

# Efficient synthesis of 1,3-benzodioxin-4-one and benzoxazine-2,4-diones

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Submitted to honor the 75<sup>th</sup> anniversary of Jan Epsztajn

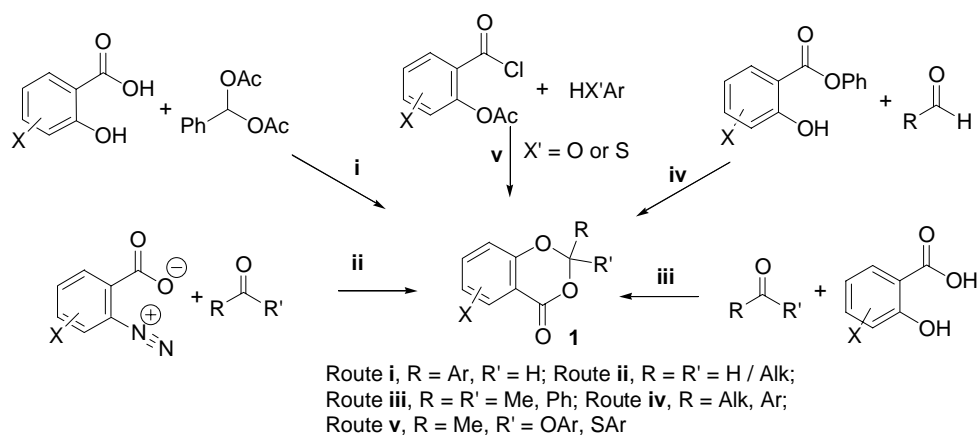
## Abstract

Reactions of stable *N*-(*o*-hydroxyarylacetyl)benzotriazoles **4a–c** / **6a–c** with various aldehydes in the presence of base afforded 1,3-benzodioxin-4-ones **1a–d** and naphtho-1,3-dioxinones **7a–c**. Reaction with isocyanates under similar conditions afforded high yields of benzoxazine-2,4-diones **2a–c** and naphthoxazine-1,3-diones **9a–b**.

**Keywords:** Benzotriazole, 1,3-benzodioxin-4-ones, benzoxazine-2,4-diones

## Introduction

1,3-Benzodioxin-4-ones **1** have been used (i) as protected forms of salicylic acids in the synthesis of salicylhalamide A and B, apicularen A<sup>1</sup> and gustastatin,<sup>2</sup> biologically active natural products and potential drug candidates<sup>1,3-5</sup> and (ii) for the flash photolytic generation of  $\alpha$ -oxo ketenes.<sup>2,6</sup>



