

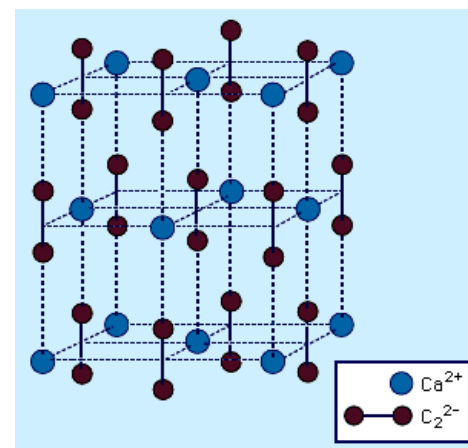
Calcium carbide

A long hidden reactant

Abolfazl Hosseini

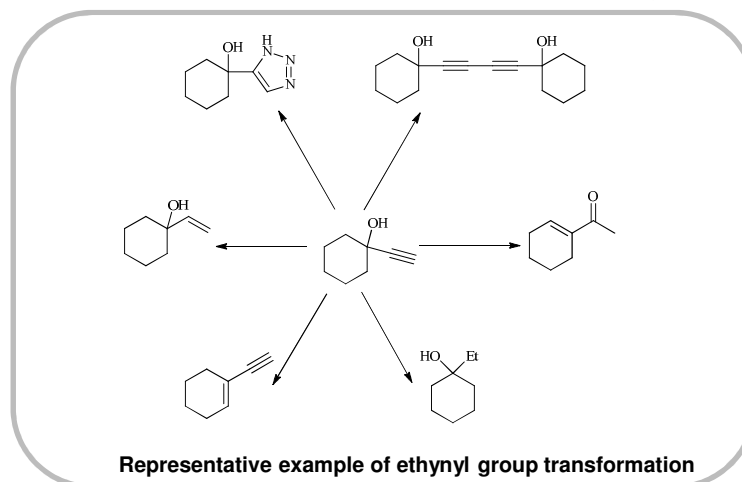
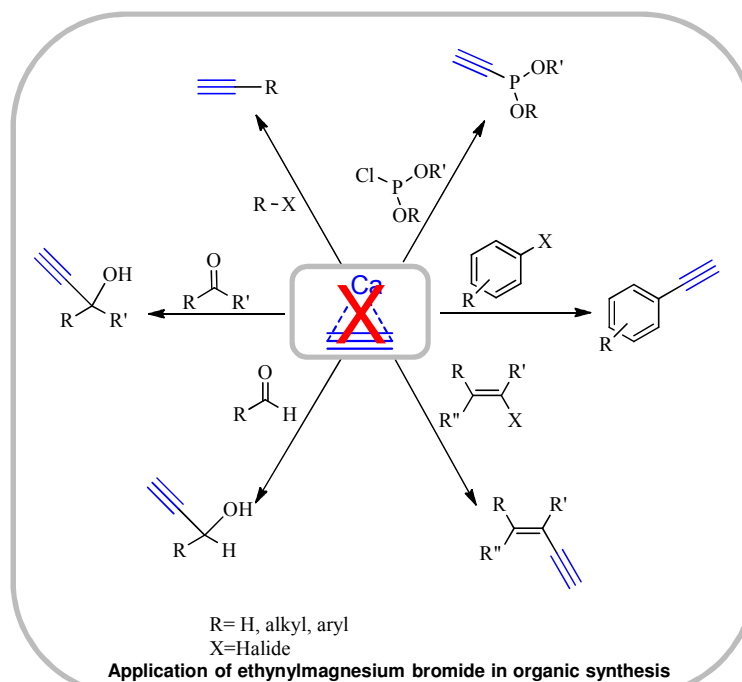
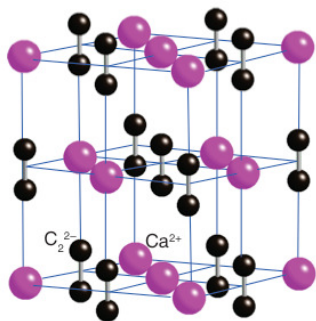
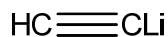
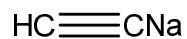
24.1.2014

