



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

SYNTHESIS AND NUCLEOPHILIC REACTIONS OF N-(1-NAPHTHYL)- 3,4-METHYLENEDIOXYBENZYL-IDINEHOMOPHTHALISOIMIDIUM PERCHLORATE

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Published online: 16 Aug 2006.

To cite this article: M. E. Azab, H. M. F. Madkour & M. R. Mahmoud (2002) SYNTHESIS AND NUCLEOPHILIC REACTIONS OF N-(1-NAPHTHYL)- 3,4-METHYLENEDIOXYBENZYL-IDINEHOMOPHTHALISOIMIDIUM PERCHLORATE, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:3, 393-402

To link to this article: <http://dx.doi.org/10.1081/SCC-120002123>

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SYNTHETIC COMMUNICATIONS, 32(3), 393–402 (2002)

**SYNTHESIS AND NUCLEOPHILIC
REACTIONS OF *N*-(1-NAPHTHYL)-
3,4-METHYLENEDIOXYBENZYL-
IDINEHOMOPHTHALISOIMIDIUM
PERCHLORATE**

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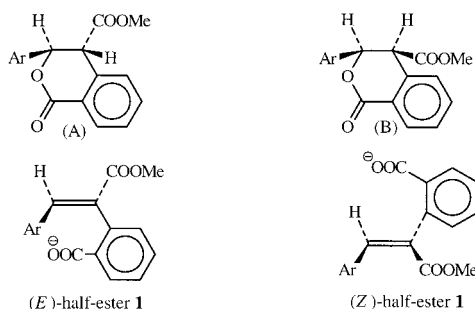
ABSTRACT

N-(1-Naphthyl)-3,4-methylenedioxybenzylidenehomophthalisoimidium perchlorate **6** was obtained via treatment of *N*-(1-naphthyl)-3,4-methylenedioxybenzylidene homophthalamic acid **5** with perchloric acid in acetic anhydride. The behaviour of **6** towards active methylene-containing compounds, Grignard reagents and aromatic primary amines and hydrocarbons, has been investigated.

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A connection with our previous interest in developing new approach for the synthesis of heterocycles utilizing readily obtainable starting materials,¹⁻⁴ we report in the present work the synthesis of some new heterocyclic systems utilizing the title compound.

Thus, when 3,4-methylenedioxybenzaldehyde was condensed with dimethyl homophthalate in the presence of sodium hydride as a condensing agent, the *Z*-half-ester **1** was obtained in approximately 90% yield (cf. Scheme 1). The preferential formation of the *Z*-configuration for the half-ester may be rationalized by considering the high strain associated with the *E*-isomer due to steric interference between the *ortho*-carboxyphenyl and the bulky substituted aryl group.



Scheme 1.

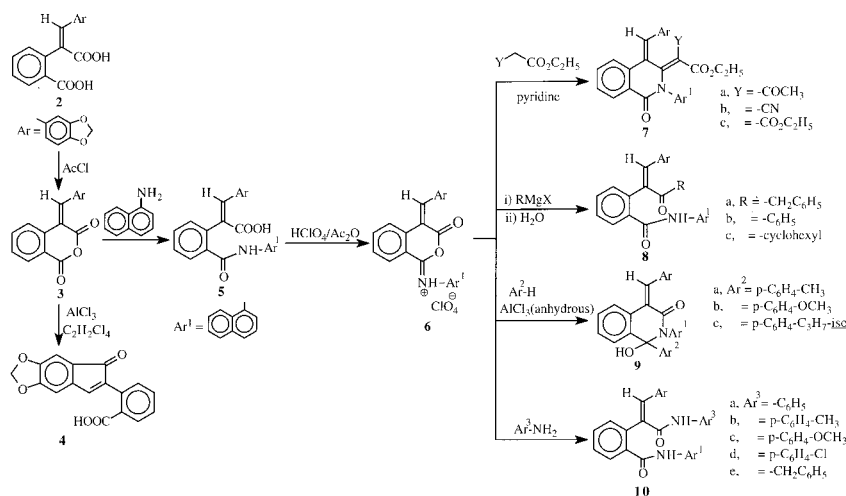
The half-ester **1** was saponified to the corresponding acid **2**. The structure assigned for the dicarboxylic acid **2** was based on its spectroscopic data. A chemical evidence for the structure assigned for the acid **2** was obtained from its conversion to the corresponding anhydride **3** by the action of acetyl chloride (cf. Scheme 2).

