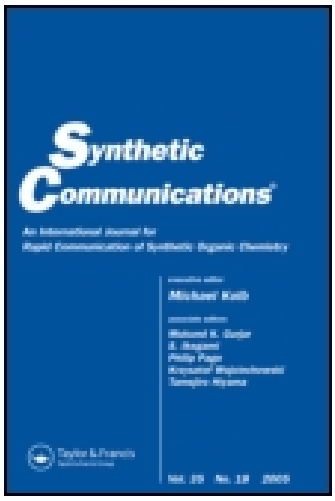


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Efficient Sonochemical Synthesis of 3- and 4-Electron Withdrawing Ring Substituted N-Alkyl-1,8-naphthalimides from the Related Anhydrides

Eduardo Rezende Triboni [a] , Pedro Berci Filho [a] , Roberto Gomes de Souza Berlinck [a] & Mario José Politi [b]

[a] Instituto de Química de São Carlos , Universidade de São Paulo , CP 780, CEP 13560-970, São Carlos, SP, Brazil

[b] Instituto de Química , Universidade de São Paulo , São Paulo, SP, Brazil

Published online: 20 Aug 2006.

To cite this article: Eduardo Rezende Triboni , Pedro Berci Filho , Roberto Gomes de Souza Berlinck & Mario José Politi (2004) Efficient Sonochemical Synthesis of 3- and 4-Electron Withdrawing Ring Substituted N-Alkyl-1,8-naphthalimides from the Related Anhydrides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:11, 1989-1999, DOI: 10.1081/SCC-120037911

To link to this article: http://dx.doi.org/10.1081/SCC-120037911

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 11, pp. 1989–1999, 2004

Efficient Sonochemical Synthesis of 3- and 4-Electron Withdrawing Ring Substituted *N*-Alkyl-1,8-naphthalimides from the Related Anhydrides

Eduardo Rezende Triboni,[1] Pedro Berci Filho,[1,*] Roberto Gomes de Souza Berlinck,[1] and Mario José Politi[2]

[1]Instituto de Química de São Carlos, Universidade de São Paulo, São Carlos, SP, Brazil
[2]Instituto de Química, Universidade de São Paulo, São Paulo SP, Brazil

ABSTRACT

1,8-*N*-alkyl-naphthalimides substituted with electron withdrawing groups were readily prepared in high yields using ultrasound in aqueous media.

Key Words: *N*-alkyl-1,8-naphthalimides; Sonochemistry; Aqueous media; Alkyl derivative; Heterogeneous sonochemistry; Alkyl amines.

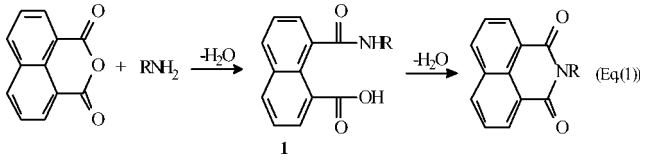
*Correspondence: Pedro Berci Filho, Instituto de Química de São Carlos, Universidade de São Paulo, CP 780, CEP 13560-970, São Carlos, SP, Brazil; E-mail: berci@iqsc.usp.br.

DOI: 10.1081/SCC-120037911 0039-7911 (Print); 1532-2432 (Online)

INTRODUCTION

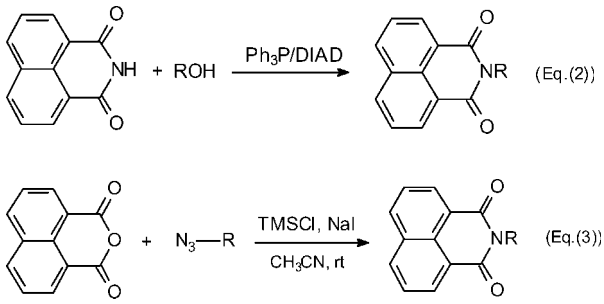
Naphthalimide derivatives are quite important as anti-neoplastic and anti-viral agents,[1–3] as fluorescent probes for a series of biological (probes of hypoxic cells,[4] DNA cleaving agents,[5] and fluorescent reporters[6]) and non-biological (optical brighteners, day-light fluorescent pigments[7]) applications. Naphthalimides have also been utilized as probes in several biophysical and photophysical studies in both homogeneous and micro-heterogeneous media.[8,9]

Despite numerous studies involving 1,8-naphthalimides, there are very few routes for the synthesis of *N*-alkyl derivatives.[4,10] Two well-established methods have been described: the *N*-alkylation of the 1,8-naphthalimide potassium salt with alkyl halides[11] and a more general method[10] involving the reaction of an amine with 1,8-naphthalic anhydride under reflux, followed by the cyclization of the corresponding *N*-substituted amic **1** intermediate [Eq. (1)].