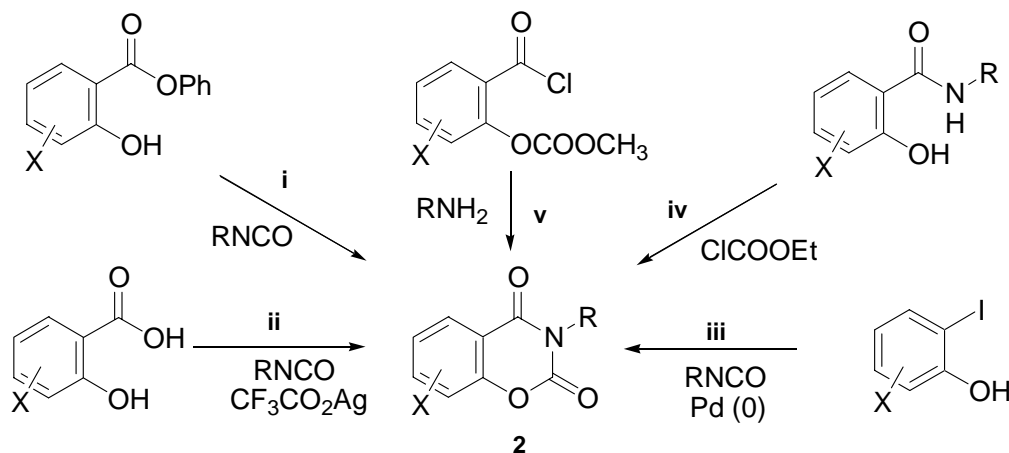
Scheme 1

Preparations (Scheme 1) of 1,3-benzodioxin-4-ones include i) the first description by Mowry,<sup>7</sup> ii) reaction between *o*-carboxybenzenediazonium salts and ketones,<sup>8</sup> iii) acid catalyzed synthesis from symmetrical ketones,<sup>2,9-11</sup> iv) base promoted reaction of phenyl salicylates with aliphatic aldehydes,<sup>12,13</sup> and v) reaction of *o*-acetoxybenzoyl chloride and phenols or thiophenols<sup>14</sup> which required the continuous removal of the HCl gas formed.

Aliphatic and heteroaryl aldehydes did not give the desired dioxinones under the conditions employed by Mowry<sup>7</sup> (Route i), while the reactions with aromatic aldehydes failed under the base-promoted conditions<sup>12</sup> (Route iv) (Scheme 1). One example has however been reported for the synthesis 1,3-benzodioxin-4-ones of aromatic aldehydes in the case of 4-methoxysalicylic acid.<sup>13</sup> Synthesis from *o*-carboxybenzenediazonium salts (Route ii) has limited synthetic utility since it is accompanied by the formation of phenol, salicylic acid and benzoic acid<sup>8</sup> (Scheme 1).

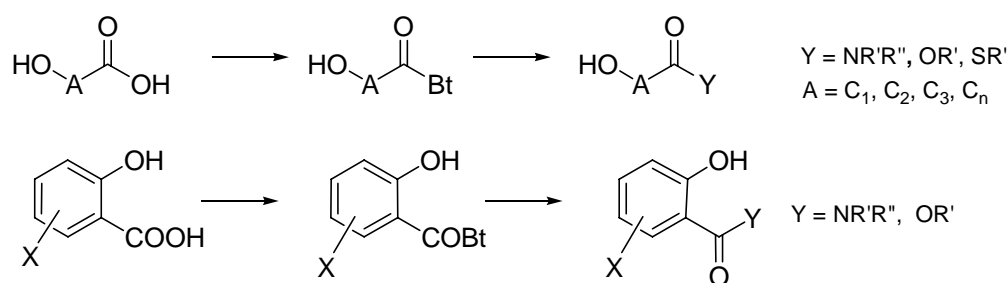
Benzoxazine-2,4-diones **2** (Scheme 2) have interested synthetic chemists due to their potential utilities in pharmacology<sup>15-17</sup> and photography.<sup>18</sup>

The reported methods for the synthesis of substituted benzoxazine-2,4-diones **2** include i) reaction of phenyl salicylates with isocyanates,<sup>19</sup> ii) silver trifluoroacetate mediated reaction of salicylic acid with isocyanates,<sup>20</sup> iii) palladium catalyzed cyclocarbonylation of *o*-iodophenols,<sup>21</sup> iv) reaction of salicylamides with ClCO<sub>2</sub>Et<sup>22-23</sup> and v) from 2-(methoxycarbonyloxy)benzoyl chloride<sup>24-25</sup> (Scheme 2).



