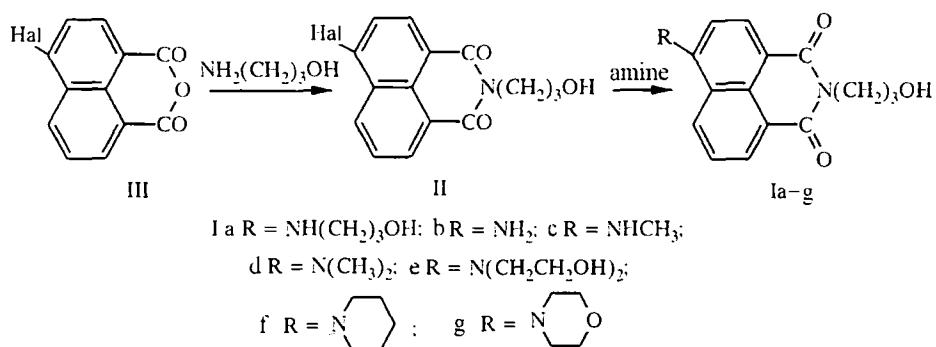


SYNTHESIS OF HYDROXYL
CONTAINING N-IMIDES
OF 4-SUBSTITUTED
NAPHTHALIC ACID

R. A. Minakova, A. I. Bedrik, V. M. Shershukov, Yu. N. Surov, and N. S. Pivnenko

A convenient, one-step method for synthesis of the N-(3-hydroxypropyl)imide of 4-(3'-hydroxypropyl)-aminonaphthalic acid is proposed. It has been found that ethylene glycol monoethyl ether can be successfully used to replace solvents previously used for these reactions.

Naphthalic acid derivatives are widely used as efficient luminophores with a yellow-green luminescence, especially high values being shown for derivatives in this series which contain groups like amino, sulfamido, carboxy etc. [1, 2]. Amongst these, the most important position is occupied by hydroxyl containing naphthalimide derivatives. We have synthesized N-(3-hydroxypropyl)imides of 4-substituted naphthalic acids Ia-g containing electron donor substituents (including hydroxypropyl) in the naphthalene ring.



Substituted naphthalimides are usually synthesized in two stages [3]. In the first there is formed an imide through the reaction of 4-chloronaphthalic anhydride and a primary amine and in the second the prepared imide is heated in DMF with the corresponding amine. It is noteworthy that 1-aminopropan-3-ol undergoes reaction with chloronaphthalic anhydride (III) with significantly greater difficulty (yield 25%) than various aliphatic and even aromatic amines. Using IR spectroscopy, we have shown that a prolonged reaction time gives rise to an increase in the probability of an alternative reaction involving the hydroxyl group in acetic acid medium, i.e. formation of a compound with an ester group. Moreover, in the second stage there arises the possibility of halogen atom exchange for a dimethylamino group in DMF. This reaction becomes predominant upon lowering the basicity of the amine used in the reaction [4]. Because both stages involve bimolecular nucleophilic substitution reactions, the reaction rate can be increased by increasing the dielectric constant and the polarity of the solvent. We conclude that the optimal solvent appropriate for technological use must be ethyl cellosolve which has a higher dielectric constant and dipole moment than acetic acid, DMF, and N-methylpyrrole, while remaining a proton donor. In fact, use of ethyl cellosolve in the synthesis of the naphthalimide Ia give good results (yield 70%).

Institute of Monocrystals, Ukrainian Academy of Sciences, Kharkov 310001. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 692-695, May, 1999. Original article submitted April 14, 1998.