1

More sophisticated or recent methods are the Mitsunobu reaction[12] [Eq. (2)] and the reaction of an aryl azide with naphthalic anhydride in the presence of iodomethylsilane[13] [Eq. (3)].



Substituents on 1,8-naphthalic anhydrides play a decisive role on their reactivity toward amines in the overall imidization process,[14] determining the conditions to be employed, which are largely solvent-dependent.[10] The reactivity pattern follows this "rule of thumb": *N*-alkyl-1,8-naphthalimides bearing electron-donating substituents, such as –OR, –NHR, Cl, and Br, are smoothly obtained in protic solvents like water,[15,16] methanol,[17] and ethanol,[18,19] giving moderate to good yields. On the other hand,

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

N-alkyl-1,8-naphthalimides with substituents that withdraw electrons, such as a nitro group, are better prepared in polar aprotic medium[20] like DMSO, DMSO/THF, DMF, and NMP, giving poor to moderate yields.

The present work reports the aqueous sonochemical synthesis of 4-nitro-*N*-alkyl-1,8-naphthalimides and other *N*-alkyl imides with electron withdrawing sustituents attached on the naphthalene ring.

Sonication of 4-nitro-1,8-naphthalic anhydride in aqueous suspension employing lower primary amines as nucleophiles gave the corresponding imides **2e**–**2i** in high yield (Table 1). No amic acid intermediates or nitro displacement side products could be detected, suggesting a tandem reaction[21] pattern with high regioselectivity. The reaction mechanism appears to follow the proposed pathways for the imidization reaction in protic solvents,[22] showing no sonochemical switching effect.[23]

This sonochemical method was also highly effective for the synthesis of the unsubstituted *N*-alkyl-1,8-naphthalimide derivatives **2a**–**2d**, as well as for the 4-chloro **2j**–**2n** (Table 1) and 3-nitro **3a**–**3d** substituted derivatives (Table 2 and Sch. 1).

In contrast, no reaction was observed between ethylamine and 4-nitro-1,8-naphthalic anhydride. This should be due to some intrinsic sonochemical interference, since this reaction can be carry out by other conventional

Table 1. Derivatives of 4-substituted *N*-alkyl-1,8-naphthalimides.

Product	R_1	R_2	Yield (%)[a]	Time (hr)
2a	Me	H	84[b]	1.5
2b	Et	H	57[c]	3
2c	*n*-Propyl	H	30[d]	4
2d	*n*-Butyl	H	41[c]	2
2e	Me	NO_2	96[b]	1.5
2f	Et	NO_2	—	—
2g	*n*-Propyl	NO_2	75[b]	2
2h	*n*-Butyl	NO_2	80[b]	2
2i	Allyl	NO_2	85[b]	2.5
2j	Me	Cl	80[b]	2
2l	Et	Cl	80[d]	2.5
2m	*n*-Propyl	Cl	70[d]	3
2n	*n*-Butyl	Cl	50[c]	2

[a]Isolated yield.
[b]Without need of purification.
[c]Purified by recrystallization (from ethanol).
[d]Purified by flash chromatography (chloroform/silica-gel); Sonicating bath US 150 W/25 kHz.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 2. Derivatives of 3-nitro-*N*-alkyl-1,8-naphthalimides.

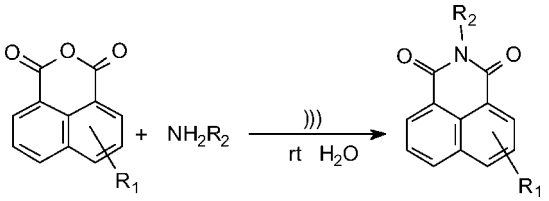
Product	R_1	Yield (%)[a]	Time (hr)
3a	Me	95	1.5
3b	Et	89	1.5
3c	*n*-Propyl	83	1.5
3d	*n*-Butyl	71	1.5

[a]Isolated yield with no need of purification. Sonicating bath US 150 W/25 kHz.

synthetic routes and works well to the 3-nitro isomer. The use of an ultrasonic apparatus with different specifications (150 W/25 kHz and 50 W/45 kHz) did not cause significant changes in the overall yield or in the reactions time.

