SHORT PAPER

J. Chem. Research (S),
2002, 136–138

Reaction of 4-amino-3-hydroxy-1-naphthalenesulfonic acid with orthoesters: a new facile one-pot synthesis of 2-substituted naphth[1,2-d]oxazole-5-sulfonates†

Mohammad S. Khajavi* and Ali A. Mohammadi

Department of Chemistry, Faculty of Sciences, Shahid Beheshti University, Shahid Chamran Highway, Evin 19834, Tehran, Iran

The synthesis of 2-substituted naphth[1,2-d]oxazole-5-sulfonate by the reaction of 4-amino-3-hydroxy-1-naphthalenesulfonic acid and orthoesters under classical heating and microwave irradiation is described.

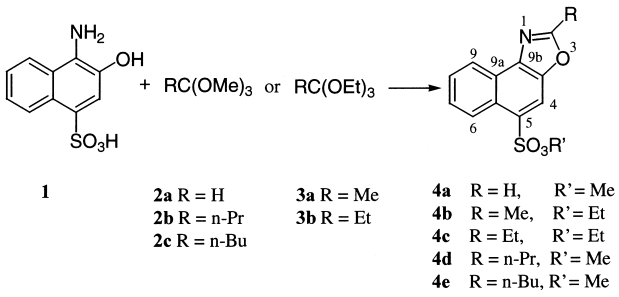
Keywords: 4-amino-3-hydroxy-1-naphthalenesulfonic acid, orthoesters, 2-substituted naphth[1,2-d]oxazole synthesis

Naphth[1,2-d]oxazoles are an important class of condensed heterocyclic compounds because of their potential applications in different fields such as sensitising dyes in photographic material,[1] fluorescent whitening agents,[2] dyestuffs,[3] and biological activity.[4] A number of synthetic routes for the preparation of 2-substituted naphth[1,2-d]oxazoles have been described. The most common approaches are: (i) the oxidation of the imines formed from 1-amino-2-naphthol and appropriate aromatic aldehydes,[3] (ii) the interaction of 1-nitroso-2-naphthol with various arylmethylamines,[3a, 5] (iii) the 1,3-dipolar cycloaddition of 3-aroylaziridines to 1-nitroso-2-naphthol,[6] (iv) the reaction of acetic anhydride with aminonaphthols,[7] and (v) by means of the Horner–Wadsworth–Emmons reaction.[4] Here we wish to report a convenient efficient one-flask procedure for the synthesis of ethyl or methyl 2-substituted naphth[1,2-d]oxazole-5-sulfonate by the simultaneous esterification and oxazole ring formation of 4-amino-3-hydroxy-1-naphthalenesulfonic acid with orthoesters under classical heating or microwave irradiation.

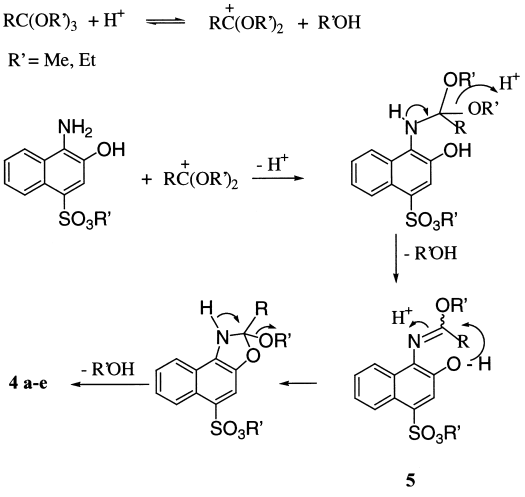
Following our earlier studies on the efficient synthesis of 2-substituted 4*H*-3,1-benzoxazin-4-ones,[8] quinazolin-4(3*H*)-ones[9] and 6-substituted benzimidazo[1,2-c] quinazolines[10] from appropriate starting materials and orthoesters, we have found that the esterification and oxazole ring formation occurs by refluxing the various commercially available orthoesters **(2a–c** and **3a–b)** with 4-amino-3-hydroxy-1-naphthalenesulfonic acid **(1)** under dry conditions (Scheme 1). Thus the parent heterocyclic compound, methyl naphth[1,2-d] oxazole-5-sulfonate **(4a)** was prepared in 72% yield by heating a mixture of **(1)** with an excess of trimethyl orthoformate. It has been reported earlier that **(1)** upon fusion with formamide, is converted to naphth[1,2-d]oxazole-5-sulfonic acid at 220°C in 30 % yield.[11] The esterifications of sulfonic acids and carboxylic acids by trimethyl or triethyl orthoformate previously have been reported.[12]

