Catalytic Coupling of Arene C-H Bonds and Alkynes for the Synthesis of Coumarins: the Substrate Scope and Application to the Development of Neuroimaging Agents

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Supporting Information

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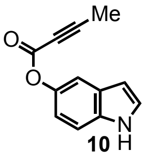
Acid Screen Results: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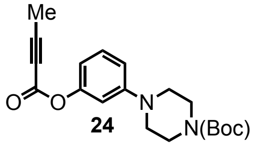
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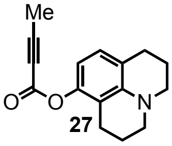
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entry	substrate	acid	temp.	observations
1	**10**	HCl	rt	no reaction, starting material re-isolated
2	**10**	HCl	80 °C	decomposition
3	**10**	$HSbF_6$	rt	decomposition
4	**10**	$HSbF_6$	80 °C	decomposition
5	**10**	TfOH	rt	complex mixture by ^1H NMR; no product detected
6	**10**	TfOH	80 °C	decomposition
7	**24**	HCl	rt	no reaction, starting material re-isolated
8	**24**	HCl	80 °C	no reaction, starting material re-isolated
9	**24**	$HSbF_6$	rt	no reaction, starting material re-isolated
10	**24**	$HSbF_6$	80 °C	complex mixture by ^1H NMR; no product detected
11	**24**	TfOH	rt	no reaction, starting material re-isolated
12	**24**	TfOH	80 °C	partial alkyne hydration & starting material by ^1H NMR
13	**27**	HCl	rt	complex mixture by ^1H NMR; no product detected
14	**27**	HCl	80 °C	decomposition
15	**27**	$HSbF_6$	rt	no reaction, starting material re-isolated
16	**27**	$HSbF_6$	80 °C	partial alkyne hydration & starting material by ^1H NMR
17	**27**	TfOH	rt	no reaction, starting material re-isolated
18	**27**	TfOH	80 °C	partial alkyne hydration & starting material by ^1H NMR

To determine the potential role of trace protic acids as the true hydroarylation catalysts we undertook a screen of the corresponding acids, namely HCl in place of both $PtCl_4$ and $Au(PPh_3)Cl$, and $HSbF_6$ in place of $AgSbF_6$. During our investigations of potential hydroarylation catalysts we also examined $Au(PPh_3)Cl/AgOTf$, which we found to be effective, but delivered lower yields than the optimized $Au(PPh_3)Cl/AgSbF_6$ catalyst (76% versus 93% for lead substrate **8**). However, this result prompted us to also investigate triflic acid, as a potential hidden acid catalyst. The *in situ* formation of triflic acid from intended metal triflate catalysts has previously been demonstrated in the literature.[1]