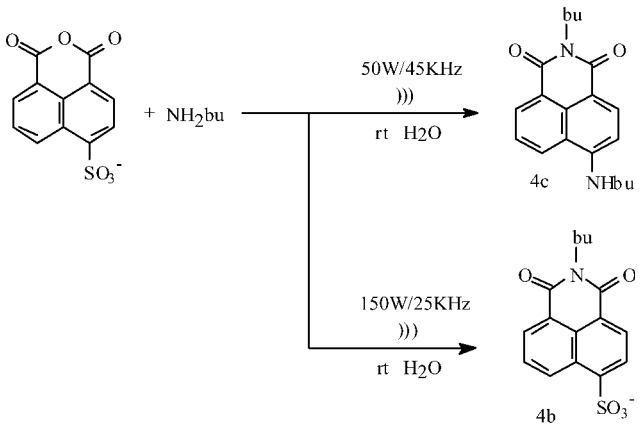
Since the aforesaid results would be due simply to a mixing effect, the same reactions were performed under magnetic stirring conditions (silent mode), giving very poor yields and in some cases no reaction at all. The sonochemical imidization results presented here are in agreement with the literature and follow general trend for sonochemical ionic reactions.[24,25] In this study, the undesired solvolytic processes usually provided by sonication[25] did not interfere with the desired reactions.

Finally, we studied the extension of this sonochemical procedure to an aqueous homogeneous solution. Sonication of potassium 4-sulfonic-1,8-naphthalic anhydride in aqueous solution with *n*-butylamine led to a more complex reaction approach (Sch. 2). The sonication with an ultrasonic cleaner of 50 W and 45 kHz resulted in loss of reaction selectivity, 4-*n*-butylamino-*N*-butyl-1,8-naphthalimide **4c** being the only detectable product. At the same time, the sonication with an ultrasonic cleaner of 150 W and 25 kHz yielded 4-sulfonic-*N*-butyl-1,8-naphthalimide **4b** as the only product (Table 3). The explanation of this behavior, which is dependent on sonochemical conditions, requires further studies.



Scheme 1. Imidization of 3- and 4-substituted-1,8-naphthalic anhydrides in heterogeneous media. R_2 = methyl, ethyl, *n*-propyl, *n*-butyl; R_1 = H, NO_2, Cl;))) = sonication.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Scheme 2. Imidization of 4-sulfonic-1,8-naphthalic anhydride in homogeneous media.

In conclusion, we developed a new sonochemical method for the synthesis of *N*-alkyl-1,8-naphthalimides in aqueous media, resulting in a shorter reaction times, a "cleaner" final products and in a greater yields.

EXPERIMENTAL

General Procedures

All 1,8-naphthalic anhydrides were purchased from Aldrich. The amines: *n*-butylamine (Carlo Erba), *n*-propylamine (Acros), Allylamine (Acros), ethylamine 70% aqueous solution (Fluka), and methylamine 40% aqueous solution (Fluka) were used without further purification. Water utilized in the experiments was doubly distilled. Other solvents were of spectroscopic

Table 3. Derivatives of 4-sulfonic-*N*-alkyl-1,8-naphthalimides.

Product	R_1	R_2	Yield (%)[a]	Time (hr)
4a	Me	SO_3H	88[b]	1.5
4b	*n*-Butyl	SO_3H	85[b]	1.5
4c	*n*-Butyl	*n*-Butyl	93[c]	0.5

[a]Isolated yield.
[b]US 150 W/25 kHz.
[c]US 50 W/45 KHz.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

grade and used without further purification. Melting points were determined in an electrothermal melting point apparatus. ^{1}H-NMR spectra were recorded on a Bruker AC-200 in $CDCl_3$ and DMSO-d_6. The chemical shifts were reported as parts per million (δ, ppm) from TMS as an internal standard. Infrared (IR) spectra were recorded on a BOMEM-MB 102-FT-IR spectrometer, employing KBr plates. Capillary GC analyses were performed on a HP-5890 coupled to a MSD-5970 mass selective detector. Two ultrasonic cleaner baths (Bransonic) 150 W/25 kHz and 50 kHz/40 kHz were used.

Method A (For Heterogeneous Suspension)

To a suspension of 4- or 3-nitro- or 4-chloro-1,8-naphthalic anhydride (1 mmol for all compounds) and 50 mL of distilled water in a 125-mL Erlenmeyer flask was added 10 mmol of the primary amine. The suspension was submitted to sonication using an ultrasonic cleaning bath with 150 W and 25 kHz of power and frequency, respectively. In the course of the reaction, the temperature was kept at 22–25°C. After the reaction was completed, a diluted HCl solution was added and the crude product was filtered off and washed with water. The products were dried in a vacuum oven.

