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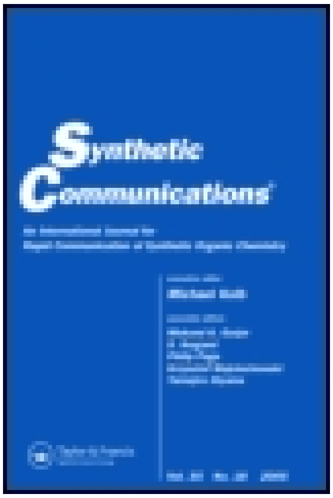

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Efficient One-Pot Synthesis of 2-Amino-4,6-diarylbenzene-1,3-dicarbonitrile under Solvent-Free Conditions

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Efficient One-Pot Synthesis of 2-Amino-4,6-diarylbenzene-1,3-dicarbonitrile under Solvent-Free Conditions

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Abstract: A facile parallel synthesis of 2-amino-4,6-diarylbenzene-1,3-dicarbonitrile derivatives via a one-pot reaction of aromatic aldehydes, aromatic ketone, and malononitrile under solvent-free conditions has been developed. This new protocol has the advantages of shorter time, higher yields, lower cost, and environmental friendliness.

Keywords: grinding, *m*-triphenyls, solvent-free condition

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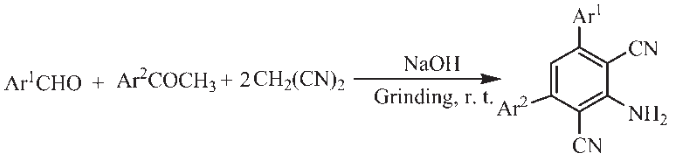
The grinding method has been used more and more frequently in organic synthesis in the past three decades.[1] Compared with traditional methods, this method is more convenient and easily controlled. A great number of organic reactions can be carried out in higher yields, shorter times, or milder conditions by the grinding method. It can even set off some reactions that cannot be carried out under traditional conditions.[2]

m-Triphenyls[3] are useful intermediates and act as building blocks for cyclophanes[4] to create a large molecular cavity[5] and host–guest complexes.[6] Some *m*-triphenyls have importment optical properties.[7] Though many methods for the synthesis of *m*-terphenyls have been reported,[8] these methods suffer from several drawbacks such as multistep reactions, long reaction times, an excess of volatile organic solvents, harsh refluxing conditions, and especially lower product yields (5–20%).[7a] As part of our continued interest in the development of highly expedient methods for the synthesis of organic compounds,[9] we report here a very simple and highly efficient method for the synthesis of *m*-triphenyls via a one-pot cyclocondensation reaction using simple and inexpensive sodium hydroxide as catalyst in solvent-free conditions.

Synthetic details are summarized in Scheme 1. In a typical experiment, the aromatic aldehydes **1**, aromatic ketone **2**, and malononitrile **3** were mixed together with a mortar in the presence of NaOH. The mixture was ground with a pestle, and the reaction could be completed within 3–5 min with excellent yields. The results of the reaction are listed in Table 1.

Table 1 shows the results using a series of aromatic aldehydes, aromatic ketones, and malononitrile that undergo the reaction to give excellent yields (69–80%) of the products **4**. We studied the products of the reactions and found products **4** were obtained, accompanied by a small quantity of the α,β-unsaturated ketones **5** or α,β-unsaturated nitriles **6** as by-products. This procedure does not require the use of any organic solvent, and the reaction could be completed within only a few minutes. The structure of each product **4a–l** was established on the basis of spectroscopic data, particularly ^{1}H NMR analysis. The formation of compound **4** could be explained by a possible mechanism presented in Scheme 2.

In conclusion, we have successfully developed an easy and efficient method to prepare a variety of *m*-triphenyls via the reaction of different



1 **2** **3** **4**

Scheme 1.