**Scheme 2**

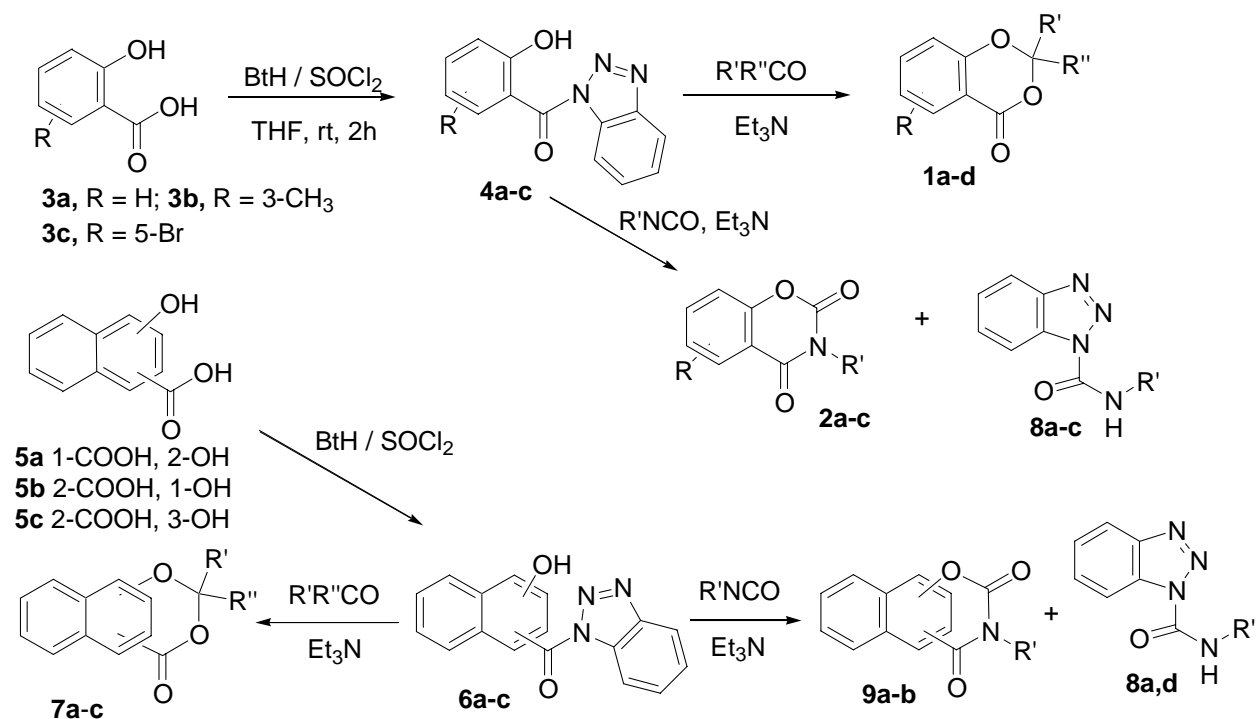
*N*-Acylbenzotriazoles<sup>26</sup> are versatile reagents for *N*-acylation,<sup>27</sup> formylation,<sup>28</sup> trifluoroacylation,<sup>29</sup> *O*-acylation,<sup>30</sup> *C*-acylation<sup>31-33</sup> and the synthesis of polycyclic heteroaromatics.<sup>34-36</sup> Recently, we utilized the *N*-(*o*-hydroxyarylacyl)benzotriazoles for the syntheses of *o*-hydroxyaryl esters / amides (Scheme 3).<sup>37</sup> Herein we report the successful use of the *N*-(*o*-hydroxyarylacyl)benzotriazoles **4** and **6** as substrates for the synthesis of 1,3-benzodioxin-4-ones **1**, **7** and benzoxazine-2,4-diones **2**, **9** (Scheme 4 and Tables 1, 2).



Scheme 3

## Results and Discussion

Crystalline *N*-(*o*-hydroxyarylacyl)benzotriazoles **4a–c** or **6a–c** isolated from corresponding salicylic acids,<sup>37</sup> were treated with 4 equivalents of the appropriate aromatic or aliphatic aldehyde in dry THF at room temperature along with 4 equivalents of triethyl amine to give **1a–d** and **7a–c** respectively in high yields (Scheme 4 and Table 1). Best results were obtained when the base was added to a well stirred mixture of aldehyde and acylbenzotriazoles **4a–c** or **6a–c**.