***N*-Methyl-1,8-naphthalimide 2a.** 84%; white crystals; mp 208–209°C (literature[26] = 204–205°C); IR (KBr) 3105, 2947, 1699, 1673, 1592, 1582, 1528, 1353, 1294, 1060 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 3.54 (s, 3H, CH_3), 7.72 (t, $J = 7.8$ Hz, 2H, Ar), 8.17 (d, $J = 7.8$ Hz, 2H, Ar), 8.68 (d, $J = 7.3$ Hz, 2H, Ar); MS (m/z) 211 (M^+, 100), 183, 167, 127, 75, 63; anal. calcd for $C_{13}H_8NO_2$: N, 6.66; C, 74.23; H, 3.85. Found: N, 6.64; C, 74.13; H, 3.87.

***N*-Ethyl-1,8-naphthalimide 2b.** 57%; white crystals; mp 156–157°C (literature[11] = 157°C); IR (KBr) 3485, 3057, 2980, 2872, 1696, 1655, 1599, 1540, 1370, 1070 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 1.94 (br s, 2H), 4.0 (br s, 2H), 4.48 (br s, 1H), 7.78 (t, $J = 7.8$ Hz, 2H, Ar), 8.22 (d, $J = 8.1$ Hz, 2H, Ar), 8.61 (d, $J = 6.66$ Hz, 2H, Ar); MS (m/z) 210, 198 (100), 180, 152, 126, 75, 63; anal. calcd for $C_{14}H_{10}NO_2$: N, 6.25; C, 75.01; H, 4.46. Found: N, 6.28; C, 74.88; H, 4.46.

***N*-Propyl-1,8-naphthamide 2c.** 30%; white crystals; mp 164–165°C (literature[11] = 160°C); IR (KBr) 3079, 2961, 2875, 1707, 1661, 1526, 1346, 1235, 1080 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 0.914 (t, 3H, CH_3), 1.64 (sextet, 2H, CH_2), 4.0 (t, 2H, CH_2), 7.85–7.92 (m, 2H, Ar), 8.46–8.51 (m, 4H, Ar); MS (m/z) 239 (M^+), 197 (100), 180, 154, 126, 75, 63, 41; anal. calcd for $C_{15}H_{12}NO_2$: N, 5.88; C, 75.63; H, 5.04. Found: N, 5.85; C, 75.53; H, 5.11.

***N*-Butyl-1,8-naphthalimide 2d.** 41%; white crystals; mp 92–94°C (literature[11] = 97–98°C); IR (KBr) 3075, 2948, 1697, 1658, 1623, 1589,

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

1352, 1266, 1073 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.94 (t, 3H, CH_3), 1.56 (sextet, 2H, CH_2), 1.69 (quintet, 2H, CH_2), 4.17 (t, 2H, CH_2), 7.73 (t, $J = 7.5$ Hz, 2H, Ar), 8.18 (d, $J = 8.3$ Hz, 2H, Ar), 8.58 (d, $J = 7.2$ Hz, 2H, Ar); MS (m/z) 253 (M^+), 211, 197 (100), 180, 152, 126, 77; anal. calcd for $C_{16}H_{14}NO_2$: N, 5.55; C, 76.20; H, 5.55. Found: N, 5.47; C, 76.32; H, 5.58.

4-Nitro-*N*-methyl-1,8-naphthalimide 2e. 96%; yellow crystals; mp 208–209°C (literature[27] = 207–208°C); IR (KBr) 3083, 2956, 1696, 1659, 1595, 1537, 1336, 1278, 1078 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 3.60 (s, 3H, CH_3), 7.98 (t, $J = 7.9$ Hz, 1H, Ar), 8.41 (d, $J = 7.9$ Hz, 1H, Ar), 8.38 (d, $J = 7.94$ Hz, 1H, Ar), 8.67–8.85 (m, 3H, Ar); MS (m/z) 256 (M^+, 100), 210, 198, 182, 153, 125, 99, 75; anal. calcd for $C_{13}H_8N_2O_4$: N, 10.93; C, 60. 93; H, 3.09. Found: N, 10.75; C, 61.11; H, 3.07.

4-Nitro-*N*-propyl-1,8-naphthalimide 2f. 75%; yellow crystals; mp 135–136°C (literature[27] = 135.5–136.5°C); IR (KBr) 3079, 2961, 2875, 1707, 1661, 1623, 1526, 1346, 1235, 1079 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 0.92 (t, 3H, CH_3), 1.65 (sextet, 2H, CH_2), 3.98 (t, 2H, CH_2), 8.0 (t, $J = 7.3$ Hz, 1H, Ar), 8.47-8.72 (m, 4H, Ar); MS (m/z) 284 (100, M^+), 243, 255, 209, 179, 151, 126, 75, 41; anal. calcd for $C_{15}H_{12}N_2O_4$: N, 9.85; C, 63.38; H, 4.22. Found: N, 9.98; C, 63.60; H, 4.27.