Furthermore, in the case of orthoesters **(2b–c** and **3b)** it was found that addition of a catalytic amount of *p*-toluenesulfonic acid is required to increase the yields and to perform the reaction in a shorter time. All products **(4a–e)** were precipitated from reaction mixtures upon cooling and were purified by recrystallisation from ethanol. The reaction proceeds without organic solvent. The optimised results are summarised in Table 1. The structures of products **(4a–e)** were characterised by IR, ^{1}H NMR, ^{13}C NMR spectral and elemental analyses.

The reaction path way seems to proceed through the imidic ester intermediate **(5)** which undergoes the nucleophilic attack



Scheme 1



Scheme 2

by the imminent hydroxyl group to produce the oxazole ring with the elimination of a molecule of alcohol (Scheme 2).

We then examined this reaction under microwave irradiation[13] and found that process results in the rapid formation of ethyl or methyl 2-substituted naphth[1,2-d]oxazole-5-sulfonate **(4a–e)**. The reactions were performed in open vessels in a microwave oven and in order to increase the energy input to the reaction mixture in a shorter time and also providing a uniform heating, a small amount of N, N-dimethylacetamide (DMAC), an excellent energy-transfer solvent with a high dielectric constant, was added to the reaction mixture (Table 1). To control the heating process and to avoid vaporisation of the orthoesters from the reaction mixture the following procedure was adapted: (i) the irradiation sequence were interrupted with a cooling period in between; (ii) for each irradiation sequence, a different power was used (Table 1), the first

* To receive any correspondence.
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Reaction of 4-amino-3-hydroxy-1-naphthalenesulfonic acid with orthoesters

		Conventional heating		Irradiation conditions[a]					
Entry	Product	Time /h	Yield /%[b]	P/W (1)	Time /min	P (W) (2)	Time /min	DMAC /ml	Yield /%[b]
1	**4a**	4	72	210	2	210	2	1	65
2	**4b**	4	75	210	2	385	3	1	84
3	**4c**	6	68	210	3	385	3	1	86
4	**4d**	6	83	210	3	385	1.5	0.8	77
5	**4e**	6	80	210	2	385	1.5	0.5	82

[a]To control the reaction, the irradiation was carried out in two stages, with a cooling period between each radiation.

[b]Yields of pure isolated product based on 4-amino-3-hydroxy-1-naphthalenesulfonic acid.

one with a lower energy input to initiate the reaction; and (iii) all reactions were performed in a tall beaker covered with a stemless funnel. By applying these, higher degrees of conversion of the reactants were observed. The results are summarised in Table 1.

In conclusion, we have demonstrated that orthoesters and 4-amino-3-hydroxy-1-naphthalenesulfonic acid react under conventional thermal heating or microwave irradiation, providing a convenient one-step procedure for the preparation of esters of 2-substituted naphth[1,2-d]oxazole-5-sulfonate. The especial features of this method are the high purity of products and simple work-up. In these reactions, the orthoesters serve as a ''one-atom linchpin'' to form the oxazole ring.

Experimental

IR spectra were measured on a Shimadzu IR-470 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured using a JEOL EX-90A spectrometer at 90 and 22.63 MHz respectively. Elemental analyses were performed using a Heracus CHN-O-Rapid analyser. N, N-Dimethylacetamide was freshly distilled from BaO. Microwave irradiation were carried out in a National oven, model 5250, at 2450 MHz. Melting points were determined in open capillary tubes using a Thomas-Hoover apparatus and are uncorrected. 4-Amino-3-hydroxy-1-naphthalenesulfonic acid and all the orthoesters were purchased from Aldrich and were used without further purification.

General procedure under conventional heating: A stirred mixture of 4-amino-3-hydroxy-1-naphthalenesulfonic acid (1.20 g, 5 mmol) and (a) trimethly orthoformate (11 ml, 0.1 mol); (b) triethyl orthoacetate (7.3 ml, 40 mmol); (c) triethyl orthopropinate (8.0 ml, 40 mmol) and a catalytic amount of PTSA; (d) trimethyl orthobutyrate (6.4 ml, 40 mmol) and a catalytic amount of PTSA; (e) trimethyl orthovalerate (6.9 ml, 40 mmol) and a catalytic amount of PTSA in a 25 ml flask was heated to reflux for the time period as indicated in Table 1. Then the flask was disconnected and transferred to a fractional distillation assembly with a short fractionating column. Heating was continued until the reaction mixture began to boil and once the distillation of methyl or ethyl alcohol had commenced, heating was continued to maintain the distillation of alcohol. After the distillation was complete, a mixture of water/ice (30 ml) was added to the reaction mixture. The precipitate was filtered and the yellowish solid material thus obtained was recrystallised from ethanol to give the desired compound.

