New Route to Dimethylnaphthalenes Involving Cyclization of Ylidenemalonodinitriles and Ethyl Ylidenecyanoacetates; Part 2[1]. Synthesis of 1,7-, 2,6-, and 2,7-Dimethylnaphthalene

Janusz SEPIOŁ

Department of Organic Chemistry, Jagiellonian University, 30-060 Krakow, Karasia 3, Poland

In continuation of studies on applications of ylidenemalonodinitriles for the construction of aromatic carbocyclic systems, the syntheses of 1,7-, 2,6-, and 2,7-dimethylnaphthalenes are now reported.

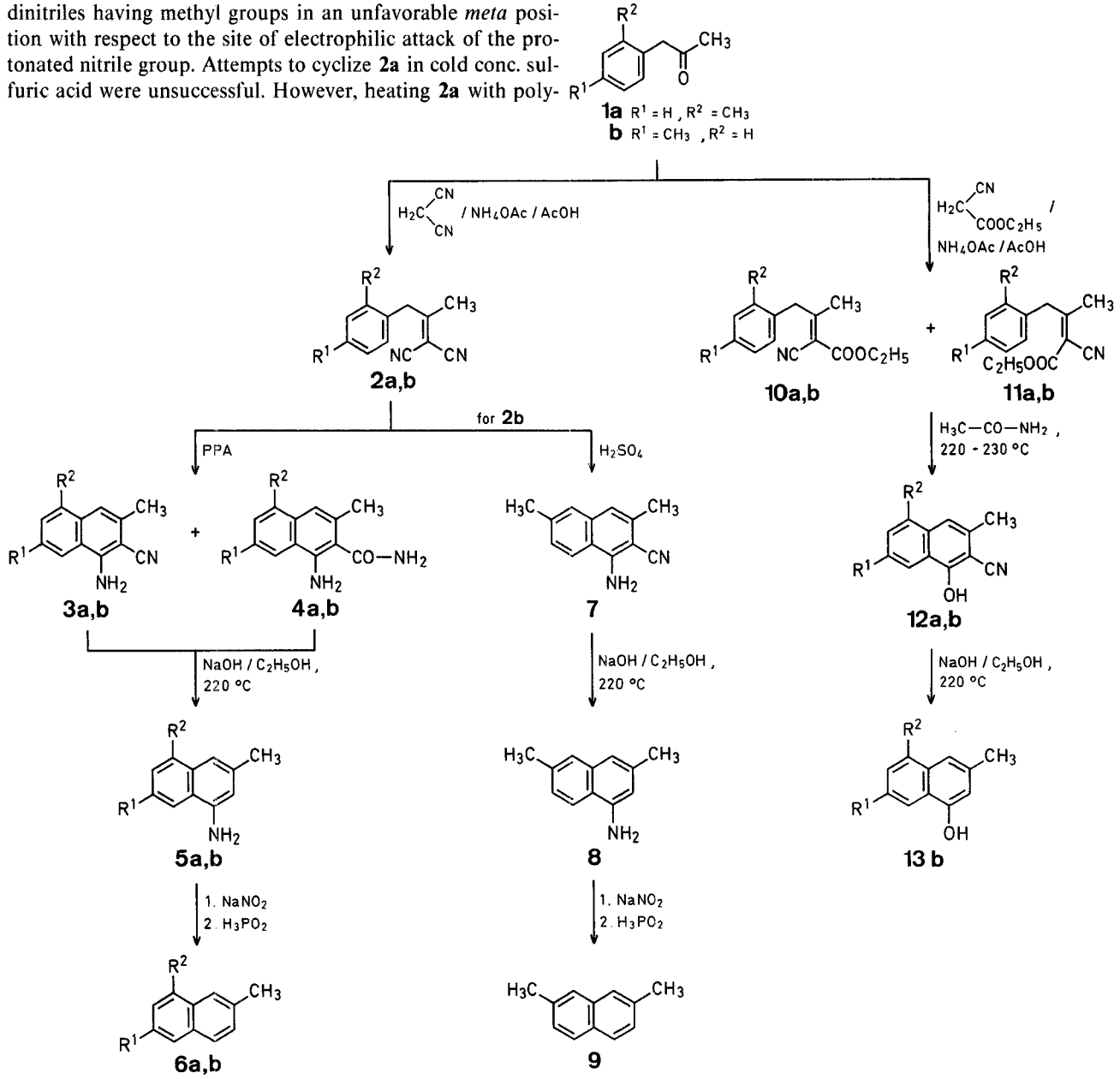
1,7-Dimethylnaphthalene **(6a)** has been synthesized from toluene and succinic anhydride[2,3] or from tolylethyl bromide

