Electronic Supplementary Information

Practical and scalable preparation of 2-methyleneglutaronitrile via an efficient and highly selective head-to-tail dimerization of acrylonitrile catalysed by low-loading tricyclohexylphosphine

Lei Yu,*[a,b,c,d] Jun Wang,[b] Xu Zhang,[a,b] Hongen Cao,[b] Genling Wang,[a,b,c] Kehong Ding,[a,b,c] Qing Xu*[a,b,c] and Mark Lautens[d]

[a] *Zhejiang Key Laboratory of Carbon Materials, College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou, Zhejiang 325035, China. E-mail: qing-xu@wzu.edu.cn; Fax: (+)-86-577-86689302; Tel: (+)-86-138-57745327*

[b] *School of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu 225002, China. Email: yulei@yzu.edu.cn; Fax: (+)-86-514-87975244; Tel: (+)-86-136-65295901*

[c] *Jiangsu Yangnong Chemical Group Co. Ltd., Yangzhou, Jiangsu, 225009, China*

[d] *Davenport Chemistry Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, ON, M5S 3H6, Canada*

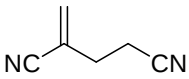
CONTENTS

Experimental

General. The chemicals such as acrylonitrile (commercial acrylonitrile contains 0.1-0.2% 1,4-hydroquinone as the stabilizer), solvents, PCy_3 and other organophosphorus catalysts were all purchased and directly used as received without further purification. All reactions were carried out under nitrogen atmosphere and monitored by gas chromatography (GC) analysis. GC analysis was performed on a JieDao TECH GC1690 instrument. GC yields of the reactions were all determined according to the internal standard curve by using biphenyl (20 mg to a standard reaction: 1 mL acrylonitrile, 15.2 mmol) as the internal standard. Figures 1-5 in the text were drawn by using Microsfot Excel 2010 as the software based on the corresponding results of GC analysis of the reactions (summarized in Tables S1-S8 in the ESI). Figure 6 in the text was drawn using Zhida (Zhejiang Univ.) N2000 Chromatography workstation. Product of the large scale reaction was purified by vacuum distillation of the reaction mixture. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 instrument (600 MHz for ^1H and 150 MHz for ^{13}C NMR spectroscopy) by using $CDCl_3$ as the solvent and Me_4Si as the internal standard. Chemical shifts for ^1H and ^{13}C NMR were referred to internal Me_4Si (0 ppm). Mass spectra were measured on a Thermo Trace DSQ II (EI).

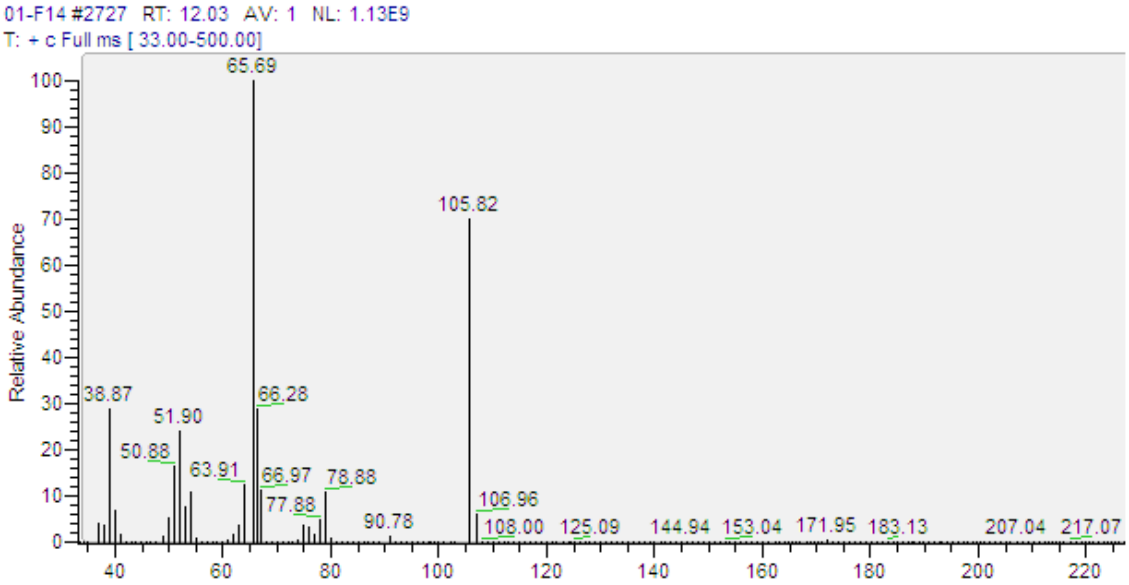
Typical Procedure for the Standard PCy_3-Catalysed Head-to-Tail Dimerization Reaction of Acrylonitrile. The mixture of acrylonitrile (AN, 1 mL, 15.2 mmol), PCy_3 (22.4 mg, 0.08 mmol, 0.5 mol%), and *t*-BuOH (2 mL) in a Schlenk tube was sealed under nitrogen and then heated at 60 ^oC for 15 h. After cooled to room temperature, biphenyl (20 mg) was added to the reaction tube as the internal standard. The mixture was then transferred into a volumetric flask, diluted with toluene to a standard 10 mL solution, and subjected to GC analysis, which indicated a 90% yield of 2-methyleneglutaronitrile (2-MGN). Reactions under other conditions were performed and analysed in similar way.

