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Two Distinct Gold-Catalyzed Oxidative Annulations of 1,5-Allenynes with Nitrones to Yield 1-Naphthol Derivatives Bearing 2,3- versus 3,4-Fused Nitroxy Rings

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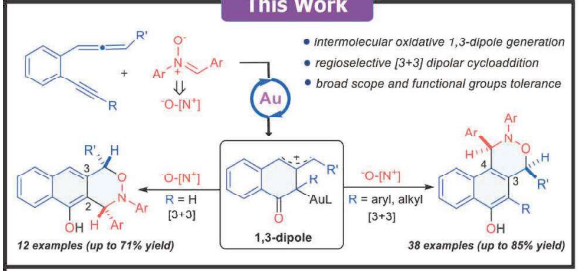
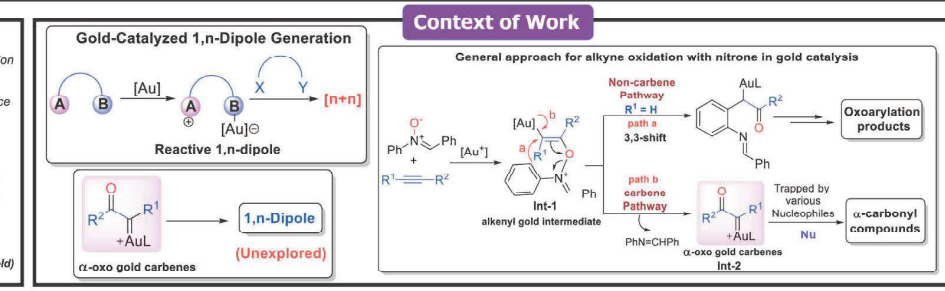
This Work

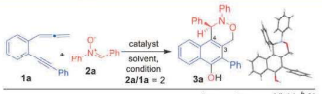


- *intermolecular oxidative 1,3-dipole generation*
- *regioselective [3+3] dipolar cycloaddition*
- *broad scope and functional groups tolerance*

Context of Work



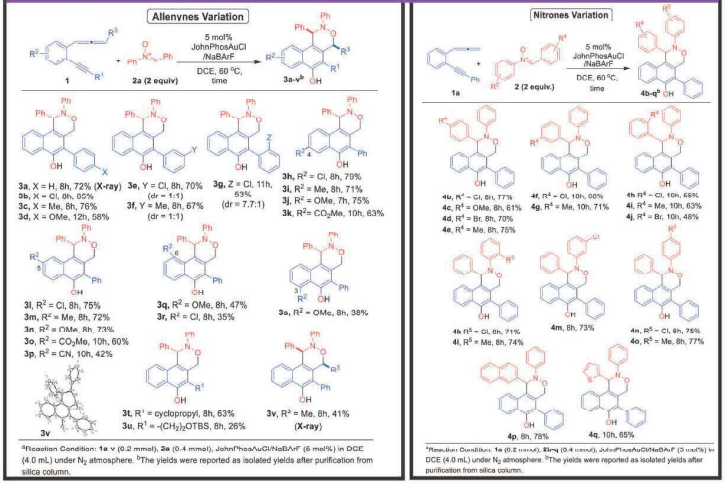
Optimization Table



Entries	catalyst (n mol%)	solvent	time (h)	temp (°C)	Yields[b] % 3a
1	$PPh_3AuCl/AgNTf_2$ (10)	DCE	18	60	27
2	$(PhO)_3PAuCl/AgNTf_2$ (10)	DCE	18	60	19
3[c]	IPrAuCl/$AgNTf_2$ (10)	DCE	18	60	16
4[d]	LAuCl/$AgNTf_2$ (10)	DCE	12	60	68
5	tBuXPhos/$AgNTf_2$ (10)	DCE	18	60	33
6	LAuCl/$AgSbF_6$ (10)	DCE	12	60	60
7	LAuCl/AgOTf (10)	DCE	12	60	45
8	LAuCl/ NaBArF (10)	DCE	08	60	74
9	LAuCl/ NaBArF (5)	DCE	08	60	72
10	LAuCl/ NaBArF (5)	DCM	18	50	50
11	LAuCl/ NaBArF (5)	Toluene	10	60	26
12	LAuCl/ NaBArF (5)	ACN	18	60	09
13[e]	LAuCl/ NaBArF (5)	DCE	48	rt	31
14[f]	LAuCl/ NaBArF (5)	DCE	20	40	42
15	$[LAu(CH_3CN)]SbF_6$ (5)	DCE	18	60	58
16	NaBArF (10)	DCE	24	60	0