4-Nitro-*N*-butyl-1,8-naphthalimide 2g. 80%; yellow needles; mp 103.5–104°C (literature[27] = 103.5–104.5°C); IR (KBr) 3074, 2961, 2872, 1706, 1656, 1624, 1530, 1347, 1231, 1082 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.96 (t, 3H, CH_3), 1.56 (sextet, 2H, CH_2), 1.72 (quintet, 2H, CH_2), 4.18 (t, 2H, CH_2), 7.96 (t, $J = 8.0$ Hz, 1H, Ar), 8.38 (d, $J = 8.0$ Hz, 1H, Ar), 8.67–8.86 (m, 3H, Ar); MS (m/z) 298 (M^+, 100), 256, 243, 225, 209, 179, 151, 126, 75; anal. calcd for $C_{16}H_{14}N_2O_4$: N, 9.39; C, 64.42; H, 4.69. Found: N, 9.33; C, 64.38; H, 4.72.

4-Nitro-*N*-allyl-1,8-naphthalimide 2h. 85%; yellow crystals; mp 104–105°C; IR (KBr) 3084, 2917, 1708, 1661, 1530, 1336, 1233, 1096 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 4.83 (d, 2H, CH_2), 5.23 (d, 1H, CH_2), 5.35 (d, 1H, CH_2), 6.0 (m, 1H, CH), 7.82 (t, 1H, Ar), 8.41 (d, 1H, Ar), 8.72 (d, 1H, Ar), 8.76 (d, 1H, Ar), 8.86 (d, 1H, Ar); MS (m/z) 282 (M^+), 267 (100), 237, 221, 179, 151, 125; anal. calcd for $C_{16}H_{14}N_2O_4$: N, 9.92; C, 63.83; H, 3.54. Found: N, 10.02; C, 63.87; H, 3.63.

4-Chloro-*N*-methyl-1,8-naphthalimide 2i. 80%; white crystals; mp 170–171°C (literature[11] = 174–175°C); IR (KBr) 3057, 2951, 2861, 1696, 1664, 1623, 1569, 1347, 1283, 1034 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 3.55 (s, 3H, CH_3), 7.80–7.91 (m, 2H, Ar), 8.5 (d, $J = 7.94$ Hz, 1H, Ar), 8.58–8.71 (m, 2H, Ar); MS (m/z) 245 (M^+, 100), 217, 188, 166, 125, 99, 75, 32; anal. calcd for $C_{13}H_8NClO_2$: N, 5.71; C, 63.56; H, 3.26. Found: N, 5.64; C, 63.48; H, 3.24.

4-Chloro-*N*-ethyl-1,8-naphthalimide 2j. 80%; white crystals; mp 167–168°C (literature[11] = 165–166°C); IR (KBr) 3385, 3068, 2968, 2888, 1695,

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

1660, 1624, 1365, 1235, 1060 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 3.61 (q, $J = 6.0$ Hz, 2H), 4.12 (t, $J = 6.3$ Hz, 2H), 4.79 (t, $J = 6.3$ Hz, 1H), 7.91–8.0 (m, 2H, Ar), 8.37 (d, $J = 7.96$ Hz, 1H, Ar), 8.50–8.54 (m, 2H, Ar); MS (m/z) 244, 232(100), 214, 160, 126, 75; anal. calcd for $C_{14}H_{10}NClO_2$: N, 5.39; C, 64.76; H, 3.85. Found: N, 5.52; C, 64.59; H, 3.82.

4-Chloro-*N*-propyl-1,8-naphthalimide 2l. 70%; white crystals; mp 141–142°C (literature[11] = 142.5–143°C); IR (KBr) 3065, 2952, 2870, 1696, 1664, 1624, 1569, 1352, 1236, 1071 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 0.91 (t, 3H, CH_3), 1.63 (sextet, 2H, CH_2), 3.97 (t, 2H, CH_2), 7.91–8.0 (m, 2H, Ar), 8.35–8.14 (m, 3H, Ar); MS (m/z) 273 (M^+), 231 (100), 214, 187, 160, 126, 75, 41; anal. calcd for $C_{15}H_{12}NClO_2$: N, 5.12; C, 65.83; H, 4.38. Found: N, 5.11; C, 65.73; H, 4.26.