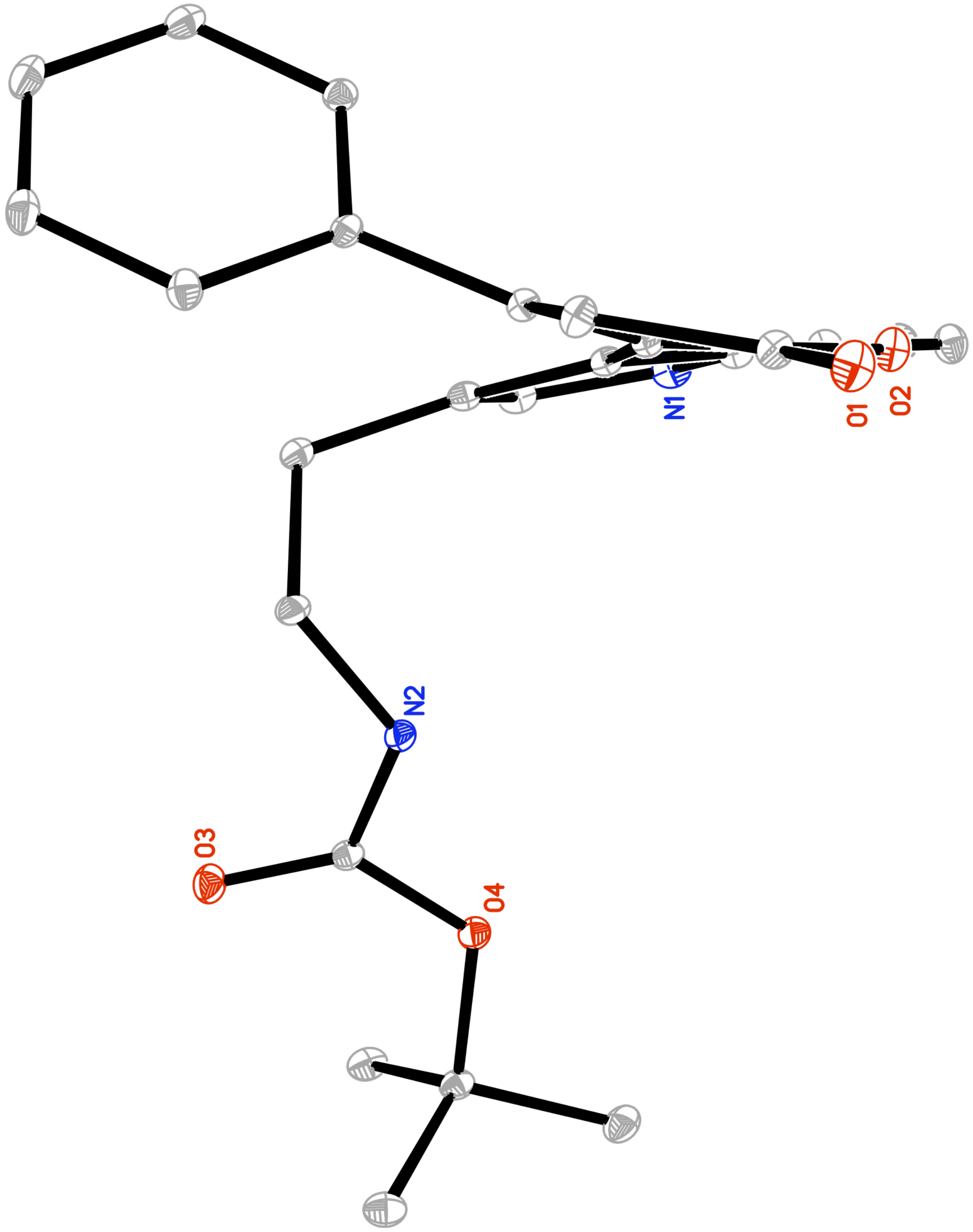
The substrates were weighed into glass vials and dissolved in a 1:1 solution of 1,2-dichloroethane:1,4-dioxane, 0.05 M to mimic the normal reaction concentration. Stir bars were added, followed by 0.5 mol % of the appropriate acid via microsyringe (the sources of the acids were: $HSbF_6$ 65% aqueous solution from Alfa Aesar; HCl 4 M in 1,4-dioxane from Aldich; neat triflic acid from Aldrich). The introduction of water in the case of the $HSbF_6$ reactions is of minimal consequence since, a) wet solvent is used for the reaction and b) the reaction has been shown to proceed, when catalyzed by $PtCl_4$, in the presence of 5% water in the solvent.

The reactions were setup in duplicate and stirred at both room temperature and 80 °C for 4 hours, after which they were analyzed by TLC and ^{1}H-NMR. The general conclusion, which can be garnered from the data below, is that trace acids, if indeed present, are not capable of promoting the hydroarylation reaction under the standard reaction conditions (i.e. standard solvent, concentration, temperature and reaction time).