[a]Reaction condition **1a** = 0.2 mmol, **2a** = 0.4 mmol, gold catalyst in solvent (4.0 mL) under N_2 atmosphere. [b] Product yields are obtained after purification from a silica column. [c]IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene. [d]L = JohnPhos. [e]50 % conversion of **1a**. [f]70 % conversion of **1a**.

Scope of Internal Alkyne Tethered 1,5-Allenynes and Nitrones



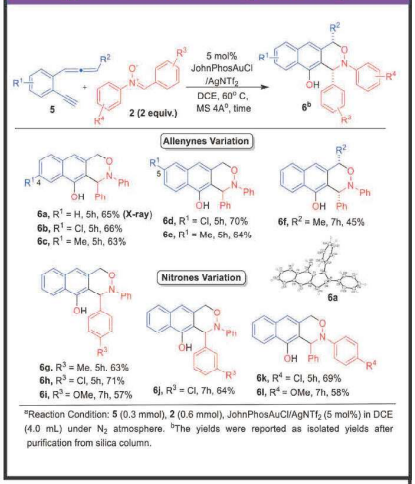
3a, X = H, 8h, 72% (**X-ray**)
3b, X = Cl, 8h, 65%
3c, X = Me, 8h, 76%
3d, X = OMe, 12h, 58%
3e, Y = Cl, 8h, 70% (dr = 1:1)
3f, Y = Me, 8h, 67% (dr = 1:1)
3g, Z = Cl, 11h, 53% (dr = 7.7:1)
3h, R^2 = Cl, 8h, 79%
3i, R^2 = Me, 8h, 71%
3j, R^2 = OMe, 7h, 75%
3k, R^2= CO_2Me, 10h, 63%
3l, R^2 = Cl, 8h, 75%
3m, R^2 = Me, 8h, 72%
3n, R^2 = OMe, 8h, 73%
3o, R^2 = CO_2Me, 10h, 60%
3p, R^2 = CN, 10h, 42%
3q, R^2 = OMe, 8h, 47%
3r, R^2 = Cl, 8h, 35%
3s, R^2 = OMe, 8h, 38%
3t, R^1 = cyclopropyl, 8h, 63%
3u, R^1 = $-(CH_2)_2OTBS$, 8h, 26%
3v, R^3 = Me, 8h, 41% (**X-ray**)

[a]Reaction Condition: **1a-v** (0.2 mmol), **2a** (0.4 mmol), JohnPhosAuCl/NaBArF (5 mol%) in DCE (4.0 mL) under N_2 atmosphere. [b]The yields were reported as isolated yields after purification from silica column.

4b, R^4 = Cl, 8h, 77%
4c, R^4 = OMe, 8h, 61%
4d, R^4 = Br, 8h, 70%
4e, R^4 = Me, 8h, 75%
4f, R^4 = Cl, 10h, 60%
4g, R^4 = Me, 10h, 71%
4h R^4 = Cl, 10h, 66%
4i, R^4 = Me, 10h, 63%
4j, R^4 = Br, 10h, 48%
4k R^5 = Cl, 8h, 71%
4l, R^5 = Me, 8h, 74%
4m, 8h, 73%
4n, R^5 = Cl, 8h, 76%
4o, R^5 = Me, 8h, 77%
4p, 8h, 78%
4q, 10h, 65%

[a]Reaction Condition: **1a** (0.2 mmol), **2b-q** (0.4 mmol), JohnPhosAuCl/NaBArF (5 mol%) in DCE (4.0 mL) under N_2 atmosphere. [b]The yields were reported as isolated yields after purification from silica column.