Scheme 4

Attempted reaction of *N*-(*o*-hydroxybenzoyl)benzotriazole **4a** with 4 equivalents of triethylamine and 1.2 equivalents of *p*-tolyl isocyanate gave a mixture of the desired compound **2a** (40%) along with the carbamoyl derivative **8a** (40%) (Scheme 4, Table 2). By using 2.2

equivalents of the isocyanate, both benzoxazine-2,4-dione **2a** and carbamoylbenzotriazole **8a** could be obtained in quantitative yields. The carbamoylbenzotriazoles **8** have been employed in our laboratories in the synthesis of various unsymmetrical ureas.<sup>38</sup> We were able to expand the method further to cover various aliphatic and aromatic isocyanates as shown in Table 2. In all cases, the benzoxazines were obtained in high yields. Employing similar reaction conditions as for the synthesis of **2** on *N*-(*o*-hydroxyarylacyl)benzotriazoles **6a–b**, other benzoxazinones **9a–b** were obtained (Scheme 4, Table 2). Sterically demanding isocyanates gave lower yields (Entry 5, Table 2).

**Table 1.** Synthesis of 1,3-benzodioxin-4-ones **1a–e** and naphtho-1,3-dioxinones **7a–d**

	<i>N</i> -Acylbenzotriazole	Product	R'	R''	Yield	Mp.
1	<b>4a</b>	<b>1a</b>	Et	H	94	Oil
2	<b>4b</b>	<b>1b</b>	Ph	H	52	83–84
3	<b>4c</b>	<b>1c</b>	Furan	H	75	87–89
4	<b>4b</b>	<b>1d</b>	Pr	H	92	62–64
5	<b>4b</b>	<b>1e</b>	(CH <sub>3</sub> ) <sub>2</sub> C:CH-	H	Mixtures	
6	<b>6a</b>	<b>7a</b>	Et	H	64	104–105
7	<b>6b</b>	<b>7b</b>	Neo-pentyl	H	75	106–108
8	<b>6b</b>	<b>7c</b>	Tolyl	H	61	242–243
9	<b>6c</b>	<b>7d</b>	PhCH:CH-	H	Mixtures	

**Table 2.** Synthesis of benzoxazin-2,4-diones **2a–c** and naphthoxazine-1,3-diones **9a–b**

	<i>N</i> -Acylbenzotriazole	R'	Product	Yield	Mp.
1	<b>4a</b>	<i>p</i> -Tolyl	<b>2a</b>	99	224–225
2	<b>4b</b>	<i>p</i> -Chlorophenyl	<b>2b</b>	Mixture	
3	<b>4c</b>	Benzyl	<b>2c</b>	96	152–154
4	<b>6a</b>	<i>p</i> -Tolyl	<b>9a</b>	86	257–258
5	<b>6b</b>	Isopropyl	<b>9b</b>	60	148–150

## Conclusions

A mild and high yielding process for synthesis of 1,3-benzodioxin-4-ones and benzoxazine-2,4-diones has been developed using benzotriazole chemistry. The synthesis of both 2-aryl and 2-alkyl 1,3-benzodioxin-4-one could be achieved under these conditions.

## Experimental Section

**General Procedures.** Melting points were determined on a hot-stage apparatus and are uncorrected. All NMR spectra were recorded in CDCl<sub>3</sub> (unless specified as DMSO-*d*<sub>6</sub>), with TMS as the internal standard for <sup>1</sup>H (300 MHz) or the solvent as the internal standard for <sup>13</sup>C (75

MHz). THF was dried over sodium/benzophenone and used freshly distilled. Column chromatography was conducted on silica gel 200–425 meshes. The compounds **4a–c** and **6a–c** were synthesized as reported.<sup>37</sup>

### General procedure for the synthesis of 1,3-benzodioxin-4-ones **1a–d** and naphtho-1,3-dioxinones **7a–c**

The appropriate aldehyde (3 eq) was added to *N*-(*o*-hydroxyarylacyl) benzotriazoles **4a–c** / **6a–c** (1mmol) in freshly dried THF (4 mL) under inert atmosphere. The mixture was stirred for 5 min before addition of triethylamine (3 eq). The reaction mixture was stirred at rt for 24 hours before concentrating under vacuum. The residue was refined by flash chromatography on silica gel using 20% ethyl acetate in hexanes to give **1a–d** and **7a–c**.