Compound **3** was subjected to an internal Friedel-Crafts acylation reaction with anhydrous aluminium chloride in dry acetylene tetrachloride to afford the respective oxoacid **4** in good yield (78%).

The assignment of the indenone structure **4** was based on analytical and spectroscopic data as well as its yellow color which is characteristic for indenones, its solubility in sodium carbonate solution and the formation of its DNP on reacting with dinitrophenyl hydrazine.

3,4-Methylenedioxybenzylidene homophthalic anhydride **3** was allowed to react with 1-naphthylamine in benzene to give 2-[*N*-(1-naphthyl)-carboxamido]-3,4-methylene-dioxybenzylidene phenylacetic acid (**5**). The interaction of 1-naphthylamine with compound **3** takes place on the benzoyl





acidic products resulting from the attack at the alternative site of the iso-imidium salt ($C=N^{\oplus}H$).

EXPERIMENTAL

All melting points are not corrected, the IR spectra were measured on a Unicam SP 1200 spectrophotometer using KBr Wafer technique. The mass spectra were determined with A.E.I.M.S. 12 single focusing mass spectrometer and the percentage of the relative abundance of a peak is shown in brackets and follows the m/z value. The 1H -NMR spectra were measured on a Varian EM 360 instrument operating at 60 MHz in DMSO- d_6 or $CDCl_3$ solution. Compounds **1–5** were prepared according to the methods described in literature.^{6–9} The physical characteristics of the new compounds are listed in Table 1.

Reaction of 3,4-Methylenedioxybenzaldehyde with Dimethyl Homophthalate; Formation of Methyl- β -(3,4-methylenedioxyphenyl)- α -(2-carboxyphenyl)acrylate **1**

A mixture of the aldehyde (15.01 g; 0.10 mol), dimethyl homophthalate (32.2 g; 0.15 mol), and sodium hydride (3.6 g, 0.15 mol) in 150 mL of dry benzene was stirred for 60 min at 60–70°C. The solid deposited was filtered off, dissolved in $NaHCO_3$ solution (10%) then acidified with dil HCl-ice. The half ester **1** separated as a colourless crystalline solid which was recrystallized from benzene (cf. Table 1).

IR spectrum of **1** exhibited strong bands at 1675 and 1720 cm^{-1} for aryl acid and α,β -unsaturated ester groups respectively. On the other hand, the 1H -NMR (DMSO- d_6) of the half-ester **1** exhibited the following signals: δ 3.28 (s, 3H, COOMe), 6.42 (s, 2H, O-CH₂-O), 7.49 (s, 1H, CH=C), 7.77–8.25 (m, 4H, Ar-H), 8.40–8.71 (m, 3H, Ar-H of piperonyl moiety) and 10.84 (s, 1H, COOH).

Saponification of the Half-Ester **1**; Formation of 3,4-Methylenedioxybenzylidene Homophthalic Acid **2**

The crystalline half-ester **1** (3.3 g; 0.01 mol) was heated under reflux in 35 mL of aqueous sodium hydroxide solution (10%) for 4 h. The alkaline solution was cooled, acidified with cold dilute hydrochloric acid and the