via malonic ester synthesis[3]. Isomerization of 1,8-dimethylnaphthalene with anhydrous hydrogen fluoride also has given **6a**[4]. 2,6-Dimethylnaphthalene **(6b)** has been prepared by methylation of 2-iodo-6-methylnaphthalene[3] or from 4-methylbenzyl chloride and 4,4-dimethoxybutan-2-one[5]. This hydrocarbon has been isolated from anthracite tar along with several other isomeric dimethylnaphthalenes[6].

Cyclizations of ylidenemalonodinitriles described previously involved compounds where ring closure leading to the naphthalene system occurred on a carbon atom at an *ortho* or *para* position with respect to the methyl group on the benzene ring[1]. Other cyclizations involved the unsubstituted benzene system[1,7]. All these reactions proceeded smoothly in cold concentrated sulfuric acid.

This communication describes cyclization of ylidenemalonodinitriles having methyl groups in an unfavorable *meta* position with respect to the site of electrophilic attack of the protonated nitrile group. Attempts to cyclize **2a** in cold conc. sulfuric acid were unsuccessful. However, heating **2a** with polyphosphoric acid (PPA) on a steam bath for a few hours afforded **3a**. Neutralization of the acidic filtrate which remained after separation of **3a** furnished the *o*-aminoamide **4a**. In the same manner, cyclization of **2b** with PPA gave **3b** and **4b**. Prolonged heating of starting nitriles **2** with PPA usually caused decreased yields of *o*-aminonitriles **3** and increased yields of *o*-aminoamides **4**. Successful cyclization of ylidenemalonodinitriles in PPA was reported earlier[8,9].

The reductive decyanation of **3** was carried out in conventional way by heating in an autoclave with ethanolic sodium hydroxide[1,10]. The same method was applied for the elimination of the aminocarbonyl group from *o*-aminoamides **4**. Thus, amines **5a** and **5b** were obtained in comparable good yields either from **3** or from **4**. Elimination of the aminocarbonyl group from *o*-aminoamides by the above method is reported here for the first time. The reaction of hypophosphorous acid with diazonium chlorides obtained from amines **5a** and **5b** afforded 1,7-dimethylnaphthalene **(6a)** and 2,6-dimethylnaphthalene **(6b)**, respectively.



	R^1	R^2
a	H	CH_3
b	CH_3	H

Scheme A

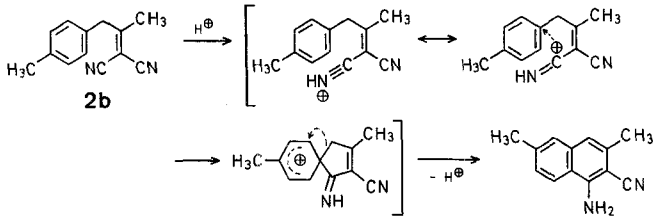
Cyclization of **2b** in cold concentrated sulfuric acid afforded colorless crystals with m.p. 178–179 °C in low yield (7%). Spectral analysis of this *o*-aminonitrile showed that instead of the expected derivative of 2,6-dimethylnaphthalene **3b** the derivative of 2,7-dimethylnaphthalene **7** was obtained. The *o*-aminonitrile **7** had the same I.R. and ^{1}H-N.M.R. spectra as an authentic sample of 1-amino-2-cyano-3,6-dimethylnaphthalene[1]. The structure of **7** was further confirmed both by decyanation which gave the amine **8** in good yield and by deamination of **8** to 2,7-dimethylnaphthalene **(9)**.