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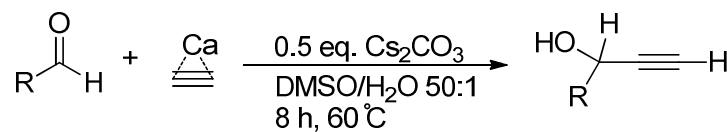
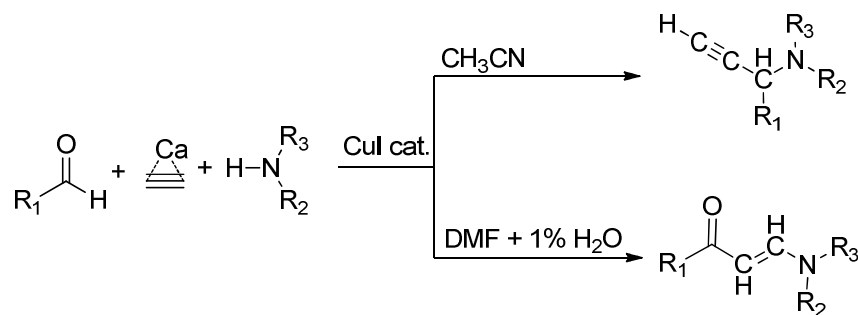
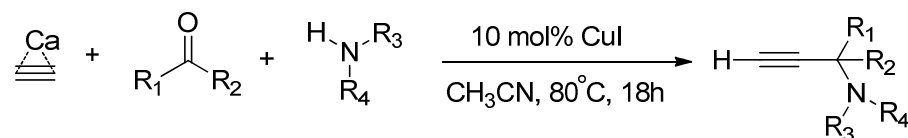
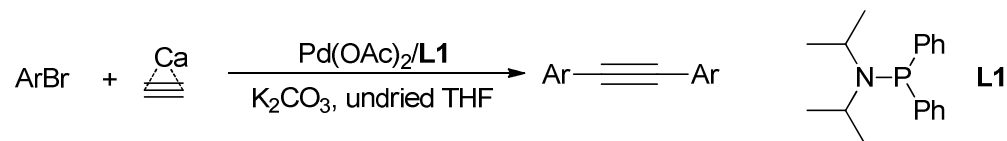