Table 1. Physical Characteristics for New Compounds

Compd. No.	Solvent of Crystallization M.P. (°C)	Yield (%)	Mol. Formula (M. wt.)	Analysis (Found/Cald.)			
				C%	H%	N%	Cl%
1	152–154 (B)*	88	C ₁₈ H ₁₄ O ₆ (326)	66.61 66.26	4.17 4.29	— —	— —
2	212–214 (B/M)	90	C ₁₇ H ₁₂ O ₆ (312)	65.01 65.38	4.14 3.85	— —	— —
3	138–139 (L.P./B)	65	C ₁₇ H ₁₀ O ₅ (294)	69.92 69.39	3.56 3.40	— —	— —
4	205–207 (B/M)	78	C ₁₇ H ₁₀ O ₅ (294)	69.49 69.39	3.21 3.40	— —	— —
5	190–200 (M)	46	C ₂₇ H ₁₉ NO ₅ (437)	74.35 74.14	4.19 4.35	3.70 3.20	— —
6	196 (T)	42	C ₂₇ H ₁₇ NO ₈ Cl (518.5)	62.05 62.40	3.61 3.28	4.42 2.70	6.86 6.85
7a	92–94 (L.P.)	41	C ₃₃ H ₂₅ NO ₆ (531)	74.42 74.58	4.79 4.71	2.77 2.64	— —
7b	210–212 (B)	36	C ₃₂ H ₂₂ N ₂ O ₅ (514)	74.38 74.71	4.66 4.29	5.59 5.45	— —
7c	110–112 (L.P.)	38	C ₃₄ H ₂₇ NO ₇ (561)	72.87 72.73	4.59 4.81	2.58 2.50	— —
8a	220–221 (T)	69	C ₃₄ H ₂₅ NO ₄ (511)	79.82 79.84	4.81 4.89	2.61 2.74	— —
8b	240–242 (M)	65	C ₃₃ H ₂₃ NO ₄ (497)	79.63 79.68	4.66 4.63	2.61 2.82	— —
8c	213–215 (B)	72	C ₃₃ H ₂₉ NO ₄ (503)	78.51 78.73	5.88 5.77	2.87 2.78	— —
9a	260 (B/M)	32	C ₃₄ H ₂₅ NO ₄ (511)	79.55 79.84	5.14 4.89	2.78 2.74	— —
9b	206 (M)	35	C ₃₄ H ₂₅ NO ₅ (527)	77.17 77.42	4.91 4.74	2.82 2.66	— —
9c	182–184 (B)	42	C ₃₆ H ₂₉ NO ₄ (539)	80.03 80.15	5.29 5.38	2.82 2.60	— —
10a	214–216 (B)	73	C ₃₃ H ₂₄ N ₂ O ₄ (512)	77.13 77.34	4.79 4.69	5.10 5.47	— —
10b	220–222 (T)	69	C ₃₄ H ₂₆ N ₂ O ₄ (526)	77.33 77.57	5.21 4.94	5.50 5.32	— —
10c	191–192 (B)	60	C ₃₄ H ₂₆ N ₂ O ₅ (542)	75.17 75.28	4.90 4.80	5.11 5.17	— —
10d	146–148 (T)	54	C ₃₃ H ₂₃ N ₂ O ₄ Cl (546.5)	72.08 72.46	4.13 4.21	5.28 5.12	6.30 6.50
10e	253 (M)	70	C ₃₄ H ₂₆ N ₂ O ₄ (526)	77.19 77.57	5.20 4.94	5.23 5.32	— —

*B = benzene; M = methanol; L.P. = light petroleum 80–100°C; T = toluene.



precipitated substance was filtered off and recrystallized from the suitable solvent to give **2** (cf. Table 1).

IR spectrum of **2** showed a single absorption band at 1680 cm^{-1} for both aryl conjugated and α,β -unsaturated acids. The $^1\text{H-NMR}$ (CDCl_3) of **2** indicates the presence of olefinic and aromatic protons: δ 6.49 (s, 2H, O-CH₂-O), 7.46 (s, 1H, CH=C), 7.70–8.34 (m, 4H, Ar-H), 8.52–8.77 (m, 3H, Ar-H of piperonyl moiety), 10.74 (s, 1H, CO₂H) and 10.84 (s, 1H, CO₂H). The MS of **2** exhibited the following peaks: 312 (50), 294 (53), 249 (20), 193 (33), 165 (100), 152 (62), 135 (45), 63 (82) and 51 (39).

Conversion of the Diacid **2** to 3,4-Methylenedioxybenzylidene Homophthalic Anhydride **3**

Refluxing the diacid **2** (3.12 g, 0.01 mol) in acetyl chloride (35 mL, 0.5 mol) for 2 h, followed by distilling off the excess acetyl chloride afforded a yellow solid which upon recrystallization gave the anhydride **3** (cf. Table 1).

IR spectrum of **3** showed the carbonyl absorption bands at 1725 and 1790 cm^{-1} characteristic for six-membered ring anhydride fused aromatic system.¹⁰ The $^1\text{H-NMR}$ (DMSO-d_6) of **3**: δ 6.39 (s, 2H, O-CH₂-O), 7.51 (s, 1H, HC=C), 7.75–8.19 (m, 4H, Ar-H), 8.59–8.84 (m, 3H, Ar-H of piperonyl moiety). The MS of **3**: 294 (20), 264 (8), 249 (6), 257 (4), 221 (12), 192 (30), 180 (8), 163 (100), 152 (18), 137 (16), 129 (22), 111 (19), 101 (60), 87 (80), 75 (82), 63 (72) and 50 (37).