It appears that during cyclization of **2b** in sulfuric acid a rearrangement of the carbocyclic system occurred (Scheme **B**). This rearrangement seems to involve the attack of the protonated nitrile group of **2b** on the carbon atom at a *para* position with respect to the methyl group. Subsequent breakdown of the cationic intermediate leads to the *o*-aminonitrile **7**.

Table. Compounds **1–13** prepared

Product	Yield [%]	m.p. [°C] (solvent) or b.p. [°C]/torr (n_D)	Molecular Formula[a] or Lit. Data	M.S. *m/e* (rel. intens. %)	I.R. (neat or KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
1a	62	91°/4 (n_D^{22}: 1.5182)	87°/3.5[12]	—	1720 (C=O)	2.12 (s, 3H); 2.25 (s, 3H); 3.68 (s, 2H); 7.2 (m, 4H)
1b	56	74°/4 (n_D^{20}: 1.5141)	70°/0.3[13]	—	1720 (C=O)	2.13 (s, 3H); 2.33 (s, 3H); 3.63 (s, 2H); 7.1 (m, 4H)
2a	70	140°/4 (n_D^{20}: 1.5537)	$C_{13}H_{12}N_2$ (196.3)	196 (M^+)	2232 (CN)	2.12 (s, 3H); 2.30 (s, 3H); 3.90 (s, 2H); 7.2 (m, 4H)
2b	59	135°/3 (n_D^{20}: 1.5472)	132°/0.25[13]	196 (M^+)	2230 (CN)	2.16 (s, 3H); 2.33 (s, 3H); 3.81 (s, 2H); 7.11 (m, 4H)
3a	34	148–149° (CH_3OH)	$C_{13}H_{12}N_2$ (196.3)	197 (15); 196 (M^+, 100)	3496, 3362, 3251 (NH_2); 2213 (CN)	2.52 (s, 3H); 2.56 (s, 3H); 5.05 (br. s, 2H); 7.05 (s, 1H); 7.2–7.5 (m, 3H)
3b	35	168–169° (CH_3OH)	$C_{13}H_{12}N_2$ (196.3)	197 (16); 196 (M^+, 100)	3480, 3456, 3395, 3348, 3255 (NH_2); 2212 (CN); 1642	[$(CD_3)_2CO$]: 2.42 (s, 3H); 2.46 (s, 3H); 6.00 (br. s, 2H); 6.90 (s, 1H); 7.33 (d, 1H, J=8 Hz); 7.56 (d, 1H, J=8 Hz); 7.93 (s, 1H)
4a	35	239–240° (C_2H_5OH)	$C_{13}H_{14}N_2O$ (214.3)	215 (8); 214 (M^+, 52); 197 (100)	3392, 3190 (NH_2); 1645	(DMSO-d_6): 2.45 (s, 3H); 2.54 (s, 3H); 5.63 (br. s, 2H); 7.03 (s, 1H); 7.2 (m, 2H); 7.53 (br. s, 1H); 7.73 (br. s, 1H); 8.0 (m, 1H)
4b	33	238–239° (C_2H_5OH)	$C_{13}H_{14}N_2O$ (214.3)	215 (8); 214 (M^+, 53); 197 (100)	3380, 3190 (NH_2); 1644	(DMSO-d_6): 2.39 (s, 3H); 2.46 (s, 3H); 5.57 (br. s, 2H); 6.88 (s, 1H); 7.23 (d, 1H, J=8 Hz); 7.51 (br. s, 1H); 7.53 (d, 1H, J=8 Hz); 7.75 (br. s, 1H); 7.90 (s, 1H)
