolar amount of benzylazide at room temperature to afford Huisgen reaction product **1** in quantitatively.



*N*Ts,*N*Ts-DACN quant. **1**

※Reaction rate of *N*Ts, *N*Ts-DACN is ca. 2.3 times faster than that of cyclooctyne (OCT).

Order of reactivity for Huisgen reaction with benzyl azide.



OCT (2.4×10^{-3}) [2)] | *N*Ts,*N*Ts-DACN (5.5×10^{-3}) [1)] | *N*Ts-AOCN (1.9×10^{-2}) [1)] | DIFO (7.6×10^{-2}) [3)] | DIBAC (3.1×10^{-1}) [4)]

*The figures in parentheses are reaction rate constants in $M^{-1}s^{-1}$.

References

1) R. Ni, N. Mitsuda, T, Kashiwagi, K. Igawa, K. Tomooka, *Angew. Chem. Int. Ed.* **2015**, *54*, 1190.
2) N. J. Agard, J. A. Prescher, C. R. Bertozzi, *J. Am. Chem. Soc.* **2004**, *126*, 15046.
3) J. A. Codelli, J. M. Baskin, N. J. Agard, C. R. Bertozzi, *J. Am. Chem. Soc.* **2008**, *130*, 11486.
4) M. F. Debets, S. S. van Berkel, S. Schoffelen, F. P. J. T. Rutjes, J. C. M. van Hest, F. L. van Delft, *Chem. Commun.* **2010**, *46*, 97.
5) H. Stöckmann, A. A. Neves, S. Stairs, H. Ireland-Zecchini, K. M. Brindle, F. J. Leeper, *Chem. Sci.* **2011**, *2*, 932.
6) R. van Geel, G. J. M. Pruijn, F. L. van Delft, W. C. Boelens, *Bioconjugate Chem.* **2012**, *23*, 392.

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