Action of Aluminium Chloride upon the Anhydride **3**; Formation of 2-(2-Carboxyphenyl)-5,6-methylenedioxyind-2-enone **4**

To a solution of the anhydride **3** (2.94 g; 0.01 mol) in excess acetylene tetrachloride (50 mL), anhydrous aluminium chloride (1.6 g; 0.012 mol) was added dropwise and the reaction mixture was stirred for 15 h at room temperature, left to stand overnight and hydrolyzed with ice-cold dilute hydrochloric acid. The solvent was removed by steam distillation and the product was taken up in ether, washed with Na₂CO₃ solution (10%). The alkaline extract on acidification afforded the oxoacid **4** (cf. Table 1).

IR spectrum of **4** exhibited $\nu_{\text{C=O}}$ at 1690 and 1700 cm^{-1} for aryl acid and ring ketonic functions.¹⁰ $^1\text{H-NMR}$ (CDCl_3) of **4** exhibited the following signals: δ 6.42 (s, 2H, O-CH₂-O), 7.42–8.18 (m, 5H, Ar-H), 8.81 (s, 1H, Ar-H of piperonyl moiety), 8.98 (s, 1H, Ar-H of piperonyl moiety) and



10.81 (s, 1H, COOH). The MS of **4**: 294 (38), 250 (100), 220 (20), 173 (14), 148 (3), 120 (46) and 77 (65).

Action of 1-Naphthylamine on the Cyclic Anhydride **3;
Formation of 2-[*N*-(1-Naphthyl)carboxamido]-3,4-
methylenedioxybenzylidene-phenylacetic Acid **5****

A solution of **3** (2.94 g; 0.01 mol) and 1-naphthylamine (1.43 g; 0.01 mol) in 50 mL of benzene was refluxed for 4 h. Most of the solvent was distilled off and the solid that separated out after cooling was collected by suction and recrystallized from suitable solvent to give **5** (cf. Table 1).

IR spectrum of **5** exhibited two absorption bands at 1668 and 1703 cm^{-1} characteristic for $\nu_{\text{C=O}}$ (amide) and $\nu_{\text{C=O}}$ (α,β -unsaturated acid). The $^1\text{H-NMR}$ (CDCl_3) of **5** exhibited the following signals: δ 6.46 (s, 2H, O-CH₂-O), 7.48 (s, 1H, HC=C), 7.63–8.28 (m, 11H, Ar-H), 8.45–8.77 (m, 3H, Ar-H of piperonyl moiety) and 10.77 (s, 1H, COOH). The MS of **5**: 437 (61), 419 (32), 393 (8), 315 (24), 267 (20), 251 (12), 222 (100), 170 (12), 143 (9) and 77 (37).

**Reaction of *N*-(1-Naphthyl)-3,4-methylenedioxybenzylidene
Homophthalamic Acid **5** with Acetic Anhydride and Perchloric Acid;
Formation of *N*-(1-Naphthyl)-3,4-methylenedioxybenzylidene
Homophthalisoimidium Perchlorate **6****

Perchloric acid (10 mL) was slowly added for 15 min to a suspension of **5** (4.37 g; 0.01 mol) in freshly distilled acetic anhydride (100 mL) kept in an ice bath. The solid salt that precipitated was collected by filtration, washed with petroleum ether (60–80°C), dried and recrystallized from the proper solvent to afford **6** (cf. Table 1).

IR spectrum of **6** was found to be consistent with the proposed structure. Thus compound **6** displayed $\nu_{\text{C=O}}$ at 1830 cm^{-1} together with strong absorption band at 1662 cm^{-1} ($\nu_{\text{C=N}^+}$). The $^1\text{H-NMR}$ (DMSO-d_6) of **6**: δ 6.39 (s, 2H, O-CH₂-O), 6.27–7.95 (m, 12H, Ar-H and HC=C^+), 8.50–8.78 (m, 3H, Ar-H of piperonyl moiety) and 9.00 (s, 1H, $=\text{N}^+\text{H}$).



**Reaction of 6 with Active Methylene Containing Compounds
Namely: Ethyl Acetoacetate, Ethyl Cyanoacetate, and Diethyl
Malonate; Formation of the Lactams 7a–c**

A solution of **6** (5.19 g; 0.01 mol) in pyridine (30 mL) was stirred with the appropriate active methylene compound (0.1 mol) at room temperature for 1 h. The reaction solution was left overnight, then, cold hydrochloric acid was added with stirring. The solid that deposited down was collected by filtration and recrystallized from the suitable solvent (cf. Table 1).