5a	80–81	79–80° (n-C_6H_{14})	$C_{12}H_{13}N$ (171.2)	172 (14); 171 (M^+, 100)	3426, 3360, 3230 (NH_2); 2915, 1640	2.42 (s, 3H); 2.62 (s, 3H); 3.88 (s, 2H); 6.55 (s, 1H); 7.2 (m, 3H); 7.6 (m, 1H)
5b	77–85	91–92° (n-C_6H_{14})	93–94°[14]; 85–86°[15]	172 (13); 171 (M^+, 100)	3422, 3340, 3232 (NH_2); 3025, 2914, 1630	2.37 (s, 3H); 2.47 (s, 3H); 3.87 (s, 2H); 6.52 (s, 1H); 7.02 (s, 1H); 7.20 (d, 1H, J=8 Hz); 7.46 (s, 1H); 7.57 (d, 1H, J=8 Hz)
6a	35	82°/0.05 (n_D^{20}: 1.6075)	263°/760[3] (n_D^{20}: 1.6072)[3]	157 (12); 156 (M^+, 100)	3055, 2973, 2945, 2920, 1636	2.52 (s, 3H); 2.65 (s, 3H); 7.2–7.4 (m, 3H); 7.6–7.8 (m, 3H)
6b	37	110–110.5°	110–111°[3]	157 (13); 156 (M^+, 100)	2915, 2862, 1610	2.45 (s, 6H); 7.21 (d, 2H, J=8 Hz); 7.49 (s, 2H); 7.59 (d, 2H, J=8 Hz)
7	7	178–179°	177–179°[1]	see Ref.[1]		
8	69	110°/0.05	$C_{12}H_{13}N$ (171.2)	172 (16); 171 (M^+, 48); 170 (100)	3482, 3380, 3273 (NH_2); 2938, 1636	2.37 (s, 3H); 2.44 (s, 3H); 3.85 (s, 2H); 6.43 (s, 1H); 6.95 (s, 1H); 7.13 (d, 1H, J=8 Hz); 7.42 (s, 1H); 7.56 (d, 1H, J=8 Hz)
9	50	94–95°	94.5–95°[1]; 95°[16]	see Ref.[1]		
10a, 11a	60	138°/4 (n_D^{20}: 1.5355)	$C_{15}H_{17}NO_2$ (243.3)	243 (M^+)	2220 (CN); 1720 (C=O)	**10a:** 1.40 (t, 3H, J=7 Hz); 2.24 (s, 3H); 2.28 (s, 3H); 3.95 (s, 2H); 4.33 (q, 2H, J=7 Hz); 7.2 (m, 4H) **11a:** 1.40 (t, 3H, J=7 Hz); 2.15 (s, 3H); 2.34 (s, 3H); 4.25 (s, 2H); 4.33 (q, 2H, J=7 Hz); 7.2 (m, 4H)
10b, 11b	67	143°/4 (n_D^{20}: 1.5341)	$C_{15}H_{17}NO_2$ (243.3)	243 (M^+)	2220 (CN); 1720 (C=O)	**10b:** 1.42 (t, 3H, J=7 Hz); 2.35 (s, 3H); 2.40 (s, 3H); 3.90 (s, 2H); 4.32 (q, 2H, J=7 Hz); 7.2 (m, 4H) **11b:** 1.42 (t, 3H, J=7 Hz); 2.22 (s, 3H); 2.40 (s, 3H); 4.18 (s, 2H); 4.36 (q, 2H, J=7 Hz); 7.2 (m, 4H)
12b	23	195–196° (C_2H_5OH)	$C_{13}H_{11}NO$ (197.2)	198 (15); 197 (M^+, 100)	3255 (OH); 2227 (CN); 1605	(DMSO-d_6): 2.52 (s, 6H); 4.75 (br. s, 1H); 7.27 (s, 1H); 7.45 (d, 1H, J=8 Hz); 7.70 (d, 1H, J=8 Hz); 8.15 (s, 1H)
13b	82	103–104° (n-C_6H_{14})	105–106°[14]	173 (14); 172 (M^+, 100)	3335 (OH); 2920, 1610	2.37 (s, 3H); 2.47 (s, 3H); 5.17 (br. s, 1H); 6.52 (s, 1H); 7.12 (s, 1H); 7.20 (d, 1H, J=8 Hz); 7.57 (d, 1H, J=8 Hz); 7.83 (s, 1H)

[a] Satisfactory microanalyses obtained: C ±0.25, H ±0.09, N ±0.19.