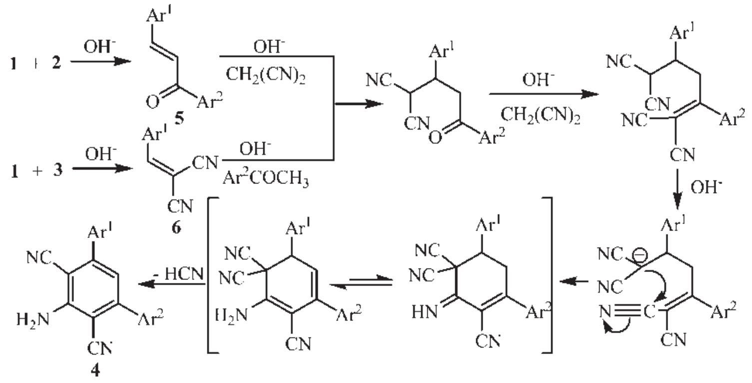
Table 1. Synthesis of compounds **4**

Entry	Ar^1	Ar^2	Product	Yields
1	4-$CH_3C_6H_4$	C_6H_5	**4a**	79
2	4-$CH_3C_6H_4$	4-ClC_6H_4	**4b**	80
3	4-FC_6H_4	C_6H_5	**4c**	73
4	4-ClC_6H_4	C_6H_5	**4d**	76
5	4-BrC_6H_4	C_6H_5	**4e**	78
6	2-ClC_6H_4	C_6H_5	**4f**	71
7	3-ClC_6H_4	C_6H_5	**4g**	73
8	3,4-$Cl_2C_6H_3$	C_6H_5	**4h**	70
9	C_6H_5	3-ClC_6H_4	**4i**	72
10	4-ClC_6H_4	4-BrC_6H_4	**4j**	69
11	4-ClC_6H_4	4-$CH_3OC_6H_4$	**4k**	70
12	4-ClC_6H_4	4-ClC_6H_4	**4l**	70

aromatic aldehydes, aromatic ketones, and malononitrile under solvent-free conditions. The short reaction time coupled with the simplicity of the reaction procedure make this method one of the most efficient methods for the synthesis of this class of compounds.

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting-point apparatus and are uncorrected. IR spectra were recorded on a FT IR-8101 spectrometer. ^1H NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as internal standard using a Bruker-400 spectrometer. Microanalyses were carried out using a Perkin-Elmer 2400 II analyzer.



Scheme 2.

General Procedure for the Synthesis of 2-Amino-4,6-diarylbenzene-1,3-dicarbonitrile (4)

Aromatic aldehyde **1** (2 mmol), aromatic ketone **2** (2 mmol), malononitrile **3** (5 mmol), and NaOH (3 mmol) were added to a mortar. The mixture was ground with a pestle at room temperatures. The reaction was completed in 3–5 min, and the reaction mixture was poured into water. The product was filtered, dried, and recrystallized from 95% ethanol.

Spectral Data

2-Amino-6-phenyl-4-p-tolylpropylbenzene-1,3-dicarbonitrile (**4a**): Mp 201–202°C; IR (KBr, ν, cm^{-1}): 3472, 3364, 3235, 3052, 2216, 1638, 1579, 1568, 1543, 1515, 1448, 1426, 1315, 1283, 1241, 1176, 866, 810, 774, 765, 732, 700; ^1H NMR (400 MHz, DMSO-d_6) δ: 7.63–7.65 (2H, m, ArH), 7.53–7.56 (5H, m, ArH), 7.34 (2H, d, $J = 8.0$ Hz, ArH), 6.82 (2H, s, NH_2), 6.78 (1H, s, C^5-H), 2.39 (3H, s, CH_3). $C_{21}H_{15}N_3$: C, 81.53: H, 4.89; N, 13.58. Found: C, 81.65; H, 4.81; N, 13.47. Anal. calcd. for $C_{21}H_{15}N_3$: C, 81.53; H, 4.89; N, 13.58. Found: C, 81.45; H, 4.96; N, 13.42.

2-Amino-6-(4-chlorophenyl)-4-p-tolylpropylbenzene-1,3-dicarbonitrile (**4b**): Mp 191–192°C; IR (KBr, ν, cm^{-1}): 3470, 3360, 3232, 3050, 2210, 1675, 1573, 1564, 1498, 1420, 1315, 1278, 1170, 860, 811, 764, 698; ^1H NMR (400 MHz, DMSO-d_6) δ: 7.11–7.46 (8H, m, ArH), 6.96 (2H, s, NH_2), 6.65 (1H, s, C^5-H), 2.33 (3H, s, CH_3). Anal. calcd. for $C_{21}H_{14}ClN_3$: C, 73.36; H, 4.10; N, 12.22. Found: C, 73.45; H, 4.00; N, 12.31.

2-Amino-4-(4-fluorophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4c**): Mp 221–223°C; IR (KBr, ν, cm^{-1}): 3478, 3366, 3240, 3050, 2217, 1646, 1606, 1571, 1557, 1513, 1287, 1233, 1163, 834, 818, 764, 695; ^1H NMR (400 MHz, DMSO-d_6) δ: 7.72 (2H, dd, $J = 5.6$ Hz, $J = 5.6$ Hz, ArH), 7.64 (2H, t, $J = 5.6$ Hz, $J = 5.6$ Hz, ArH), 7.54 (3H, t, $J = 5.6$ Hz, $J = 5.6$ Hz, ArH), 7.38 (2H, d, $J = 8.8$ Hz, ArH), 6.87 (2H, s, NH_2), 6.81 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{12}FN_3$: C, 76.67; H, 3.86; N, 13.41. Found: C, 76.75; H, 3.73; N, 13.32.