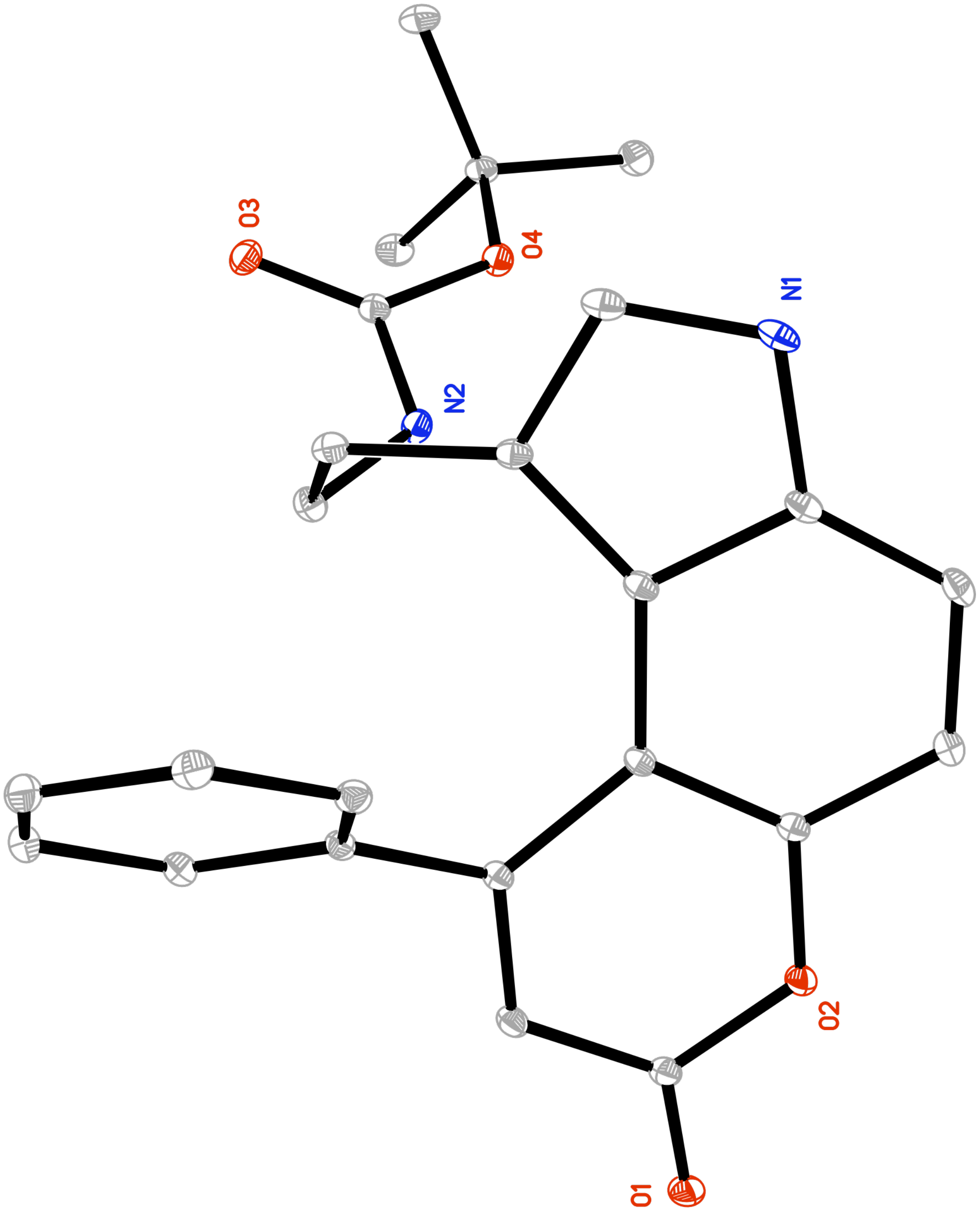
1. Dang, T. T.; Boeck, F.; Hintermann, L. *J. Org. Chem.* **2011**, *76*, 9353-9361.

X-ray data for Compound 14:

Compound	**14**
Empirical formula	$C_{24}H_{24}N_2O_4$
Formula weight	404.17 g/mol
Temperature	125(2) K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P1
Unit cell dimensions	*a* = 9.4174(4) Å alpha = 107.8320(10)°
	b = 10.2417(2) Å beta = 90.81°
	c = 13.5578(4) Å gamma = 93.4290(10)°
Volume, Z	1241.88(8) Å^3, 2
Density (calculated)	1.290 Mg/m^3
Absorption coefficient	0.086 mm^{-1}
F (000)	512
Crystal size	0.20 x 0.10 x 0.10 mm
Θ range for data collection	1.58 to 32.69°
Limiting indicies	$-14 \leq h \leq 14$, $-14 \leq k \leq 15$, $-20 \leq l \leq 20$
Reflections collected	21718
Independent reflections	8503 ($R_{int} = 0.0262$)
Completeness to $\Theta = 32.69°$	93.0%
Absorption correction	EMPIRICAL
Max. and min. transmission	0.9915 and 0.9830
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	8053 / 0 / 325
Goodness-of-fit on F^2	1.031
Final R indices [$I>2\sigma(I)$]	R1 = 0.0476, wR2 = 0.1220
R indicies (all data)	R1 = 0.0673, wR2 = 0.1341
Largest diff. peak and hole	0.460 and -0.374 eÅ^{-3}



ORTEP of compound 14



ORTEP of compound 14