4-Chloro-*N*-butyl-1,8-naphthalimide 2m. 50%; white needles; mp 89–90°C (literature[11] = 92–94°C); IR (KBr) 2954, 1701, 1652, 1589, 1461, 1350, 1076 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.95 (t, 3H, CH_3), 1.54 (sextet, 2H, CH_2), 1.69 (quintet, 2H, CH_2), 4.15 (t, 2H, CH_2), 7.7–7.9 (m, 2H, Ar), 8.4–8.6 (m, 3H, Ar); MS (m/z) 287 (M^+), 247, 231 (100), 214, 186, 160, 126, 75; anal. calcd for $C_{16}H_{14}NClO_2$: N, 4.87; C, 66.80; H, 4.87. Found: N, 4.80; C, 66.95; H, 4.87.

3-Nitro-*N*-methyl-1,8-naphthalimide 3a. 95%; yellow crystals; mp 204–205°C; IR (KBr) 3083, 2956, 1696, 1659, 1624, 1537, 1336, 1278, 1070 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 3.58 (s, 3H, CH_3), 7.94 (t, $J = 8.0$ Hz, 1H, Ar), 8.43 (d, $J = 8.2$ Hz, 1H, Ar), 8.79 (d, $J = 8.0$ Hz, 1H, Ar), 9.13 (d, $J = 2.2$ Hz, 1H, Ar), 9.31 (d, $J = 2.2$ Hz, 1H, Ar); MS (m/z) 256 (M^+, 100), 210, 198, 182, 153, 125, 99, 75; anal. calcd for $C_{13}H_8N_2O_4$: N, 10.93; C, 60.93; H, 3.12. Found: N, 10.88; C, 60.82; H, 3.12.

3-Nitro-*N*-ethyl-1,8-naphthalimide 3b. 89%; yellow crystals; mp 231–232°C; IR (KBr) 3383, 3051, 2986, 1697, 1655, 1624, 1540, 1335, 1080 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 3.64 (br s, 2H), 4.14 (t, $J = 5.5$ Hz, 2H), 4.8 (br s, 1H), 8.02 (t, $J = 8.3$ Hz, 1H, Ar), 8.63 (d, $J = 7.2$ Hz, 1H, Ar), 8.73 (d, $J = 8.4$ Hz, 1H, Ar), 8.91 (d, $J = 2.0$ Hz, 1H, Ar), 9.43 (d, $J = 2.3$ Hz, 1H, Ar); MS (m/z) 255, 243 (100), 225, 197, 171, 126, 75, 32; anal. calcd for $C_{14}H_{10}N_2O_4$: N, 10.37; C, 62.22; H, 3.70. Found: N, 10.45; C, 60.31; H, 3.76.

3-Nitro-*N*-propyl-1,8-naphthalimide 3c. 83%; yellow crystals; mp 166–167°C; IR (KBr) 3087, 2959, 2871, 1702, 1660, 1542, 1351, 1243, 1085 cm^{-1}, ^{1}H-NMR (DMSO-d_6) δ 0.925 (t, 3H, CH_3), 1.65 (sextet, 2H, CH_2), 4.0 (t, 2H, CH_2), 8.0 (t, $J = 8.0$ Hz, 1H, Ar), 8.61 (d, $J = 7.1$ Hz, 1H, Ar), 8.64 (d, $J = 7.2$ Hz, 1H, Ar), 8.91 (d, $J = 2.3$ Hz, 1H, Ar), 9.41 (d, $J = 2.3$ Hz, 1H, Ar); MS (m/z) 284 (100, M^+); 243, 209, 179, 153, 126, 75, 41; anal. calcd for $C_{15}H_{12}N_2O_4$: N, 9.85; C, 63.38; H, 4.22. Found: N, 9.78; C, 63.48; H, 4.17.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

3-Nitro-*N*-butyl-1,8-naphthalimide 3d. 71%; yellow crystals; mp 97.5–98°C (literature[27] = 98–98.5°C); IR (KBr) 3082, 2956, 1706, 1663, 1595, 1545, 1348, 1234, 1087 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.92 (t, 3H, CH_3), 1.57 (sextet, 2H, CH_2), 1.72 (quintet, 2H, CH_2), 4.18 (t, 2H, CH_2), 7.92 (t, $J = 7.24$ Hz, 1H, Ar), 8.39 (d, $J = 8.2$ Hz, 1H, Ar), 8.74 (d, $J = 7.2$ Hz, 1H, Ar), 9.11 (d, $J = 2.4$ Hz, 1H, Ar), 9.28 (d, $J = 2.4$ Hz, 1H, Ar); MS (m/z) 298 (M^+, 100), 243, 225, 209, 179, 151, 126, 75; anal. calcd for $C_{16}H_{14}N_2O_4$: N, 9.39; C, 64.43; H, 4.69. Found: N, 9.38; C, 64.53; H, 4.60.