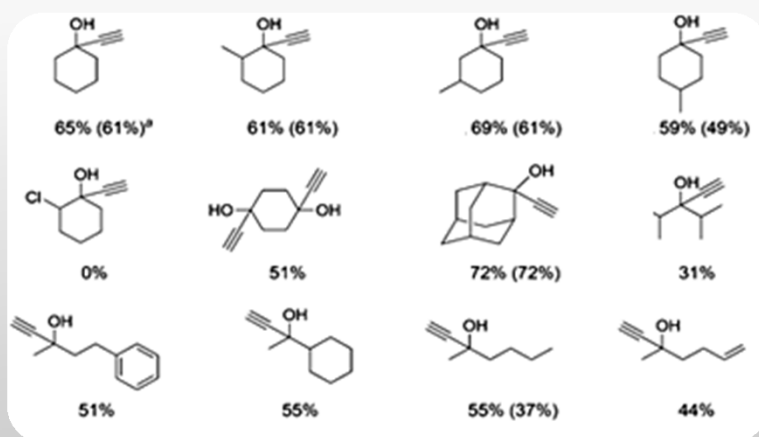
Terminal alkynes

Acetylide reagents

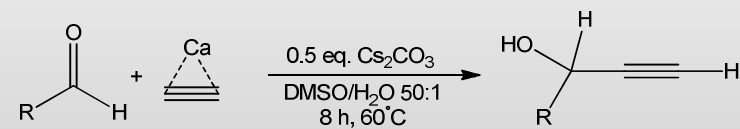


The use of calcium carbide in organic synthesis



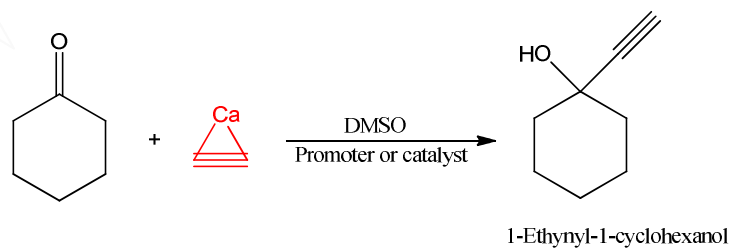


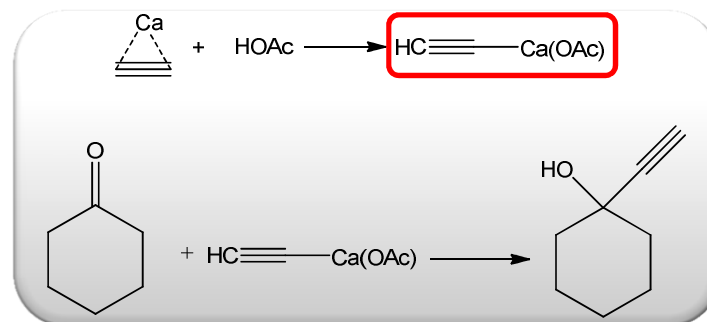
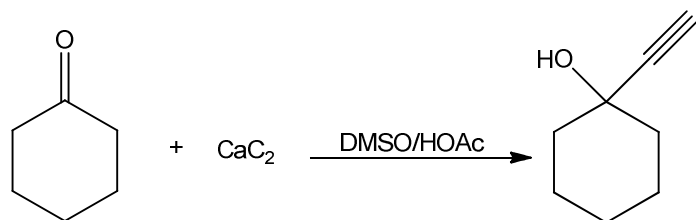
^a NMR yield. Isolated yield is in parentheses.



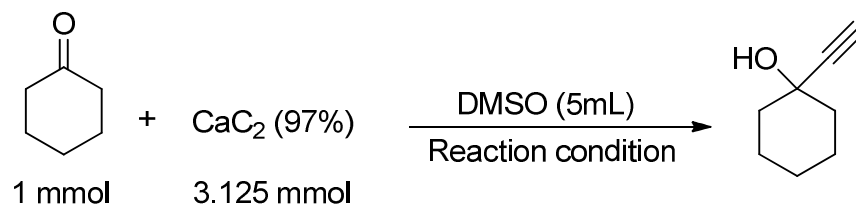
Sum, Y. N.; Yu, D.; Zhang, Y. *Green Chem.* **2013**, *15*, 2718.

Model reaction





Reaction scheme showing cyclohexanone reacting with CaC_2 (97%) in DMSO (5mL) under reaction conditions to form 1-ethynylcyclohexanol.				
	1 mmol	3.125 mmol		
Entry	Additive (mol%)	Temp. ($^{\circ}\text{C}$)	Time (h)	GC Conv. (%)
1	Acetic acid (100)	60	72	46
2	Acetic acid (300)	60	60	45
3	2-ethylhexanoic acid (100)	60	26	0
4	L-Proline (100)	60	26	0



Entry	Additive (mol%)	Water (μL)	Temp. ($^{\circ}\text{C}$)	Time (h)	GC Conv. (%)
1	CS_2CO_3 (50)*	60	60	1.5	93
2	CS_2CO_3 (50)*	60	R.T.	3	26
3	TBAF (70)	-	R.T.	3	99
4	TBAF (20)	-	R.T.	8	71
5	TBAF (20)	40	R.T.	1	99
6	TBAF (5)	40	R.T.	2	95
7	TBAF (1)	40	R.T.	4	0
8	-	60	R.T.	22	0
9	-	60	60	22	0
10	TBACl (5)	60	R.T.	17	0
11	TBABr (5)	60	R.T.	45	0
12	TBAI (5)	60	R.T.	45	trace
13	TBAAc (5)	60	R.T.	17	7

6 * This is according to known procedure (Green Chem., **2013**, 15, 2718) they got 65% yield (NMR yield) by using 80% purity CaC_2 , in this case the CaC_2 with 97% purity was used and because of the yield might changed.