TABLE 1. Characteristics of Synthesized Compounds

| Compound | Empirical formula | Found, % | | | mp, °C | λ_{max} , nm | UV spectrum (ϵ) | IR spectrum, ν , cm ⁻¹ | Yield, % |
|----------|---|----------------|--------------|----------------|-----------|-----------------------------|-------------------------------|---------------------------------------|----------|
| | | C | H | N | | | | | |
| Ia | C ₁₈ H ₂₀ N ₂ O ₄ | 68.90 68.98 | 6.20 6.09 | 8.50 5.53 | 203...204 | 422 | 12265 | 1670 1643 | 70 |
| Ib | C ₁₃ H ₁₄ N ₂ O ₃ | 75.38 75.50 | 4.72 4.63 | 10.20 10.37 | 198...199 | 405 | 9509 | 1673 1663 | 35 |
| Ic | C ₁₆ H ₁₆ N ₂ O ₃ | 67.43 67.60 | 5.34 5.07 | 9.72 9.85 | 229...230 | 415 | 10500 | 1670 1658 | 60 |
| Id | C ₁₇ H ₁₈ N ₂ O ₃ | 68.69 68.45 | 5.87 6.04 | 9.15 9.40 | 128...129 | 405 | 9750 | 1690 1655 | 65 |
| Ie | C ₁₉ H ₂₂ N ₂ O ₅ | 63.81 63.69 | 6.29 6.15 | 7.57 7.82 | 209...210 | 405 | 10050 | 1685 1648 | 67 |
| If | C ₂₀ H ₂₂ N ₂ O ₃ | 70.85 71.00 | 6.36 6.50 | 8.09 8.28 | 118...119 | 401 | 9654 | 1690 1657 | 62 |
| Ig | C ₁₉ H ₂₀ N ₂ O ₄ | 66.89 67.06 | 5.73 5.88 | 8.05 8.23 | 127...128 | 390 | 9762 | 1680 1650 | 70 |

For the synthesis of N-(3-hydroxypropyl)imides of the 4-substituted naphthalic acids Ib,c,d,f,g which do not contain a hydroxyl group in the naphthalene ring, the first stage is carried out in ethyl cellosolve and the second (depending on the basicity of the amine) can be carried out both in ethyl cellosolve and in DMF. Aqueous solutions of the amines (methylamine, dimethylamine) are employed in a two to threefold excess. In the case of N-imides of 4-chloronaphthalic anhydride where the reaction with ammonia occurs only under pressure, compound Ib was synthesized by reduction of the N-(3-hydroxypropyl)imide of 4-nitronaphthalic acid.

Besides the fact that the use of ethyl cellosolve excludes secondary reactions, it has a number of advantages in a technical sense.

The IR spectra of the synthesized compounds show a marked lowering of the stretching frequency for the carbonyl group when compared with the starting anhydride and this agrees well with literature data [5] for cyclic imides of dicarboxylic acids. Substituents in the naphthalene ring have little effect on $\nu_{C=O}$. The PMR spectra of the investigated compounds show characteristic multiplets for the naphthalene fragment, the methylene chain of the aminopropanol, and the proton containing groups of the substituent (see Experimental section). Investigation of the absorption spectra in toluene confirm the structure of the compounds prepared since they absorb in the region 390-417 nm which is a characteristic of imides of substituted naphthalic acids (Table 1).

EXPERIMENTAL

PMR spectra were obtained on a Tesla BS-487A spectrophotometer at 80 MHz using TMS as internal standard and $CDCl_3$ as solvent. IR Spectra were recorded on a Specord IR-75 instrument for KBr tablets. Absorption spectra were measured on a Specord M-40 instrument using toluene as solvent.

N-(3-Hydroxypropyl)imide of 4-(3'-Hydroxypropyl)aminonaphthalic Acid (Ia). A mixture of 4-chloronaphthalic anhydride (11.6 g, 0.05 mol), 1-aminopropan-3-ol (12 ml, 0.16 mol), and ethyl cellosolve (60 ml) was refluxed for 6 h. The reaction mixture was cooled, slowly poured into iced water (300 ml), and held at room temperature for 15 h. The precipitate formed was filtered off and refluxed for 30 min in an aqueous solution of sodium carbonate (3%, 300 ml). The precipitate was filtered off, washed with water to a neutral and dried. Yield 11.3 g (70%); mp 203-204°C (benzene). Found, %: N 8.50. $C_{18}H_{20}N_2O_4$. Calculated, %: N 8.53.

N-(3-Hydroxypropyl)imide of 4-Nitronaphthalic Acid. A mixture of 4-nitronaphthalic anhydride (4.8 g, 0.02 mol) and 1-aminopropan-3-ol (1.9 g, 0.025 mol) was refluxed for 6 h in ethyl cellosolve (50 ml). The reaction mixture was cooled and slowly poured into cold water (200 ml). The precipitate formed was filtered off, washed with water, and refluxed for 30 min in aqueous sodium carbonate solution (3%, 100 ml). The hot mixture was filtered, the precipitate was washed with water to neutrality using a solution of hydrochloric acid (7%) and then water. Yield 4 g (70%); mp 132°C (propan-2-ol). Found, %: N 9.10. $C_{15}H_{12}N_2O_5$. Calculated, %: N 9.33.

