Electronic Supplementary Material (ESI) for RSC Advances.

Continuous-Flow Synthesis of 3,5-Disubstituted Pyrazoles *via* Sequential Alkyne Homocoupling and Cope-Type Hydroamination

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Supporting Information

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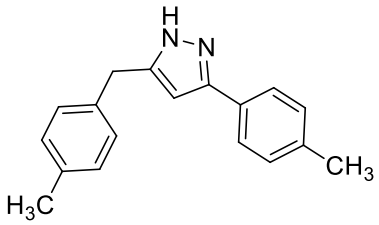
1. Additional tables

Table S1. Solubility test of the copper sources.[a]

Entry	Catalyst	Solvent	Test No. 1.[b]	Test No 2.[c]
1	CuOAc	DMSO	did not dissolve	-
2	CuOAc	EtOH	did not dissolve	-
3	$Cu(OAc)_2$	DMSO	did not dissolve	-
4	$Cu(OAc)_2$	EtOH	did not dissolve	-
5	$CuBr(PPh_3)_3$	DMSO	did not dissolve	-
6	$CuBr(PPh_3)_3$	EtOH	did not dissolve	-
7	$Cu(NCCH_3)_4\ CF_3SO_3$	DMSO	dissolved	failed
8	$Cu(NCCH_3)_4\ CF_3SO_3$	EtOH	dissolved	failed
9	$Cu(MeCN)_4BF_4$	DMSO	dissolved	failed
10	$Cu(MeCN)_4BF_4$	EtOH	did not dissolve	-
11	$[Cu(phen)(PPh_3)_2]NO_3$	DMSO	dissolved	succeeded
12	$[Cu(phen)(PPh_3)_2]NO_3$	EtOH	dissolved	succeeded
13	$CuBr_2$	DMSO	dissolved	succeeded
14	$CuBr_2$	EtOH	did not dissolve	-

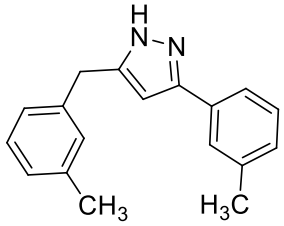
[a] Conditions: 0.045 mmol catalyst in 10 mL solvent, 3 equiv. hydrazine.
[b] Solubility probe of the catalyst, addition of hydrazine monohydrate in case of dissolution.
[c] Subsequent addition of 4-ethynyltoluene in case of successful Test No. 1.

2. Analytical data



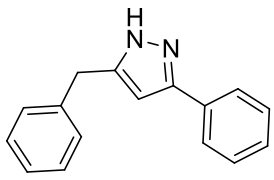
5-(4-Methylbenzyl)-3-(*p*-tolyl)-1*H*-pyrazole:

White solid, mp 92−95 °C. ^{1}H NMR (400.1 MHz, CDCl3): δ = 7.57-7.55 (d, *J* = 8 Hz, 2H), 7.19-7.12 (m, 6H), 6.31 (s, 1H), 3.99 (s, 2H), 2.36 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 136.2, 135.4, 129.4, 129.3, 128.7, 125.4, 32.8, 21.3, 21.1 NMR data is in agreement with the literature reference.[S1]



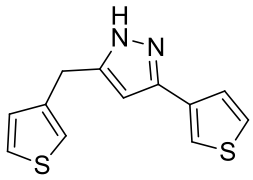
5-(3-Methylbenzyl)-3-(*m*-tolyl)-1*H*-pyrazole:

Colorless oil. ^{1}H NMR (400.1 MHz, CDCl3): δ = 7.50 (s, 1H), 7.48-7.46 (d, *J* = 8 Hz, 1H), 7.29-7.27 (m, 1H), 7.23-7.20 (m, 1H), 7.13-7.11 (d, *J* = 8 Hz, 1H), 7.13-7.06 (m, 4H), 6.36 (s, 1H), 2.37 (s, 1H), 2.33 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 138.3, 129.5, 128.8, 128.6, 127.4, 126.2, 125.8, 122.6, 33.1, 21.5.,21.4. NMR data is in agreement with the literature reference.[S1]



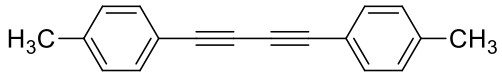
5-Benzyl-3-phenyl-1*H*-pyrazole:

White solid, mp 90−93 °C.^{1}H NMR (400.1 MHz, CDCl3): δ = 7.68-7.66 (d, *J* = 7.3 Hz, 2H), 7.40-7.27 (m, 8H), 6.36 (s, 1H), 4.04 (s, 2H). 264.02. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.1, 132.1, 128.6, 128.5, 128.4, 126.3, 125.4, 101.5, 33.1. NMR data is in agreement with the literature reference.[S1]



3-(Thiophen-3-yl)-5-(thiophen-3-ylmethyl)-1*H*-pyrazole:

White solid, mp 99−102 °C. ^{1}H NMR (400.1 MHz, CDCl3): δ = 7.53 (s, 1H), 7.40-7.39 (m, 1H), 7.34-7.32 (m, 1H), 7.28-7.26 (m, 1H), 7.04 (s, 1H), 6.99-6.98 (m, 1H), 6.26 (s, 1H), 4.03 (s, 2H). 247.81. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 133.4, 128.3, 126.1, 125.9, 121.6, 120.6, 27.9. NMR data is in agreement with the literature reference.[S1]

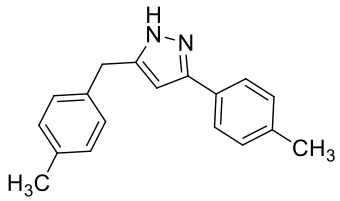


1,4-Di-*p*-tolylbuta-1,3-diyne:

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.41-7.40 (d, *J* = 7.9 Hz, 4H), 7.15-7.13 (d, *J* = 7.9 Hz, 4H), 2.36 (s, 6H). NMR data is in agreement with the literature reference.[S2]

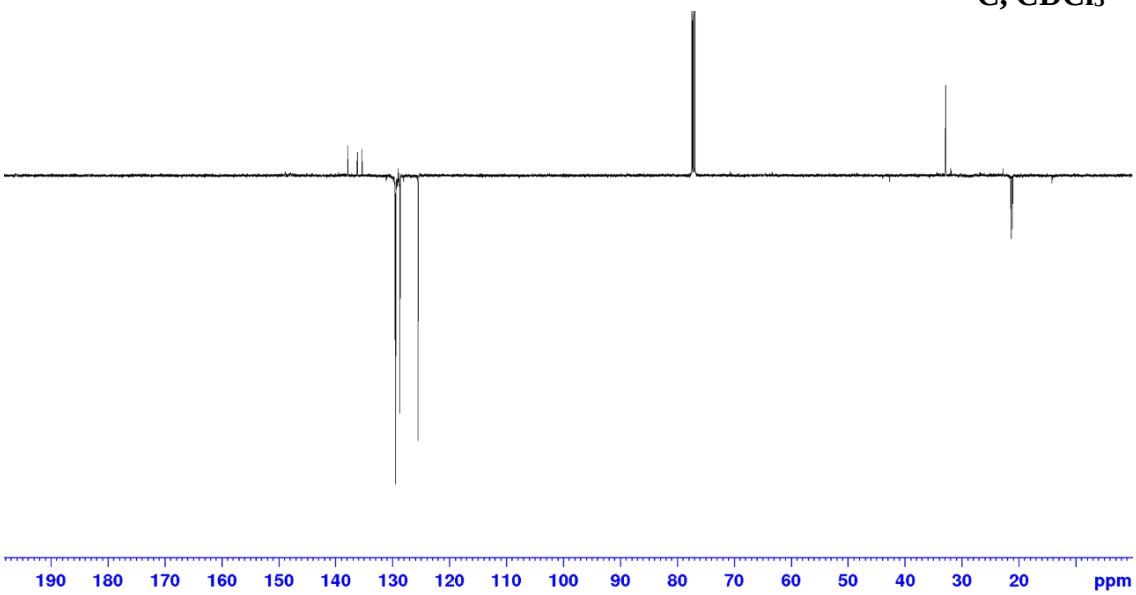
3. Collection of NMR spectra

5-(4-Methylbenzyl)-3-(*p*-tolyl)-1*H*-pyrazole:

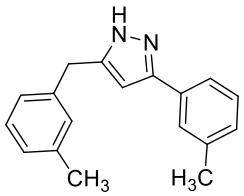


^{1}H, CDCl$_3$

^{13}C, CDCl$_3$

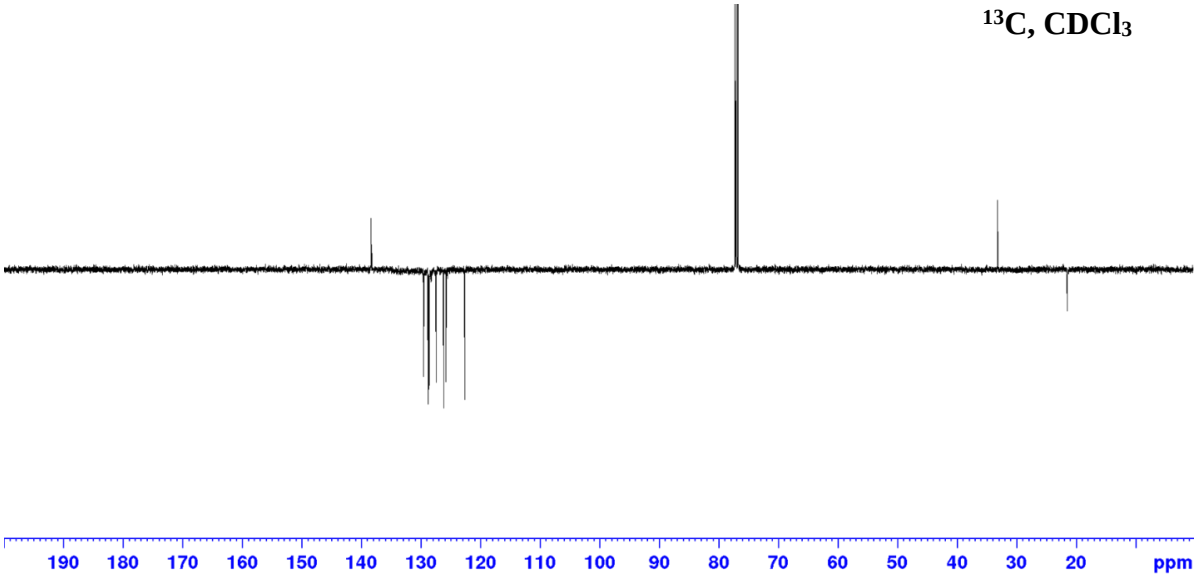


5-(3-Methylbenzyl)-3-(*m*-tolyl)-1*H*-pyrazole:

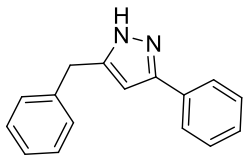


^{1}H, $CDCl_3$

^{13}C, $CDCl_3$

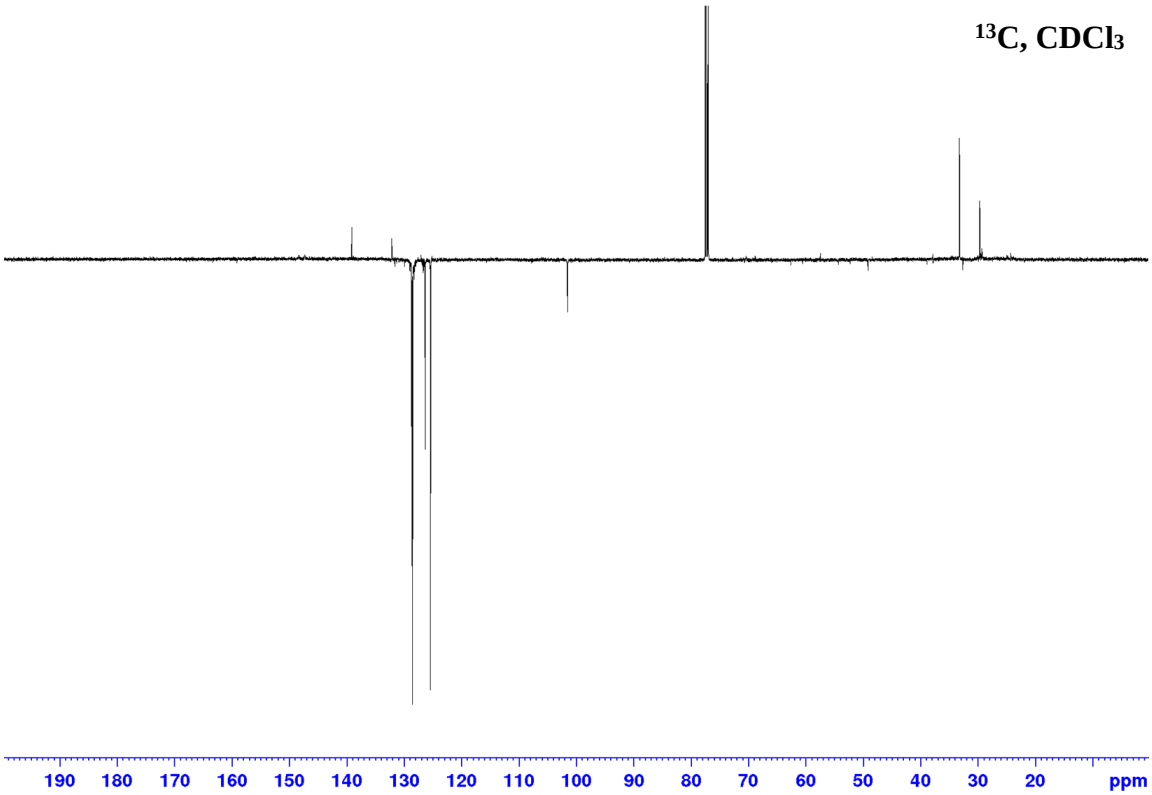


5-Benzyl-3-phenyl-1*H*-pyrazole:



^{1}H, CDCl$_3$

^{13}C, CDCl$_3$



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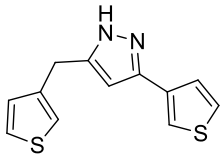
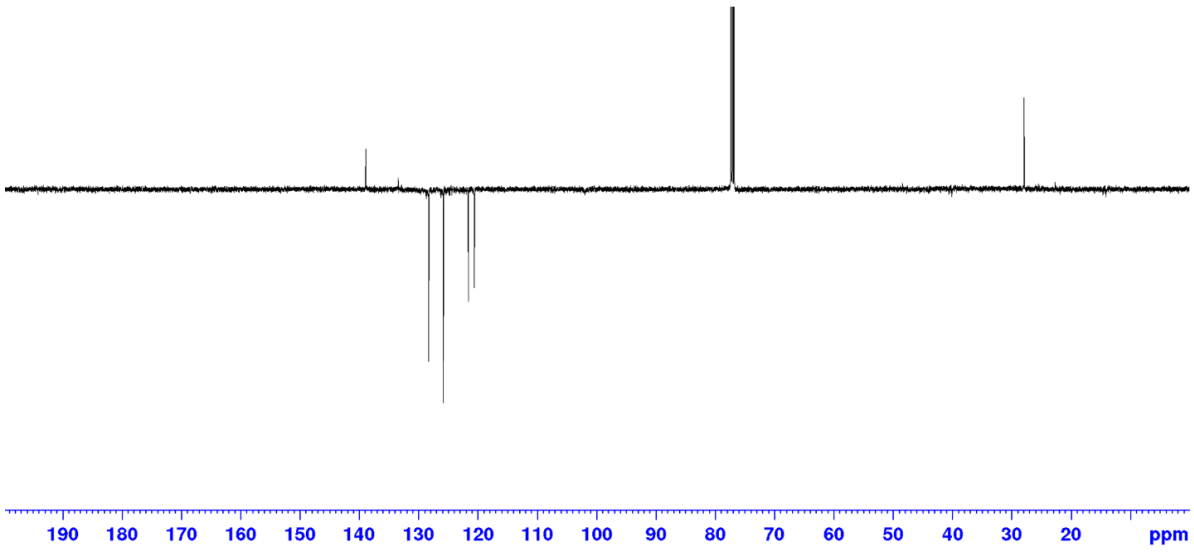
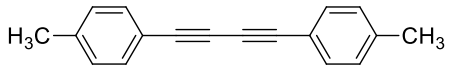


^{1}H, CDCl$_3$

^{13}C, CDCl$_3$



1,4-Di-*p*-tolylbuta-1,3-diyne:



^{1}H, CDCl$_3$

4. References

[S1] L. Wang, X. Yu, X. Feng, M. Bao, *J. Org. Chem.*, **2013**, *78*, 1693-1698.

[S2] A. Kusuda, X.-H. Xu, X. Wang, E. Tokunaga, N. Shibata, *Green Chem.*, **2011**, *13*, 843-846.