General procedure under microwave irradiation: A mixture of 4-amino-3-hydroxy-1-naphthalenesulfonic acid (1.20 g, 5 mmol) and (a) trimethly orthoformate (11 ml, 0.1 mol) and DMAC (1 ml), (b) triethyl orthoacetate (7.3 ml, 40 mmol) and DMAC (1 ml), (c) triethyl orthopropionate (8.0 ml, 40 mmol) and DMAC (1 ml) plus a catalytic amount of PTSA, (d) trimethyl orthobutyrate (6.4 ml, 40 mmol) and 0.8 ml of DMAC plus a catalytic amount of PTSA, (e) trimethyl orthovalerate (6.9 ml, 40 mmol) and DMAC (0.5 ml) plus a catalytic amount of PTSA, in a tall beaker was placed in the microwave oven. The beaker was covered with a stemless funnel and irradiated with power and time as indicated in Table 1. Then the reaction mixture was allowed to cool to room temperature. A mixture of water/ice (30 ml) was added and the yellow solid precipitate was collected with filtration which after drying it was recrystallised from ethanol to give pure products.

4a: White powder; m.p. 121–122°C (decom); IR (KBr): ν max/cm^{-1} 3100, 1618, 1582, 1332, 1239, 1182, 1155; ^{1}H NMR ($CDCl_3$): δ ppm 3.74 (s, 3H, OCH_3), 7.65–8.82 (m, 6H, Ar–H and oxazole-H);.^{13}C NMR($CDCl_3$): δppm 56.73 (OCH_3), 116.71, 122.94, 125.87, 126.64, 127.71, 128.03, 128.43, 128.84 (C_4–C_9, C_{5a} and C_{9a}), 144.80, 154.69 (C_{3a} and C_{9b}), 177.38 (C_2); Calcd. for $C_{12}H_9NO_4S$; C, 54.74; H, 3.45; N, 5.32. Found: C, 54.43; H, 3.38; N, 5.14.

4b: White powder; m.p. 205–206°C; IR (KBr): ν max/cm^{-1} 3075, 2925, 1583, 1551, 1345, 1231, 1162; ^{1}H NMR ($CDCl_3$): δ ppm 1.20 (t, 3H, CH_3), 2.78 (s, 3H, CH_3), 4.17 (q, 2H, OCH_2), 7.62–8.83 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$): δppm 14.65 (CH_3), 15.83 (C_2-Me), 67.52 (OCH_2), 116.12, 122.88, 125.68, 126.37, 126.78, 127.32, 127.83, 128.16 (C_4–C_9, C_{5a} and C_{9a}), 142.22, 145.33 (C_{3a} and C_{9b}), 172.43 (C_2); Calcd. for $C_{14}H_{13}NO_4S$; C, 57.72; H, 4.49; N, 4.81. Found: C, 57.80; H, 4.41; N, 4.72.

4c: White powder; m.p. 160–162°C; IR (KBr): ν max/cm^{-1} 3070, 2930, 1622, 1586, 1550, 1513, 1346, 1217, 1153; ^{1}H NMR ($CDCl_3$): δ ppm 1.17 (t, 3H, CH_3), 1.42 (t, 3H, CH_3), 3.15 (q, 2H, CH_2), 4.17 (q, 2H, OCH_2), 7.65–8.79 (m, 5H, Ar-H); ^{13}C NMR ($CDCl_3$): δppm 11.12 (C_2–Me), 14.70 (CH_3), 22.48 (C_2–CH_2), 67.47 (CH_2), 115.93, 122.89, 125.74, 126.52, 126.72, 127.49, 127.86, 128.11 (C_4–C_9, C_{5a} and C_{9a}), 142.07, 145.29 (C_{3a} and C_{9b}), 170.98 (C_2); Calcd. for $C_{15}H_{15}NO_4S$; C, 58.99; H, 4.95; N, 4.59. Found: C, 58.84; H, 4.74; N, 4.63.