**2-Ethyl-1,3-benzodioxin-4-one (1a)**. Oil (94%), <sup>1</sup>H NMR: δ 7.98 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.57 (td, *J* = 8.1, 1.8 Hz, 1H), 7.17 (td, *J* = 7.8, 0.9 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 5.57 (t, *J* = 4.8 Hz, 1H), 5.57 (t, *J* = 4.8 Hz, 1H), 2.12–2.02 (m, 2H), 1.15 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR: δ 162.3, 158.4, 136.1, 130.1, 123.1, 116.6, 114.4, 102.2, 26.8, 7.1. Anal. Calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>: C, 67.41; H, 5.66. Found: C, 67.09; H, 5.81.

**8-Methyl-2-phenyl-4H-1,3-benzodioxin-4-one (1b)**. Colorless microcrystals (52%) from hexanes / ethyl acetate, m.p. 83.0–84.0 °C; <sup>1</sup>H NMR : δ 7.88 (ddq, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.65–7.70 (m, 2H), 7.51–7.44 (m, 4H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.54 (s, 1H), 2.31 (s, 3H); <sup>13</sup>C NMR: δ 162.3, 156.4, 137.4, 134.2, 130.2, 128.6, 127.4, 126.5, 123.0, 114.2, 100.2, 100.1, 15.0. Anal. Calcd for C<sub>15</sub>H<sub>12</sub>O<sub>3</sub>: C, 74.99; H, 5.03. Found: C, 74.92; H, 4.98.

**6-Bromo-2-(2-furyl)-4H-1,3-benzodioxin-4-one (1c)**. Colorless needles (75%) from hexanes / ethyl acetate, m. p. 87.2–89.2 °C; <sup>1</sup>H NMR: δ 8.04 (d, *J* = 2.6 Hz, 1H), 7.60 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.43 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.63 (d, *J* = 3.3 Hz, 1H), 6.51 (s, 1H), 6.38 (dd, *J* = 3.3, 1.8 Hz, 1H); <sup>13</sup>C NMR: δ 159.8, 156.4, 146.2, 144.2, 139.3, 132.6, 118.9, 116.2, 115.8, 111.2, 110.7, 94.5. Anal. Calcd for C<sub>12</sub>H<sub>7</sub>BrO<sub>4</sub>: C, 48.84; H, 2.39. Found: C, 48.76; H, 2.34.

**8-Methyl-2-propyl-4H-1,3-benzodioxin-4-one (1d)**. Colorless microcrystals (92%) from hexanes / ethyl acetate, m. p. 62.0–64.0 °C; <sup>1</sup>H NMR: δ 7.82 (ddq, *J* = 7.7, 1.1, 0.8 Hz, 1H), 7.40 (ddq, *J* = 7.7, 1.1, 0.6 Hz, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 5.59 (t, *J* = 5.2 Hz, 1H), 2.26 (s, 3H), 2.09–2.01 (m, 2H), 1.64 (sextet, *J* = 7.6 Hz, 2H), 1.04 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR: δ 162.8, 156.7, 137.0, 127.6, 126.1, 122.6, 114.1, 101.2, 35.5, 16.5, 14.9, 13.7. Anal. Calcd for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>: C, 69.89; H, 6.84. Found: C, 69.83; H, 6.89.

**3-Ethyl-naphtho[2,1-*d*][1,3]dioxin-1-one (7a)**. White needles from methanol (64%), m.p. 104.0–105.0 °C; <sup>1</sup>H NMR: δ 9.12 (br d, *J* = 8.6 Hz, 1H), 7.83 (br d, *J* = 8.8 Hz, 1H), 7.69 (ddd, *J* = 8.8, 7.0, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.0, 1.2 Hz, 1H), 7.17 (d, *J* = 8.9 Hz, 1H), 5.60 (t, *J*<sub>AX</sub> = *J*<sub>BX</sub> = 5.0 Hz, X part of ABX spin system), 2.15 (dd, *J*<sub>AB</sub> = 7.4, *J*<sub>BX</sub> = 5.0 Hz, 1H, B part of ABX spin system), 2.11 (dd, *J*<sub>AB</sub> = 7.4, *J*<sub>AX</sub> = 5.0 Hz, 1H, A part of ABX spin system), 1.19 (t, *J* = 7.6 Hz, 3H); <sup>13</sup>C NMR: δ 161.9, 160.1, 137.6, 131.9, 130.0, 129.5, 128.7, 125.7, 125.5, 116.5, 106.6, 101.4, 26.7, 7.3. Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>3</sub>: C, 73.67; H, 5.30. Found: C, 73.59; H, 5.23.