Scheme B

Careful analysis of intermediate compounds used for the preparation of **2b** showed that 4-methylbenzaldehyde and 1-(4-methylphenyl)-propan-2-one were free from their *meta* isomers. Samples for cyclization in PPA or sulfuric acid were taken from the same bath of ylidenemalonodinitrile **2b**. Furthermore, compounds **3b** and **4b** showed no contamination by derivatives of 2,7-dimethylnaphthalene. All this evidence supports our conclusion that the rearrangement of the carbocyclic system is responsible for formation of **7** from the nitrile **2b**.

Since *o*-aminonitrile **7** and the amine **8** were not contaminated by their isomers, the synthetic sequence reported here may be of some importance as an alternative route to **8** or 2,7-dimethylnaphthalene **(9)**.

As in the previous report[1], the application of ethyl ylidenecyanoacetates for synthesis of some dimethylnaphthalene derivatives was only of limited success. Attempted cyclizations of ylidenecyanoacetates **10a, 11a** in boiling acetamide were unsuccessful and the *o*-hydroxynitrile **12a** was not isolated. However, under the same conditions ylidenecyanoacetates **10b, 11b** gave **12b** in low yield which was subsequently decyanated to 1-hydroxy-3,7-dimethylnaphthalene **(13b)** (Scheme A).

All spectral and analytical data were obtained on the same instruments as described previously[1].

Preparation of Ketones 1; General Procedure:
Ketones **1a** and **1b** are synthesized from 2-methylbenzaldehyde and 4-methylbenzaldehyde (Fluka AG), respectively, by condensation with nitroethane using piperidine as a catalyst and then reducing the nitro derivative with iron powder and hydrochloric acid. This procedure is essentially the same as reported earlier for the preparation of *m*-tolylacetone[11].

Preparation of Ylidenemalonodinitriles 2 and Ethyl Ylidenecyanoacetates 10, 11:
These nitriles and cyanoesters are synthesized in the same manner as reported previously[1]. Liquid cyanoesters are mixtures (1:1 ratio) of two isomers **10** and **11** (see Table).

Cyclization of Ylidenemalonodinitriles 2; General Procedure:
The ylidenemalonodinitrile **2a** or **2b** (2.0 g, 10 mmol) and polyphosphoric acid (100 g) are mixed in a flask protected from moisture. The flask is heated on a steam bath for 3 h with occasional swirling. The brown mixture is poured into water (300 ml), the precipitated solid is filtered off, washed with water, sublimed in vacuo, and recrystallized from methanol to give **3a** or **3b** as colorless needles. The acidic filtrate is neutralized with sodium hydroxide solution. The precipitated solid is filtered off on a Büchner funnel, washed with water, sublimed in vacuo, and recrystallized from ethanol to afford **4a** or **4b** as colorless needles.

Elimination of the Nitrile Group from 3a, 3b or the Aminocarbonyl Group from 4a, 4b; General Procedure:
The *o*-aminonitrile **3a, 3b** (392 mg, 2 mmol) or the *o*-aminoamide **4a, 4b** (428 mg, 2 mmol) and sodium hydroxide (0.8 g) are dissolved in ethanol (50 ml) and heated in a 250 ml autoclave for 4 h. The mixture is diluted with water (50 ml) and ethanol is removed by distillation. The precipitated black oil solidifies on standing at room temperature. The solid amine is filtered off, washed with water, sublimed in vacuo and recrystallized from *n*-hexane. The amine **5a** is obtained as colorless fluffy crystals and **5b** as colorless long needles.