2-Amino-4-(4-chlorophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4d**): Mp 244–246°C (lit.[7d] 249–250°C); IR (KBr, ν, cm^{-1}): 3467, 3365, 3241, 3057, 2215, 1644, 1564, 1548, 1500, 1286, 1237, 1095, 1013, 829, 757, 695; ^1H NMR (400 MHz, DMSO-d_6) δ: 7.53–7.70 (9H, m, ArH), 6.90 (2H, s, NH_2), 6.82 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{12}ClN_3$: C, 72.84; H, 3.67; N, 12.74. Found: C, 72.76; H, 3.73; N, 12.88.

2-Amino-4-(4-bromophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4e**): Mp 251–254°C; IR (KBr, ν, cm^{-1}): 3458, 3362, 3237, 2214, 1640, 1561, 1544, 1497, 1286, 1075, 1010, 826, 757, 696; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.74 (2H, d, $J = 8.4$ Hz, ArH), 7.60–7.64 (4H, m, ArH), 7.53 (3H, m, ArH), 6.89 (2H, s, NH$_2$), 6.81 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{12}BrN_3$: C, 64.19; H, 3.23; N, 11.23. Found: C, 64.30; H, 3.18; N, 11.06.

2-Amino-4-(2-chlorophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4f**): Mp 208–210°C; IR (KBr, ν, cm^{-1}): 3441, 3347, 3238, 3050, 2219, 1636, 1577, 1556, 1421, 1286, 1057, 1033, 870, 760, 704; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.62–7.66 (3H, m, ArH), 7.50–7.55 (6H, m, ArH), 6.96 (2H, s, NH$_2$), 6.74 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{12}ClN_3$: C, 72.84; H, 3.67; N, 12.74. Found: C, 72.93; H, 3.58; N, 12.63.

2-Amino-4-(3-chlorophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4g**): Mp 221–223°C; IR (KBr, ν, cm^{-1}): 3464, 3354, 3238, 3053, 2218, 1640, 1579, 1567, 1428, 1402, 1285, 1081, 859, 794, 703, 668; ^{1}H NMR (400 MHz, DMSO-d6) δ: 7.47–7.62 (9H, m, ArH), 7.28 (2H, s, NH$_2$), 6.89 (1H, s, C5-H). Anal. calcd. for $C_{20}H_{12}ClN_3$: C, 72.84; H, 3.67; N, 12.74. Found: C, 72.75; H, 3.77; N, 12.83.

2-Amino-4-(3,4-dichlorophenyl)-6-phenylbenzene-1,3-dicarbonitrile (**4h**): Mp 143–145°C; IR (KBr, ν, cm^{-1}): 3462, 3357, 3236, 3068, 2215, 1638, 1575, 1542, 1286, 1137, 1031, 870, 830, 765, 700; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.52–7.74 (8H, m, ArH), 7.15 (2H, s, NH$_2$), 6.87 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{11}Cl_2N_3$: C, 65.95; H, 3.04; N, 11.54. Found: C, 65.86; H, 3.15; N, 11.45.

2-Amino-6-(3-chlorophenyl)-4-phenylbenzene-1,3-dicarbonitrile (**4i**): Mp 197–199°C; IR (KBr, ν, cm^{-1}): 3464, 3352, 3238, 3050, 2218, 1641, 1568, 1558, 1332, 1286, 1211, 1050, 773, 761, 698; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.49–7.90 (9H, m, ArH), 6.92 (2H, s, NH$_2$), 6.85 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{12}ClN_3$: C, 72.84; H, 3.67; N, 12.74. Found: C, 72.72; H, 3.75; N, 12.65.

2-Amino-6-(4-bromophenyl)-4-(4-chlorophenyl)benzene-1,3-dicarbonitrile (**4j**): Mp 278–280°C; IR (KBr, ν, cm^{-1}): 3463, 3358, 3243, 3050, 2219, 1645, 1576, 1558, 1497, 1287, 1093, 1011, 820, 669; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.75 (2H, d, $J = 8.4$ Hz, ArH), 6.68 (2H, d, $J = 8.4$ Hz, ArH), 7.61 (4H, d, $J = 8.4$ Hz, ArH), 6.96 (2H, s, NH$_2$), 6.83 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{11}BrClN_3$: C, 58.78; H, 2.71; N, 10.28. Found: C, 58.67; H, 2.84; N, 10.07.