Procedure for the Large Scale Reaction (eq. 2 in the Text). To a 250 mL round-bottomed flask equipped with a condenser was added PCy_3 (1.12 g, 3.8 mmol, 5 mol%), AN (50 mL, 760 mmol), *t*-BuOH (100 mL) under nitrogen. The mixture was then heated at 60 ^oC for 15 h under nitrogen. After cooled to room temperature, the solvent was quickly removed by rotary evaporation under reduced pressure. The concentrated residue was transferred to a 100 mL round-bottomed flask. A careful vacuum distillation of the residue under reduced pressure afforded 31.0 g of 2-MGN (77% isolated yirld, 79-86 ^oC/0.6 mmHg).



2-Methyleneglutaronitrile (2-MGN). Oil. b.p. 79-86 ^{o}C/0.6 mmHg. IR (film): 2932, 2252, 1653, 1457, 1415, 1333, 1252, 1050, 974, 915, 742, 655, 543 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$, TMS): δ 6.07 (s, 1H), 5.96 (s, 1H), 2.67-2.62 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): *δ* 133.4, 119.3, 117.7, 117.3, 30.3, 16.1. MS (EI, 70 eV): *m/z* (%) 107 (6) [M^{+}+1], 106 (70) [M^{+}], 79 (11), 67 (12), 66 (29), 65 (100). This compound was known: CAS No. 1572-52-7; M. M. Baizer, J. D. Anderson, *J. Org. Chem.* 1965, **30**, 1357.