Method B (For Homogeneous Solution)

To a solution of potassium 4-sulfonic-1,8-naphthalic anhydride (1 mmol) in 50 mL of distilled water in a 125-mL Erlenmeyer flask was added 10 mmol of the primary amine. The solution was sonicated using ultrasonic cleaning baths with 150 W/25 kHz or 50 W/40 kHz of power and frequency, respectively. The temperature was maintained between 22 and 25°C. After the reaction was completed, the solvent was evaporated under vacuum and the crude product washed with diethyl ether. The products were dried in a vacuum oven.

4-Sulfonic-*N*-methyl-1,8-naphthalimide acid 4a. 88%; yellow needles; IR (KBr) 3094, 2960, 2857, 1693, 1639, 1589, 1349, 1231, 1160, 1067 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 2.88 (s, 3H, CH_3), 7.35 (t, 1H, Ar), 7.68–7.80 (m, 3H, Ar), 8.39 (d, 1H, Ar).

4-Sulfonic-*N*-butyl-1,8-naphthalimide acid 4b. 85%; yellow needles; IR (KBr) 3092, 2956, 2857, 1707, 1652, 1587, 1348, 1225, 1160, 1077 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.98 (t, 3H, CH_3), 1.55 (sextet, 2H, CH_2), 1.70 (quintet, 2H, CH_2), 4.21 (t, 2H, CH_2), 7.65 (t, 1H, Ar), 8.01–8.21 (m, 3H, Ar), 8.69 (d, 1H, Ar).

4-Butyl-*N*-butyl-1,8-naphthalimide 4c. 93%; yellow crystals; mp 125–126°C (literature[20] = 127–128°C); IR (KBr) 3346, 2956, 1701, 1658, 1589, 1201, 1084 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 0.93–1.06 (m, 6H, $2CH_3$), 1.34–1.87 (m, 8H, $4CH_2$), 3.17 (q, 2H, CH_2), 4.16 (t, 2H, CH_2), 5.18–5.25 (br s, 1H, NH), 6.72 (d, $J = 8.2$ Hz, 1H, Ar), 7.67 (t, $J = 8.4$ Hz, 1H, Ar), 8.06 (d, $J = 7.3$ Hz, 1H, Ar), 8.46 (d, $J = 8.4$ Hz, 1H, Ar), 8.57 (d, $J = 7.3$ Hz, 1H, Ar); MS (m/z) 324 (M^+), 307, 271, 268, 225, 207, 182 (100), 154; anal. calcd for $C_{16}H_{14}N_2O_4$: N, 8.64; C, 70.07; H, 7.40. Found: N, 8.62; C, 70.05; H, 7.25.

ACKNOWLEDGMENTS

The authors thank FAPESP for providing financial support, CNPq and CAPES for a scholarship to ERT. The authors thank Dr. Frank H. Quina (IQ–USP) for useful discussions.

REFERENCES

1. Middleton, R.W.; Parrick, J.; Clark, D.E.; Wardman, P. Synthesis and fluorescence of *N*-substituted 1,8-naphthalimides. J. Heterocyclic. Chem. **1986**, *23*, 849–855.
2. Chanh, T.C.; Lewis, D.E.; Allan, J.S.; Soganders-Bernal; Judy, M.M.; Utecht, R.E.; Mattheus, J.L. Neutralization of HIV-1 and inhibition of HIV-1-induced syncytia by 1,8-naphthalimide photoactive compound. AIDS Res. Human Retrov. **1993**, *9*, 891–896.
3. Chang, S.; Utrech, R.E.; Lewis, D.E. Synthesis and bromination of 4-alkylamino-*N*-alkyl-1,8-naphthalimides. Dyes Pigments **1999**, *43*, 83–94.
4. Middleton, R.W.; Parrick, J. Preparation of 1,8-naphthalimides as candidate fluorescent probes of hypoxic cells. J. Heterocyclic. Chem. **1985**, *22*, 1567–1572.
5. Saito, I. Photochemistry of highly organized biomolecules: sequence-selective photoreaction of DNA. Pure Appl. Chem. **1992**, *64*, 1305–1310.
6. Dubey, K.K.; Singh, R.K.; Misra, K. A novel bifunctional fluorescent tag for use in molecular-biology. Ind. J. Chem. **1995**, *34B*, 876–878.
7. Haremsa, S. Naphthalimide dyes and pigments. In *Ullman's Encyclopedia of Industrial Chemistry*; Elvers, B., Hawkins, S., Eds.; VCH: Basel, (Switzerland), 1991; Vol. 17, 59–65.
8. Barros, T.C.; Berci Filho, P.; Toscano, V.G.; Politi, M.J. Intramolecular excimer formation from 1,8-*N*-alkyldinaphthalimides. J. Photochem. Photob. A: Chem. **1995**, *89*, 141–146.
9. Brochsztain, S.; Rodrigues, M.A.; Politi, M.J. Inclusion complexes of naphthalimides derivatives with cyclodextrins. J. Photochem. Photob. A: Chem. **1997**, *107*, 195–200.
10. Alexiou, M.S.; Tychopoulos, V.; Ghorbanian, S.; Tyman, J.H.P.; Brown, R. The UV-visible absorption and fluorescence of some substituted 1,8-naphthalimides and naphthalic anhydrides. J. Chem. Soc. Perkin Trans. 2 **1990**, 837–842.
11. Karishin, A.P.; Baklan, V.F. *N*-alkyl derivatives of naphthalimide and halonaphthalimides. Zhur. Obshchei Khim. **1959**, *29*, 3048; Chem. Abstr. **1960**, *54*, 13,073.
12. Hamilton, D.G.; Feeder, N.; Teat, S.J.; Sanders, J.K.M. Reversible synthesis of π-associated [2] catenanes by ring-closing metathesis: towards dynamic combinatorial libraries of catenanes. New J. Chem. **1998**, *22*, 1019–1021.
13. Kamal, A.; Laxman, E.; Laxman, N.; Rao Venugopal, N. Efficient one-pot synthesis of *N*-substituted phthalimides/naphthalimides from azides and anhydrides by iodotrimethylsilane. Tetrahedron Lett. **1998**, *39*, 8733–8734.
14. Silva, D.; Machado, V.G.; Nome, F. In *Studies of 1,8 Naphthalic Anhydrides Aminolysis. The Effect of the Substituent and Amine Structure*