IR spectrum of **7** showed one carbonyl absorption band at ca. 1685–1672 (6-membered lactam). The ¹H-NMR (DMSO-*d*₆) of **7b**: δ 1.66 (t, 3H, CH₂CH₃), 3.97 (q, 2H, CH₂CH₃), 6.42 (s, 2H, O-CH₂-O), 6.27–7.85 (m, 12H, Ar-H and HC=C) and 8.42–8.57 (m, 3H, Ar-H of piperonyl moiety).

**Reaction of 6 with Grignard Reagents; Formation of
Aralkyl-2-[N-(1-naphthyl)carboxamido]-3,4-
methylenedioxybenzylidenebenzyl Ketone 8a–c**

A solution of the appropriate Grignard's reagent (0.3 mol) in dry ether (50 mL) was added dropwise to a solution of **6** (5.19 g; 0.01 mol) in dry ether (50 mL) with occasional shaking. The reaction mixture was refluxed for 6 h on water bath, then left overnight and decomposed with saturated aqueous ammonium chloride solution. The organic layer was separated then evaporated to afford the crude solid product which recrystallized to afford **8** (cf. Table 1).

IR spectra of **8** showed two absorption bands for the carbonyl stretching frequencies of ketones and amides at ca. 1695 and 1662 cm^{−1} as well as ν_{NH} of amides at ca. 3310 cm^{−1}. The ¹H-NMR (DMSO-*d*₆) of **8a** exhibited the following signals: δ 4.06 (s, 2H, -CH₂C₆H₅), 5.57 (s, 1H, -NH), 6.42 (s, 2H, O-CH₂-O), 7.54 (s, 1H, HC=C) and 7.72–7.93 (m, 5H, Ar-H of benzyl moiety), 8.10–8.33 (m, 11H, Ar-H) and 8.42–8.57 (m, 3H, Ar-H of piperonyl moiety).

**Reaction of 6 with Aromatic Hydrocarbons; Formation
of Hydroxy-3,4-methylenedioxybenzylidene
Homophthalimidine Derivatives 9a–c**

To a stirred cold solution or suspension of **6** (5.19 g; 0.01 mol) in aromatic hydrocarbon (50 mL), anhydrous AlCl₃ (0.03 mol) was added portionwise. The mixture was, then stirred for 5 h at room temperature and left overnight, then, hydrolyzed with ice cold hydrochloric acid. The resulting



organic product was filtered off, washed with cold water, dried and crystallized from the proper solvent to give **9** (cf. Table 1).

IR spectra of **9** exhibited one carbonyl absorption band at ca. $1674\text{--}1660\text{ cm}^{-1}$ and a broad band at $3100\text{--}3460\text{ cm}^{-1}$ (ν_{OH}). The $^1\text{H-NMR}$ (DMSO-d_6) of **9b** exhibited the following signals: δ 3.27 (s, 3H, OCH_3), 5.81 (s, 1H, OH), 6.45 (s, 2H, $\text{O-CH}_2\text{-O}$), 7.69 (s, 1H, HC=C) and 7.80–8.54 (m, 18H, Ar-H).

Reaction of **6** with Primary Aromatic Amines; Formation of *N,N'*-Disubstituted-3,4-methylenedioxybenzylidine Homophthalamide **10a–e**

Compound **6** (5.19 g; 0.01 mol) was added to a stirred solution of the appropriate amine (0.01 mol) namely, aniline, *p*-toluidine, *p*-anisidine, *p*-chloroaniline and benzylamine in benzene (30 ml). The reaction mixture was then stirred for one hour at room temperature. Excess solvent was distilled off to afford a solid product which on recrystallization from suitable solvent gave **10a–e** (cf. Table 1).

IR spectra of **10** exhibited $\nu_{\text{C=O}}$ at $1652\text{--}1636\text{ cm}^{-1}$ (amide) and ν_{NH} at $3250\text{--}3152\text{ cm}^{-1}$. The $^1\text{H-NMR}$ (DMSO-d_6) of **10b** showed the following signals: δ 2.00 (s, 3H, CH_3), 5.54 (s, def., 2H, 2NH), 6.42 (s, 2H, $\text{O-CH}_2\text{-O}$), 7.69 (s, 1H, HC=C) and 7.81–8.54 (m, 18H, Ar-H).

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