MS Spectra of 2-MGN



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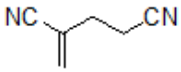
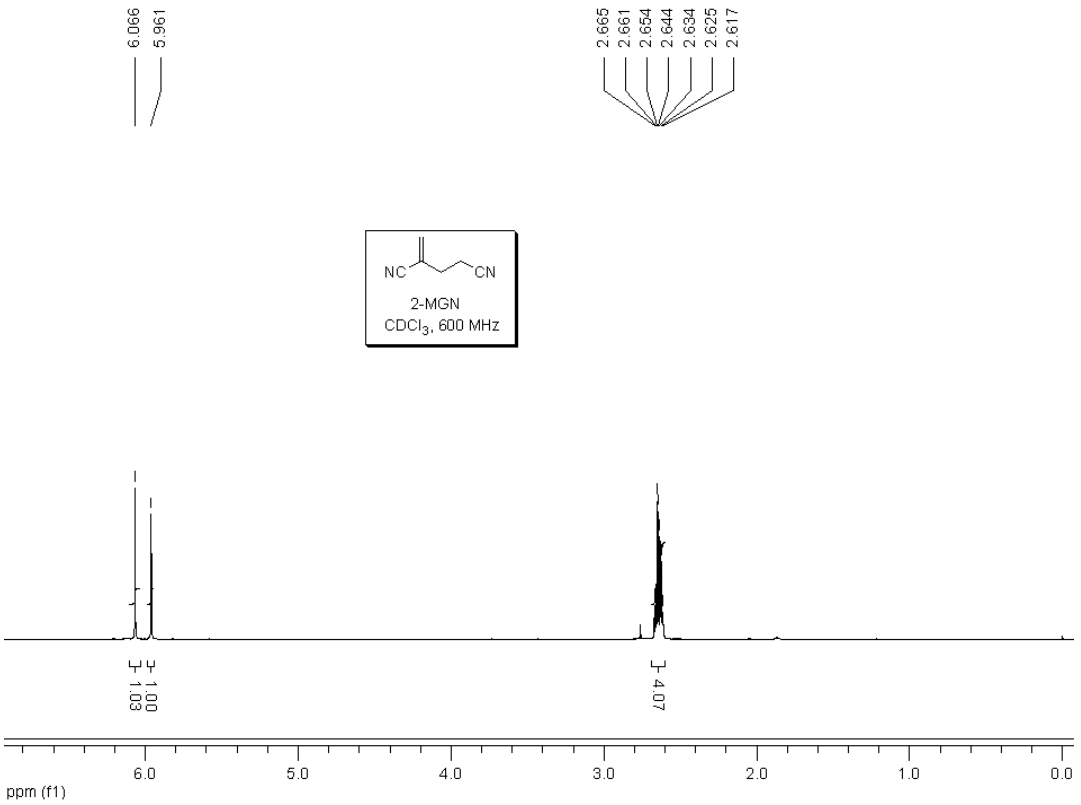
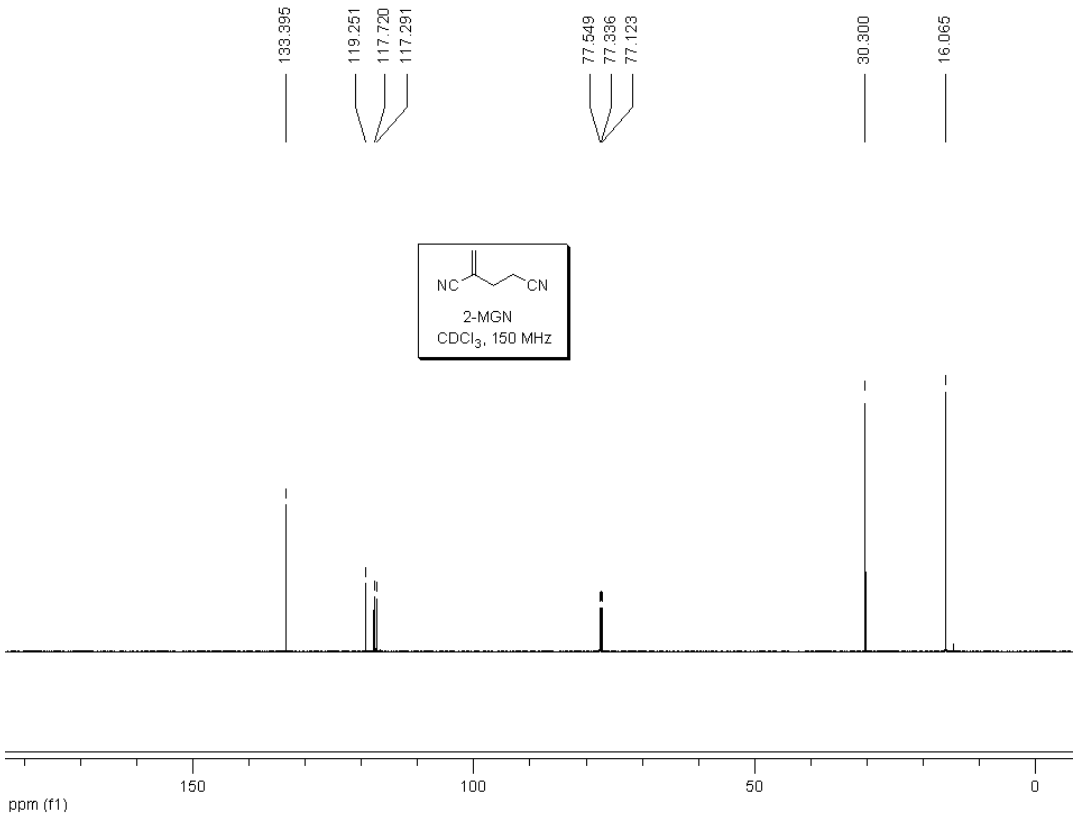
F014		106

m/z	Absolute Intensity	Relative Intensity
38.87	327149824	28.89
50.88	188599808	16.65
51.90	274322944	24.22
65.69	1132403968	100.00
66.28	327915776	28.96
66.97	131150336	11.58
78.88	123645184	10.92
105.82	793763840	70.10
106.96	71846144	6.34