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

(Portuguese); Proceedings of the 25th Brazilian Chemistry Society (SBQ) Congress, Poços de Caldas, Brazil, May 20–23, 2002.
15. Kasay, T. Novel 4-Alkoxy Naphthalimides. US Patent Off. 3, 310, 564, March 21, 1967.
16. Yuan, D.; Brown, R.G. The effect of pH on the absorption and fluorescence properties of some 4-amino-*N*-alkylamino-1,8-naphthalimides. J. Chem. Res. (M) **1994**, 2345–2363.
17. Konstantinova, T.; Meallier, P.; Grabchev, I. The synthesis of some 1,8-naphthalic anhydride derivatives as dyes for polymeric materials. Dyes Pigments **1993**, *22*, 191–198.
18. Tyman, J.; Ghorbanian, S.; Muir, M.; Tychopoulous, V.; Bruce, I.; Fisher, I. Improved nucleophilic displacements in *N*-methyl pyrrolidinone as a solvent. Synth. Commun. **1989**, *19* (1,2), 179–188.
19. Rama Chandran, B.; Sankaran, N.B.; Karmakar, R.; Saha, S.; Samanta, A. Fluorescence signalling of transition metal ions by multi-component systems comprising 4-chloro-1,8-naphthalimide as fluorophore. Tetrahedron **2000**, *56*, 7041–7044.
20. Alexiou, M.S.; Tyman, J.H.P. The synthesis of alkylamino-*N*-alkyl-naphthalic-1,8-imides from 2- and 4-nitronaphthalic anhydrides by nitro group displacement. J. Chem. Res. (M) **2000**, 633–636.
21. Ho, T.-L. *Tandem Organic Reactions*; John Wiley and Sons: New York, 1992.
22. Perry, C.J.; Parveen, Z. The cyclization of substituted phthalanilic acids in acetic acid solution. A kinetic study of substituted *N*-phenylphthalimide formation. J. Chem. Soc. Perkin Trans. 2 **2001**, 512–521.
23. Ando, T.; Sumi, S.; Kawate, T.; Ichihana, J.; Hanafusa, T. Sonochemical switching of reaction pathways in solid–liquid two-phase reactions. J. C. S. Commun. **1984**, 439–440.
24. Mason, T.J. Ultrasound in synthetic organic chemistry. Chem. Soc. Rev. **1997**, *26*, 443–451.
25. Luche, J.L. Sonochemical activation in organic synthesis. Part 1. C. R. Acad. Sci. Paris, Serie II **1996**, *323*, 203–213.
26. Gompper, R. The course of the methylation of carboxylic acid amides with diazomethanes. Chem. Ber. **1960**, *93*, 198–209; Chem. Abstr. **1960**, *54*, 9955.
27. Okazaki, M.; Tanaka, T.; Taniguchi, S. Derivatives of 4-aminonaphthalimide. Yûki Gôsei Kagaku Kyôkai Shi **1956**, *14*, 344; Chem. Abstr. **1957**, *51*, 8050.

Received in the USA October 2, 2003

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016