**2-Neopentyl-4H-naphtho[1,2-*d*][1,3]dioxin-4-one (7b).** Colorless microcrystals (75%) from hexanes / ethyl acetate, m. p. 106.0–107.0 °C; <sup>1</sup>H NMR: δ 8.20 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.71–7.55 (m, 3H), 2.23 (dd, *J* = 14.7, 6.5 Hz, 1H), 2.07 (dd, *J* = 14.7, 3.7 Hz, 1H), 1.15 (s, 9H); <sup>13</sup>C NMR: δ 162.8, 157.0, 137.3, 130.0, 128.1, 126.9, 123.8, 123.2, 122.8(2C), 108.9, 101.1, 46.8, 30.1, 29.4. Anal. Calcd for C<sub>17</sub>H<sub>18</sub>O<sub>3</sub>: C, 75.53; H, 6.71. Found: C, 75.16; H, 6.85.

**2-(4-Methylphenyl)-4H-naphtho[1,2-*d*][1,3]dioxin-4-one (7c).** Colorless plates (61%), m.p. 242.0–243.0; <sup>1</sup>H NMR: δ 8.25 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.61 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.70–7.54 (m, 5H), 7.32 (d, *J* = 8.6 Hz, 2H), 6.68 (s, 1H), 2.42 (s, 3H); <sup>13</sup>C NMR: δ 162.4, 156.7, 140.6, 137.4, 131.2, 130.1, 129.3, 128.0, 126.9, 126.6, 123.8, 123.2, 123.0, 122.9, 108.8, 100.8, 21.4. Anal. Calcd for C<sub>19</sub>H<sub>14</sub>O<sub>3</sub>: C, 78.61; H, 4.86. Found: C, 78.46; H, 4.75.

### General procedure for the synthesis of benzoxazin-2,4-diones 2a–c and naphthoxazine-1,3-diones 9a–b

The appropriate isocyanate (2.2 eq) was added to *N*-(*o*-hydroxyarylacyl) benzotriazoles **4a–c** / **6a–c** (1mmol) in freshly dried THF (4 ml) under inert atmosphere. The mixture was stirred for 5 min before the addition of triethylamine (3 eq). The reaction mixture was stirred at rt for 24 hours before concentrating under vacuum. The residue was diluted with THF and impregnated onto 3 times w/w of silica gel. The dry impregnated silica gel was refined by column chromatography using varying amounts of ethyl acetate in hexane to give **2a–c** and **9a–b**. It was sometimes necessary to carry out the column chromatography twice to obtain the pure compound.

**3-*p*-Tolyl-1,3-benzoxazine-2,4-dione<sup>39</sup> (2a).** Colorless needles (99%) from methanol, m. p. 224.0–225.0 °C; <sup>1</sup>H NMR: δ 8.13 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.75 (dt, *J* = 8.7, 1.5 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 2.43 (s, 3H); <sup>13</sup>C NMR: δ 160.7, 152.7, 148.1, 139.5, 136.4, 131.5, 130.3, 128.4, 127.7, 125.6, 116.6, 114.4, 21.3.