^{1}H NMR

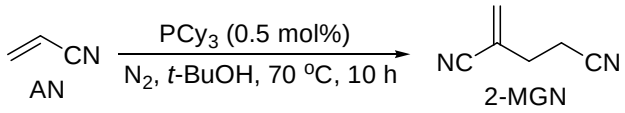


^{13}C NMR



Detailed Condition Optimization Tables Evaluating the Reaction Parameters

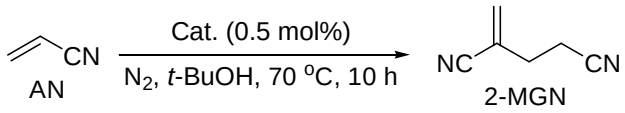
Table S1. Solvent Volume and Reaction Concentration Screening (Fig. 1 in the Text).[a]



run	*t*-C_4H_9OH, V (mL)	*t*-C_4H_9OH/AN (V/V)	2-MGN%[b]
1	0	0	21
2	1	1	75
3	2	2	85
4	3	3	60
5	4	4	54
6	6	6	52

[a] AN (1 mL, 15.2 mmol) and PCy_3 (0.08 mmol, 0.5 mol%) in different volumes of *t*-C_4H_9OH were heated at 70 °C for 10 h under N_2. [b] Determined by GC with biphenyl used as the internal standard.

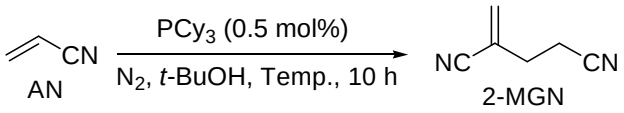
Table S2. Organophosphorous Catalyst Screening (Fig. 2 in the Text).[a]



run	Cat.	AN conversion%[b]	2-MGN%[b]
1	PMe_3	5	3
2	PBu_3	45	32
3	PCy_3	99	85
4	PCy_2Ph	72	66
5	PPh_3	12	0
6	P(*o*-Tol)$_3$	15	0
7	P(*p*-Tol)$_3$	17	0
8	$P(C_6F_5)_3$	3	0
9	Ph_2POEt	10	0
10	$P(OEt)_3$	0	0
11	$HP(O)(OEt)_2$	0	0

[a] AN (1 mL, 15.2 mmol) and an organophosphorous catalyst (0.08 mmol, 0.5 mol%) in *t*-C_4H_9OH (2 mL) were heated at 70 °C for 10 h under N_2. [b] Determined by GC with biphenyl used as the internal standard.

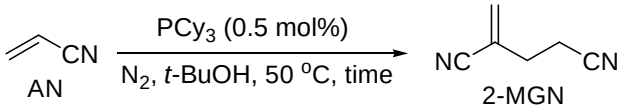
Table S3. Temperature Effect Screening (Fig. 3 in the Text).[a]



run	Temp. (°C)	2-MGN%[b]
1	25	49
2	40	62
3	50	64
4	60	83
5	70	85
6	80	66

[a] AN (1 mL, 15.2 mmol) and PCy_3 (0.08 mmol, 0.5 mol%) in t-C_4H_9OH (2 mL) were heated at different temperatures for 10 h under N_2. [b] Determined by GC with biphenyl used as the internal standard.

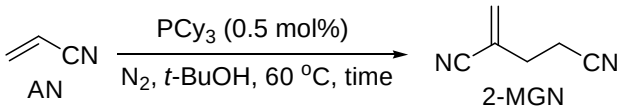
Table S4. Time Effect of the Reactions at 50 °C (Fig. 4 in the Text).[a]



run	Time (h)	2-MGN%[b]
1	1	56
2	2	59
3	5	60
4	10	64
5	15	63
6	20	55

[a] AN (1 mL, 15.2 mmol) and PCy_3 (0.08 mmol, 0.5 mol%) in t-C_4H_9OH (2 mL) were heated at 50 °C under N_2 for the time as indicated in the table. These six parallel reactions were conducted simultaneously under the same condition. After heated at the temperature for 1, 2, 5, 10, 15, or 20 h, respectively, these six reactions were successively quenched by adding toluene into the reaction tube and biphenyl (20 mg) as the internal standard. The reaction mixtures were then transferred into volumetric flasks, diluted with toluene to standard 10 mL solutions, and subjected to GC analysis. [b] Determined by GC with biphenyl used as the internal standard.