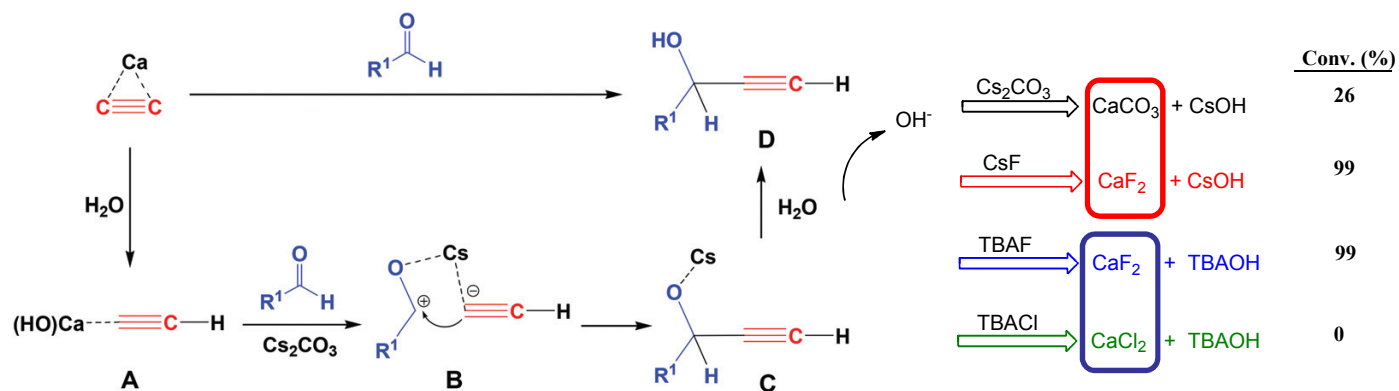
...TBAF/DMSO has subsequently been explored as a reaction medium for chemical modifications of cellulose, for example, acetylation, carboxymethylation, and benzylation. However, the dissolution mechanism of this solvent system is not fully elucidated...

Östlund, A.; Lundberg, D.; Nordstierna, L.; Holmberg, K.; Nydén, M. *Biomacromolecules* **2009**, *10*, 2401.

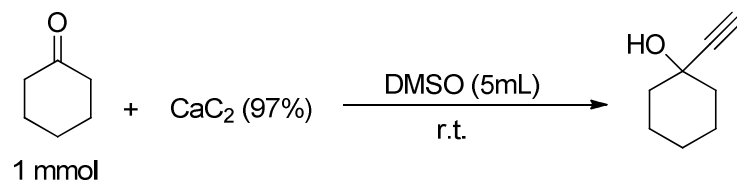
Fluorine effect

Entry	Additive (mol%)	Water (μL)	Temp. (°C)	Time (h)	GC Conv. (%)
1	CS ₂ CO ₃ (50)	60	60	1.5	93
2	CS ₂ CO ₃ (50)	60	R.T.	3	26
3	CsF (50)	60	R.T.	2	99
4	CsF (5)	60	R.T.	3.5	29
5	KF (300)	-	R.T.	12	0
6	KF (300)	60	60	1.5	94
7	KF (300)	60	R.T.	3	95
8	KF (50)	60	R.T.	22	5

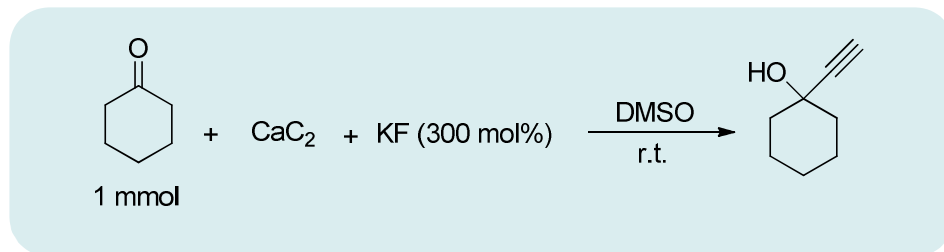
A brief review of mechanism



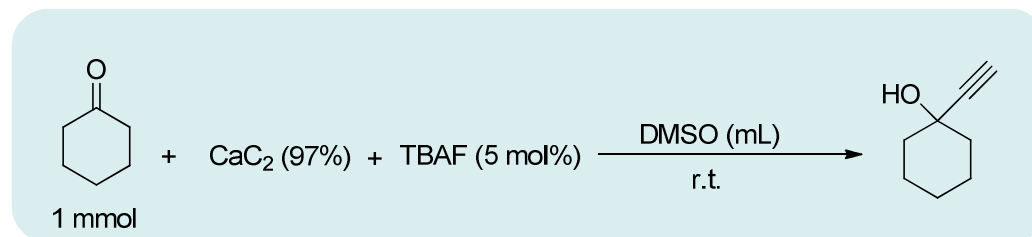
Salt	Solubility in water (g/L)	Solubility in DMSO (g/L)
Cesium hydroxide	3000 (30 °C)	
Cesium carbonate	2605 (15 °C)	361.7
Calcium carbonate	0.013 (25 °C)	
Calcium fluoride	0.016 (20 °C)	
Calcium chloride	745 (20 °C)	
Calcium hydroxide	1.73 (20 °C)	Insoluble (25 °C)
Calcium bromide	1430 (20 °C)	
Calcium iodide	660 (20 °C)	