**3-Benzyl-6-bromo-2H-1,3-benzoxazine-2,4(3H)-dione<sup>40</sup> (2c).** Colorless microcrystals (96%), m. p. 154.0–156.0 °C; <sup>1</sup>H NMR: δ 8.21 (d, *J* = 2.4 Hz, 1H), 7.77 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.53–7.50 (m, 2H), 7.34–7.31 (m, 4H), 7.16 (d, *J* = 8.5, Hz, 1H), 5.19 (s, 2H); <sup>13</sup>C NMR: δ 159.4, 155.9, 151.4, 139.1, 135.3, 130.7, 129.3, 128.6, 128.3, 118.3, 118.3, 115.7. Anal. Calcd for C<sub>15</sub>H<sub>10</sub>BrNO<sub>3</sub>: C, 54.24; H, 3.03; N, 4.22. Found: C, 54.14; H, 2.82; N, 4.00.

**2-*p*-Tolyl-naphtho[1,2-*e*][1,3]oxazine-1,3-dione (9a).** Colorless needles (86%) from methanol, m. p. 257.0–258.0 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 9.40 (d, *J* = 8.5 Hz, 1H), 8.45 (d, *J* = 9.1 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.81–7.76 (m, 1H), 7.69–7.64 (m, 1H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.34 (s, 4H), 2.40 (s, 3H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 161.7, 154.5, 147.7, 138.3, 138.0, 133.0, 130.6, 130.0, 129.7, 129.4, 128.6, 126.5, 124.7, 116.5, 107.0, 100.3, 21.0. Anal. Calcd for C<sub>19</sub>H<sub>13</sub>NO<sub>3</sub>: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.60; H, 4.27; N, 4.96.

**3-Isopropyl-2H-naphtho[2,1-*e*][1,3]oxazine-2,4(3H)-dione (9b).** Yellow microcrystals (60%), m.p. 148.0–150.0; <sup>1</sup>H NMR: δ 8.43 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 8.7 Hz, 1H), 7.90 (d, *J* =

7.28 Hz, 1H), 7.74–7.64 (m, 3 H), 5.31 (septet,  $J = 6.9$  Hz, 1H), 1.58 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR:  $\delta$  161.4, 150.7, 147.2, 137.0, 130.1, 128.0, 127.5, 125.0, 122.5, 122.0, 121.7, 109.8, 47.0, 19.1. Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{NO}_3$ : C, 70.58; H, 5.13; N, 5.49. Found: C, 70.20; H, 5.12; N, 5.51.

## Acknowledgements

The authors would like to thank Dr. C. Dennis Hall for help and advice.

## Reference and Notes

1. Yet, L. *Chem. Rev.* **2003**, *103*, 4283.
2. Garcia-Fortanet, J.; Debergh, J. R.; De Brabander, J. K. *Org. Lett.* **2005**, *7*, 685.
3. Xie, X-S.; Pardon, D.; Liao, X.; Wang, J.; Roth, M. G.; De Brabander, J. K. *J. Biol. Chem.* **2004**, *279*, 19755.
4. Hong, J.; Ishihara, K.; Zee, O.; Ohuchi, K. *Planta Med.* **2005**, *71*, 306.
5. Pettit, G. R.; Zhang, Q.; Pinilla, V.; Herald, D. L.; Doubek, D. L.; Duke, J. A. *J. Nat. Prod.* **2004**, *67*, 983.
6. Liu, R. C-Y.; Luszytk, J.; McAllister, M. A.; Tidwell, T. T.; Wagner, B. D. *J. Am. Chem. Soc.* **1998**, *120*, 6247.
7. Mowry, D. T. *J. Am. Chem. Soc.* **1947**, *69*, 2362.
8. Chiusoli, G. P.; Venturello, C. *Chem. Commun.* **1969**, 771.
9. Dushin, R. G.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1992**, *114*, 655.
10. Marriott, J. H.; Barber, A. M. M.; Hardcastle, I. R.; Rowlands, M. G.; Grimshaw, R. M.; Neidle, S.; Jarman, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4265.
11. Tisdale, E. J.; Li, H.; Vong, B. G.; Kim, S. H.; Theodorakis E. A. *Org. Lett.* **2003**, *5*, 1491.
12. Perlmutter, P.; Puniani, E. *Tetrahedron Lett.* **1996**, *37*, 3755.
13. Boontheung, P.; Perlmutter, P.; Puniani, E. *ARKIVOC* **2001**, (viii), 95.
14. Diaz-Mondejar, M. R.; Miranda, M. A. *Heterocycles* **1984**, *22*, 1125.
15. Devaux, G.; Renaudie, C.; Boineau, F.; Mesnard, P.; Demarquesz, N. *Eur. J. Med. Chem. Chim. Ther.* **1974**, *9*, 44.
16. Kahus, A. H.; Bundgaard, H. *Acta. Pharm. Nord.* **1991**, *3*, 45.
17. Waisser, K.; Gregor, J.; Kubicova, L.; Klimesova, V.; Kunes, J.; Machacek, M.; Kaustova, J. *Eur. J. Med. Chem.* **2000**, *35*, 733.
18. Masuda, T.; Sato, H.; Ono, H. *Ger. Offen.* **1977**, *2*, 721828. *Chem. Abstr. No.* 88,161490.
19. Boontheung, P.; Perlmutter, P. *Tetrahedron Lett.* **1998**, *39*, 2629.
20. Shibuya, I.; Goto, M.; Shimizu, M.; Yanagisawa, M.; Gama, Y. *Heterocycles* **1999**, *51*, 2667.
21. Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9194.