Preparation of Dimethylnaphthalenes 6a, 6b; General Procedure:
The amine **5a** or **5b** (342 mg, 2 mmol) is converted into a hydrochloride, diazotized with sodium nitrite (200 mg), and then reduced with hypophosphorous acid (5 g) in essentially the same manner as described previously for the synthesis of 1,2-dimethylnaphthalene[1]. The crude product **6a** is extracted with ether and after the work-up distilled under reduced pressure to afford **6a** as a colorless oil. The solid product **6b** is filtered off, sublimed in vacuo, and recrystallized from methanol to give **6b** as colorless fine plates.

1-Amino-2-cyano-3,6-dimethylnaphthalene (7):
The ylidenemalonodinitrile **2b** (3.0 g, 15 mmol) is slowly dissolved in ice-cold conc. sulfuric acid (10 ml). The solution immediately becomes dark-red and then magenta colored. The solution is kept in the ice-bath for 1.5 h and is then poured on to ice. The yellow precipitate is filtered off, washed with water, and sodium hydrogen carbonate solution. Attempted crystallization of this product from ethanol is unsuccessful. The solid is sublimed under reduced pressure (0.05 torr) and a small amount of crystalline substance is collected. A substantial amount of decomposed coke-like black substance remains in the sublimation apparatus. The crystalline product is further purified by recrystallization from ethanol to give **7** as colorless crystals; yield: 200 mg (7%); m.p. 178–179 °C (Ref.[1], m.p. 177–179 °C); mixture m.p. with an authentic sample[1] is not depressed.

1-Amino-3,6-dimethylnaphthalene (8):
The *o*-aminonitrile **7** (196 mg, 1 mmol) and sodium hydroxide (0.5 g) are dissolved in ethanol (50 ml) and heated in an autoclave at 220 °C for 5 h. The solution is diluted with water (40 ml) and ethanol is distilled off. The precipitated oil is extracted with ether (3 × 10 ml). The combined extracts are washed with water and dried with anhydrous magnesium sulfate. Ether is distilled off and remaining oil is distilled in vacuo to furnish **8** as very thick oil which could not be induced to crystallize; yield: 118 mg (69%); b.p. 110 °C/0.05 torr.

2,7-Dimethylnaphthalene (9):
The amine **8** (86 mg, 0.5 mmol) is converted into a hydrochloride by dissolving in hydrochloric acid (1 ml). Water (1 ml) is added and the suspension is diazotized at −4 °C with sodium nitrite (80 mg) dissolved in a small amount of water. Cold hypophosphorous acid (4.0 g) is added and the solution is left at 7 °C for two days. The crude hydrocarbon is filtered off, washed with water, sublimed in vacuo, and recrystallized from methanol to afford **9** as colorless plates; yield: 39 mg (50%); m.p. 94–95 °C (Ref.[1], m.p. 94.5–95 °C; Ref.[16], m.p. 95 °C).

1-Hydroxy-2-cyano-3,7-dimethylnaphthalene (12b):
Ethyl ylidenecyanoacetate **10b, 11b** (2.5 g, 10 mmol) and acetamide (6.0 g) are heated at 220–230 °C for 4 h. After conventional work-up[1], the product is sublimed in vacuo and recrystallized from ethanol to give **12b** as yellow needles; yield: 461 mg (23%); m.p. 195–196 °C.

1-Hydroxy-3,7-dimethylnaphthalene (13b):
The *o*-hydroxynitrile **12b** (394 mg, 2 mmol) and sodium hydroxide (0.5 g) are dissolved in ethanol (50 ml) and heated in an autoclave at 220 °C for 6 h. The mixture is diluted with water (50 ml) and ethanol is removed by distillation. The solution is neutralized with dilute sulfuric acid. The precipitate is filtered off, washed with water, sublimed in vacuo, and recrystallized from *n*-hexane to afford **13b** as colorless needles; yield: 282 mg (82%); m.p. 103–104 °C (Ref.[14], m.p. 105–106 °C).

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