Entry	Additive (mol%)	Water (μL)	CaC ₂ (mmol)	Time (h)	GC Conv. (%)
1	KF (200)	38.5	2	6.5	5
2	KF (250)	48	2.5	6.5	31
3	KF (300)	50	3	8	62
4	KF (300)	41	2.5	8	72
5	KF (300)	60	3	7	78
6	KF (300)	50	2.5	5.5	57
7	KF (300)	60	3.125	3	98
8	KF (300)	60	3.125	3	39
9	KF (300)	60	3.125	4	35

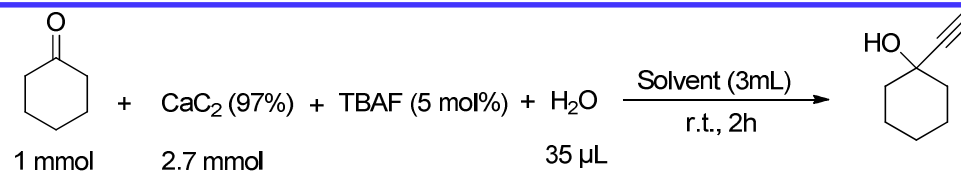


Entry	DMSO (mL)	Water (μL)	Time (h)	CaC_2 (mmol, purity)	GC Conv. (%)
1	3	H_2O (70 μL)	5.5	3.125, 97%	89
2	1.5	H_2O (60 μL)	3	3.125, 97%	72
3	3	H_2O (60 μL)	3	3.125, 97%	54
4	2	H_2O (65 μL)	2	3.125, 97%	49
5	3	H_2O (60 μL)	2	3.125, 97%	18.5
6	3	H_2O (60 μL)	3	3.125, 97%	40
7	3	H_2O (48 μL)	3	2.5, 80%	52
8	3	H_2O (60 μL)	2	3.125, 80%	56
9	3	H_2O (60 μL)	2	2.5, 80%	3



Entry	DMSO (mL)	Water (μL)	CaC_2 (mmol)	Time (h)	GC Conv. (%)
1	5	26	2	5	94.5
2	5	40	2.5	3.5	88
3	5	32	2.5	2.5	97
4	3	32	2.5	2.5	92.5
5	5	35	2.7	2	96
6	3	35	2.7	2	97
7	3	32	2.7	2	84
8	3	35	2.7	2	97
9	3	38	2.7	2	99
10	3	40	2.7	2.45	94
11	3	43.5	3	2.45	92
12	5	38.5	3	2	98.5
13	3	38.5	3	2	97
14	5	38.5	3	2	97

Scale up the reaction was successfully done according optimized condition by yielding 1 g of product (90% isolated yield after distillation).

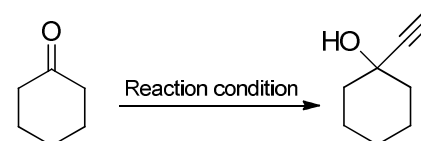


Solvent screening

Entry	Solvent	GC Conv. (%)
1	DMSO	97
2	Toluene	3.5
3	Dioxane	21
4	CH ₃ CN*	1.5
5	THF	Nothing
6	DMF	Nothing
7	CH ₂ Cl ₂	Nothing

* 24% of 1-hydroxycyclohexaneacetonitrile was produced

Comparison of other methods for synthesis of 1-Ethynyl-1-cyclohexanol



Entry	Reagent	Solvent	Time (h)	Yield (%)	Ref.
1	HC≡CNa	NH ₃ (liq.)	20	65-75	<i>Org. Synth.</i> , 1955 , <i>Coll. Vol. 3</i> , 416.
2	Na(H ₃ C) ₃ AlC≡CMgBr	Toluene-THF	3	81	<i>J. Org. Chem.</i> , 1996 , 61, 4472.
3	HC≡CMgBr	Ionic liquids	16	78	WO2006007703, 2006 .
4	HC≡CK	THF	2	88	CN102701911, 2012 .
5	CaC ₂ /Cs ₂ CO ₃	DMSO	8	61	<i>Green Chem.</i> , 2013 , 15, 2718.
6	CaC₂/TBAF	DMSO	2	90	Our protocol



Acknowledgement

- Special thanks to Professor Schreiner for his support, helpful discussions and suggestions
- Thanks are also due to Professor Seidel for his ideas and guidance
- The whole group for pleasant work environment

Thanks for your attention