4d: White powder; m.p. 128–130°C; IR (KBr): ν max/cm^{-1} 3080, 2952, 1621, 1583, 1546, 1522, 1353, 1249, 1160, 1146; ^{1}H NMR ($CDCl_3$): δ ppm 1.17 (t, 3H, CH_3), 2.02 (m, 2H, CH_2), 3.09 (t, 2H, CH_2), 3.66 (s, 3H, OCH_3), 7.62–8.81 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$): δ ppm 18.76, 20.48, 30.74 (3C-aliphatic), 56.64 (OCH_3), 116.38, 122.86, 125.62, 126.48, 126.68, 126.93, 127.58, 127.91 (C_4–C_9, C_{5a} and C_{9a}), 142.19, 145.21 (C_{3a} and C_{9b}), 170.21 (C_2); Calcd. for $C_{15}H_{15}NO_4S$: C, 58.99; H, 4.95; N, 4.59; found: C, 59.05; H, 4.90; N,4.70.

4e: White powder; m.p. 120–122°C; IR (KBr): ν max/cm^{-1} 3065, 2933, 1622, 1581, 1546, 1352, 1262, 1174; ^{1}H NMR ($CDCl_3$): δ ppm 1.02 (t, 3H, CH_3), 1.23–1.61 (m, 2H, CH_2), 1.64–2.25 (m ,2H, CH_2), 3.11 (t, 2H, CH_2), 3.81 (s, 3H, OCH_3), 7.42–8.86 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$): δ ppm 13.64, 22.27, 28.54, 28.95 (4C-aliphatic), 56.60 (OCH_3), 116.29, 122.85, 125.62, 126.47, 126.64, 126.88, 127.54, 127.86 (C_4–C_9, C_{5a} and C_{9a}), 142.19, 145.17(C_{3a} and C_{9b}), 170.36 (C_2); Calcd. for $C_{16}H_{17}NO_4S$:C, 60.17; H, 5.36; N, 4.39; found: C, 59.64; H, 5.30; N, 4.20.

Received 27 July 2001; accepted 8 September 2001
Paper 01/1004

References

1 (a) M. Yasumoto, Y. Taguchi and T. Tsucha, *Japan Kokai*, 06,220,028, *Chem. Abstr*., 1995, **122**: 10022k; (b) H. Takei and T. Ukai, *Japan Kokai*, 05,297,504, *Chem. Abstr*., 1994, **120**: 231889j; (c) S. Sudo, Y. Kawashima, M. Tanaka and R. Yamauchi, *Japan Kokai*, 05,100,349, *Chem. Abstr*., 1994, **120**: 231798d.

2 H.X. Kaempfen, *U.S. Pat*., 3,767,663, *Chem. Abstr*., 1974, **80**: 38391t.

3 (a) A.M. Osman and I. Bassiouni, *J. Org. Chem*., 1962, **27**, 558; (b) M.A. Abbady, *Ind. J. Chem., Sect. B*, 1979, 17B, 450.

4 T. Kosaka and T. Wakabayashi, *Heterocycles*, 1995, **41**, 477, and references cited therein.

5 R.R. Reddy, G.V. Reddy and C.V.C. Rao, *Indian J. Heterocycl. Chem*., 1994, **3**, 219

6 (a) J.W. Lown and J.P. Moser, *Can. J. Chem*., 1970, **48**, 2227; (b) J.W. Lown and J.P. Moser, *Chem. Commun*., 1970, 247.

7 (a) N.I. Fisher and F.M. Hamer, *J. Chem. Soc*., 1934, 962; (b) E.J. Cross, *J. Soc. Dyers Colourists*, 1962, **78**, 280.
8 M.S. Khajavi, N. Montazari and S.S.S. Hosseni, *J. Chem. Res*. (S), 1997, 286.
9 K. Rad-Moghadam and M.S. Khajavi, *J. Chem. Res*. (S), 1998, 702.
10 M.S. Khajavi, K. Rad-Moghadam and H. Hazarkhani, *Synth. Commun*., 1999, **29**, 2617.
11 A.M. Osman, M.S.K. Youssef and F.M. Atta, *J. Heterocyclic Chem*., 1982, **19**, 953.
12 A.A. Padmapriya, G. Just and N.G. Lewis, *Synth. Commun*., 1985, **15**, 1057.
13 For reviews on microwave assisted organic reaction see: (a) A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault and D. Mathe, *Synthesis*, 1998, 1213; (b) S. Caddick, *Tetrahedron*, 1995, **51**, 10403.