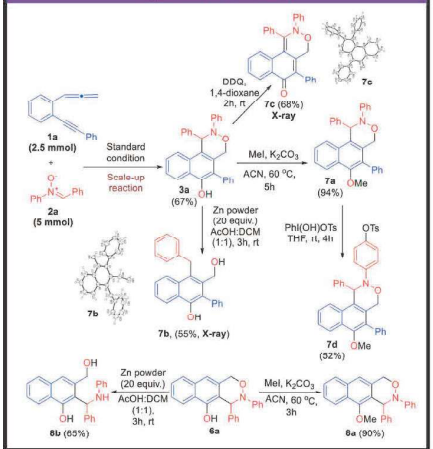
Scope of Terminal Alkyne Allenynes



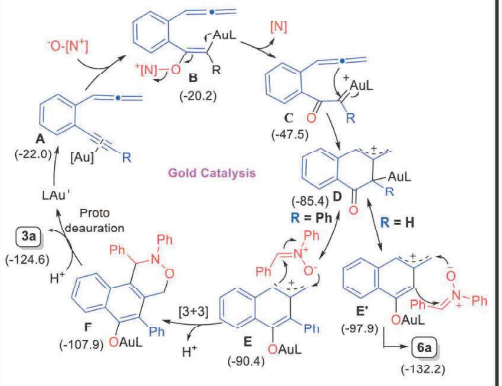
6a, R^1 = H, 5h, 65% (**X-ray**)
6b, R^1 = Cl, 5h, 66%
6c, R^1 = Me, 5h, 63%
6d, R^1 = Cl, 5h, 70%
6e, R^1 = Me, 5h, 64%
6f, R^2 = Me, 7h, 45%
6g, R^3 = Me, 5h, 63%
6h, R^3 = Cl, 5h, 71%
6i, R^3 = OMe, 7h, 57%
6j, R^3 = Cl, 7h, 64%
6k, R^4 = Cl, 5h, 69%
6l, R^4 = OMe, 7h, 58%

[a]Reaction Condition: **5** (0.3 mmol), **2** (0.6 mmol), JohnPhosAuCl/$AgNTf_2$ (5 mol%) in DCE (4.0 mL) under N_2 atmosphere. [b]The yields were reported as isolated yields after purification from silica column.

Synthetic Utility

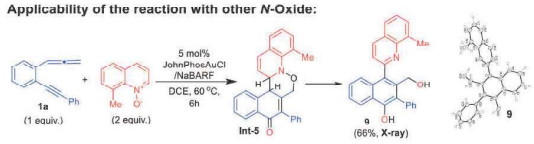


Plausible Reaction Mechanism

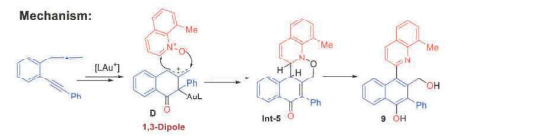


Applicability of this Reaction Protocol

Applicability of the reaction with other *N*-Oxide:



Mechanism:



Summary

- Intermolecular Oxidative 1,3-dipole generation via α-oxo gold carbene
- Regioselective [3+3] cycloaddition for internal and terminal allenynes
- Broad substrate scope of 1,5-allenynes and various N-oxides (50 examples)
- Mild reaction conditions and easy scale-up

References

(1) **Barik, D.**; Maitra, C; Hsieh, C.-T.; Cheng, M. -J; Liu, R.-S. *ACS Catal.* **2024**, *14*, 1525–1531.

(2) Ye, L.-W.; Zhu, X.-Q.; Sahani, R. L.; Xu, Y.; Qian, P.-C.; Liu, R.-S. *Chem. Rev.* **2021**, *121*, 9039– 9112.

Acknowledgments

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