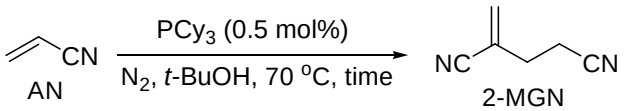
Table S5. Time Effect of the Reactions at 60 °C (Fig. 4 in the Text).[a]



run	Time (h)	2-MGN%[b]
1	1	57
2	2	66
3	5	75
4	10	83
5	15	90
6	20	71

[a] See Table S4 for similar conditions. [b] Determined by GC with biphenyl used as the internal standard.

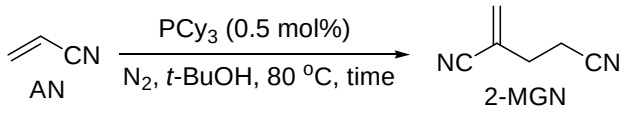
Table S6. Time Effect of the Reactions at 70 °C (Fig. 4 in the Text).[a]



run	Time (h)	2-MGN%[b]
1	1	66
2	2	67
3	5	70
4	10	85
5	15	84
6	20	64

[a] See Table S4 for similar conditions. [b] Determined by GC with biphenyl used as the internal standard.

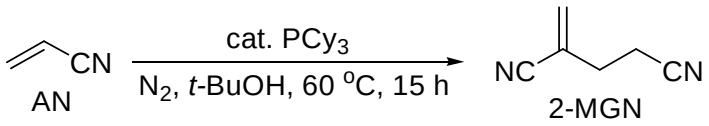
Table S7. Time Effect of the Reactions at 80 °C (Fig. 4 in the Text).[a]



run	Time (h)	2-MGN%[b]
1	1	63
2	2	64
3	5	69
4	10	66
5	15	64
6	20	58

[a] See Table S4 for similar conditions. [b] Determined by GC with biphenyl used as the internal standard.

Table S8. Screening on Catalyst Loading under the Optimized Condition (Fig. 5 in the Text).[a]

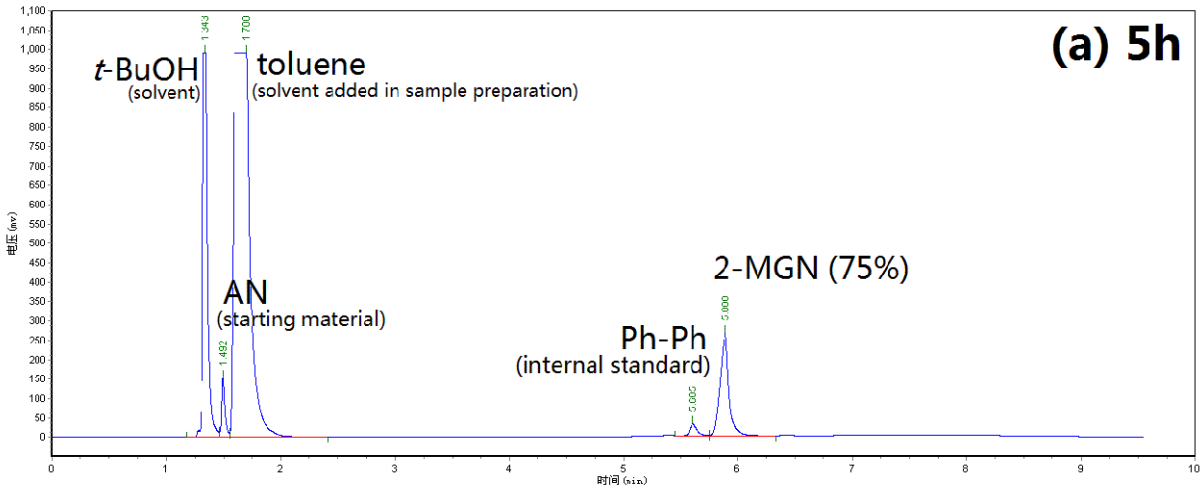


run	PCy_3 (mol%)	2-MGN%[b]
1	0.1	37
2	0.2	39
3	0.3	69
4	0.4	86
5	0.5	90
6	0.6	82
7	0.7	75
8	1.0	71

[a] AN (1 mL, 15.2 mmol) and a given loading of PCy_3 in *t*-BuOH (2 mL) was heated at 60 °C for 15 h under N_2. [b] Determined by GC with biphenyl used as the internal standard.

Selected GC Spectra of the Standard Reaction at 60 °C (Figure 6 in the Text)

(1) The reaction of Table S5, run 3: 75% GC yield of 2-MGN



(2) The reaction of Table S5, run 5: 90% GC yield of 2-MGN