22. Zhu, X.; Yu, Q.-S.; Greig, N. H.; Flippen-Anderson, J. L.; Brossi, A. *Heterocycles* **2003**, *59*, 115.
23. Kakuta, H.; Tanatani, A.; Nagasawa, K.; Hashimoto, Y. *Chem. Pharm. Bull.* **2003**, *51*, 1273.
24. Heinisch, L.; Gebhardt, P.; Heidersbach, R. Reissbrodt, R.; Mollmann, U. *Biometals* **2002**, *15*, 133.
25. Heinisch, L.; Wittman, S.; Stoiber, T.; Berg, A.; Ankel-Fuchs, D.; Mollmann, U. *J. Med. Chem.* **2002**, *45*, 3032.
26. Katritzky, A. R.; Shobana, N.; Pernak, J.; Afridi, A. S.; Fan, W.-Q. *Tetrahedron* **1992**, *48*, 7817.
27. Katritzky, A. R.; He, H.-Y.; Suzuki, K. *J. Org. Chem.* **2000**, *65*, 8210.
28. Katritzky, A. R.; Chang, H.-X.; Yang, B. *Synthesis* **1995**, 503.
29. Katritzky, A. R.; Yang, B.; Semenzin, D. *J. Org. Chem.* **1997**, *62*, 726.
30. Katritzky, A. R.; Pastor, A.; Voronkov, M. V. *J. Het. Chem.* **1999**, 777.
31. Katritzky, A. R.; Pastor, A. *J. Org. Chem.* **2000**, *65*, 3679.
32. Katritzky, A. R.; Suzuki, K.; Singh, S. K.; He, H.-Y. *J. Org. Chem.* **2003**, *68*, 5720.
33. Katritzky, A. R.; Suzuki, K.; Singh, S. K. *Croat. Chem. Acta* **2004**, *77*, 175.
34. Katritzky, A. R.; Huang, T. B.; Voronkov, M. V.; Steel, P. J. *J. Org. Chem.* **2000**, *65*, 8069.
35. Katritzky, A. R.; Singh, S. K.; Bobrov, S. *J. Org. Chem.* **2004**, *69*, 9313.
36. Katritzky, A. R.; Rogers, J. W.; Witek, R. M.; Nair, S. K. *ARKIVOC* **2004**, (viii), 52.
37. Katritzky, A. R.; Singh, S. K.; Cai, C.; Bobrov, S. *J. Org. Chem.* **2006**, *71*, 3364.
38. Katritzky, A. R.; Pleyne, D. P. M.; Yang, B. *J. Org. Chem.* **1997**, *62*, 4155.
39. Deck, J. F.; Dains, F. B. *J. Am. Chem. Soc.* **1933**, *55*, 4986.
40. Waissner, K.; Perina, M.; Kunes, J.; Klimesova, V.; Kaustova, J. *Farmaco* **2003**, *58*, 1137.