N-(3-Hydroxypropyl)imide of 4-Chloronaphthalic Acid (II) was obtained similarly. Yield 64%; mp 95°C. Found, %: N 4.60; Cl 12.10. $C_{15}H_{12}NO_3Cl$. Calculated, %: N 4.83; Cl 12.26.

N-(3-Hydroxypropyl)imide of 4-Aminonaphthalic Acid (Ib). A hot solution of $SnCl_2$ (28 g, 0.14 mol) in conc. hydrochloric acid (28 g) was added gradually to a refluxing solution of the N-(3-hydroxypropyl)imide of 4-nitronaphthalic acid (7 g, 0.023 mol) in propanol (200 ml). The mixture was refluxed for 3 h, cooled, and filtered. The precipitate was refluxed in aqueous NaOH solution (10%, 100 ml), filtered, and washed with water to neutrality. Yield 2.2 g (35%); mp 198-199°C (toluene). Found, %: N 10.20. $C_{15}H_{14}N_2O_3$. Calculated, %: N 10.37.

N-(3-Hydroxypropyl)imide of 4-Methylaminonaphthalic Acid (Ic). Aqueous methylamine solution (33%, 5.4 ml, 0.06 mol) was added in four portions (once per hour) to a refluxing solution of hydroxyimide II (5.8 g, 0.02 mol) in ethyl cellosolve (40 ml). After the addition of the last portion of methylamine, the reaction mixture was refluxed for 3 h, cooled, poured into iced water (200 ml), and left for 15 h. The precipitate was filtered off and dried. Yield 3.4 g (60%); mp 229-230°C (toluene). Found, %: N 9.72. $C_{16}H_{16}N_2O_3$. Calculated, %: N 9.85.

The remaining **N-(3-hydroxypropyl)imides of 4-Naphthalic Acids** were obtained similarly but an equimolar amount of the amine was added at once (see Table 1). PMR spectrum (**compound Id**): 2.90 (1H, s, OH); 2.05 (2H, m, 2'-CH₂); 3.10 (6H, s, N(CH₃)₂); 4.17 (2H, t, J = 7.3 Hz, OCH₂); 4.26 (2H, t, J = 6.2 Hz, CH₂);

7.11 (1H, d, 3-H); 7.64 (1H, dd, 6-H); 8.43 (1H, d, 5-H); 8.44 (1H, d, 2-H); 8.53 ppm (1H, d, 7-H). (**Compound If**): 2.90 (1H, s, OH); 2.05 (2H, m, 2'-CH₂); 1.80 (6H, m, (CH₂)₃); 3.26 (4H, m, N(CH₂)₂); 4.17 (2H, m, N-CH₂); 4.26 (2H, t, OCH₂); 7.66 (1H, dd, 6-H); 8.39 (1H, d, 5-H); 7.18 (1H, d, 3-H); 8.48 (1H, d, 2-H); 8.56 ppm (1H, d, 7-H). (**Compound Ig**): 2.90 (1H, s, OH); 2.05 (2H, m, 2'-CH₂); 3.26 (4H, m, N(CH₂)₂); 4.03 (4H, m, O(CH₂)₂); 4.17 (2H, t, N-CH₂); 4.26 (2H, t, OCH₂); 7.69 (1H, dd, 6-H); 8.41 (1H, d, 5-H); 7.23 (1H, d, 3-H); 8.51 (1H, d, 2-H); 8.56 ppm (1H, d, 7-H).

REFERENCES

1. L. N. Sal'vitskaya, T. V. Chumak, D. G. Pereyaslova, and E. E. Panasenko, *Organic Luminescent Materials* [in Russian]. Science Symposium Transactions, All Union Science Research Institute for Monocrystals, Kharkov (1989), No. 24, p. 139.
2. L. N. Sal'vitskaya, D. G. Pereyaslova, N. M. Golovina, and T. T. Kudinova, *Plastics*, No. 1, 44 (1986).
3. B. M. Krasovitskii, É. A. Shevchenko, and V. B. Distanov, *Zh. Org. Khim.*, **19**, 1305 (1983).
4. Kh. A. Kazhoka and I. A. Meirovits, *Izv. Akad. Nauk Latv. SSR, Ser. Khim.*, No. 5, 620 (1982).
5. L. J. Bellamy, *Infrared Spectra of Complex Molecules* [Russian translation], Inostr. Lit., Moscow (1963), p. 590.