2-Amino-4-(4-chlorophenyl)-6-(4-methoxyphenyl)benzene-1,3-dicarbonitrile (**4k**): Mp 188–191°C; IR (KBr, ν, cm^{-1}): 3463, 3369, 3232, 3070, 2206, 1642, 1599, 1575, 1494, 1365, 1238, 1013, 826, 809, 670; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.12 (2H, d, $J = 8.4$ Hz, ArH), 7.70 (2H, d,

$J = 8.4$ Hz, ArH), 7.63 (2H, d, $J = 8.4$ Hz, ArH), 7.24 (2H, s, ArH), 7.06 (1H, s, ArH), 7.04 (2H, s, NH_2), 7.01 (1H, s, C^5-H). Anal. calcd. for $C_{21}H_{14}ClN_3O$: C, 70.10; H, 3.92; N, 11.68. Found: C, 70.21; H, 3.83; N, 11.52.

2-Amino-4,6-bis(4-chlorophenyl)benzene-1,3-dicarbonitrile (**4l**): Mp 271–273°C; IR (KBr, ν, cm^{-1}): 3466, 3356, 3245, 3073, 2210, 1646, 1595, 1577, 1498, 1439, 1286, 1244, 1094, 1013, 865, 822, 767, 664; ^1H NMR (400 MHz, DMSO-d_6) δ: 7.68 (4H, d, $J = 8.4$ Hz, ArH), 6.61 (4H, d, $J = 8.4$ Hz, ArH), 6.94 (2H, s, NH_2), 6.83 (1H, s, C^5-H). Anal. calcd. for $C_{20}H_{11}Cl_2N_3$: C, 65.95; H, 3.04; N, 11.54. Found: C, 65.88; H, 3.11; N, 11.46.

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REFERENCES

1. (a) Tanaka, T.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025; (b) Tanaka, K.; Kishigami, S.; Toda, F. *J. Org. Chem.* **1991**, *56*, 4333; (c) Toda, F.; Kiyoshige, K.; Yagi, M. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 320; (d) Cave, G. W. V.; Raston, C. L. *Chem. Commun.* **2000**, 2199; (e) Liu, X. X.; Shen, Z. X. *Tetrahedron Lett.* **2006**, *47*, 5623.
2. (a) Wang, S. X.; Li, J. T.; Geng, L. J. *J. Chem. Res.* **2003**, 370; (b) Meng, J. B.; Du, M. D.; Wang, Y. M.; Wang, R. J.; Wang, H. G. *Chin. Chem. Lett.* **1992**, *3*, 247.
3. Saednya, A.; Hart, H. *Synthesis* **1996**, 1455.
4. Hart, H.; Rajakumar, P. *Tetrahedron* **1995**, 1313.
5. Rajakumar, P.; Kannan, A. *Tetrahedron Lett.* **1993**, *34*, 4407.
6. Bringmann, G.; Walter, R.; Weirich, R. *Synthesis* **1990**, 977.
7. Janusz, S.; Piotr, M. *Tetrahedron* **1985**, *41*, 5261.
8. (a) Pedro, V.; Jose, I. B.; Anton, V. F. *Tetrahedron Lett.* **1991**, *32*, 5375; (b) Griffiths, J.; Lockwood, M.; Roozpeikar, B. *J. Chem. Soc., Perkin Trans. 2,* **1977**, 1608; (c) Victory, P. J.; Borrell, J. I.; Vidal-Ferran, A. *Heterocycles* **1993**, *36*, 769; (d) Mazaahir, K.; Shilpi, S.; Shweta, R. *Indian, J. Chem.* **2004**, *43B*, 2423; (e) Cui, S. L.; Lin, X. F.; Gang, W. Y. *J Org. Chem.* **2005**, *70*, 2866.
9. (a) Rong, L. C.; Li, X. Y.; Wang, H. Y.; Shi, D. Q.; Tu, S. J.; Zhuang, Q. Y. *Synth. Commun.* **2006**, *36*, 2363; (b) Rong, L. C.; Li, X. Y.; Wang, H. Y.; Shi, D. Q.; Tu, S. J.; Zhuang, Q. Y. *Synth. Commun.* **2006**, *36*, 2407; (c) Rong, L. C.; Li, X. Y.; Yao, C. S.; Wang, H. Y.; Shi, D. Q. *Acta Cry* **2006**, *E62*, o35; (d) Rong, L. C.; Li, X. Y.; Yao, C. S.; Wang, H. Y.; Shi, D. Q. *Acta Crys.* **2006**, *E62*, o3004.