A Facile Synthesis of Bridged Polycyclic Naphthooxazocine Skeletons: Eight-Membered-Ring Constructions *via* Tandem Dinucleophilic Addition of Naphthalenols to Quinolinium Salts

by **Firouz Matloubi Moghaddam***[a]), **Salman Taheri**[a]), **Zohreh Mirjafary**[a]), **Hamdollah Saeidian**[b]), **Mostafa Kiamehr**[a]), and **Mohsen Tafazzoli**[a])

[a]) Laboratory of Organic Synthesis & Natural Products, Department of Chemistry, Sharif University of Technology, P.O. Box 11155-9516, Tehran, Iran (phone: +98-21-66165309; fax: +98-21-66012983; e-mail: matloubi@sharif.edu)

[b]) Department of Science, Payame Noor University (PNU), Zanjan, Iran

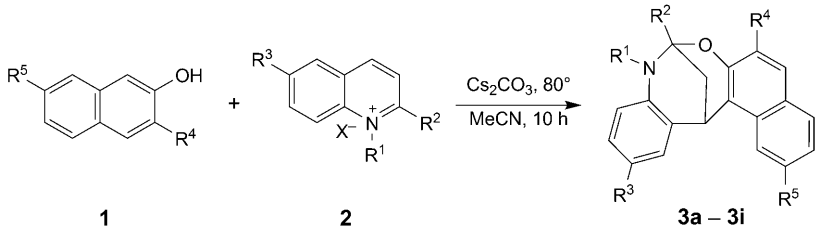
The efficient synthesis of bridged polycyclic naphthooxazocines **3** *via* addition of naphthalenols **1** as a bis-nucleophile to *N*-alkylquinolinium salts **2** is described (*Scheme 1* and *Table 2*). This new approach provides a powerful entry into polycyclic structures containing bicyclic N,O-acetals related to bioactive compounds.

Introduction. – In recent years, many researches in organic chemistry have focused on discovering new methods for ring construction [1]. In this respect, methodologies leading to the synthesis of bridgehead heterocycles containing an eight-membered ring are particularly appealing because these molecules with functional groups having cleft-like shapes have recently emerged as useful tools in molecular-recognition studies [2]. Among the members of this family, benzoxazocines have received considerable attention because of their pharmacological properties, such as their antidepressant, antithrombotic, antipsychotic (for the central nervous system (CNS)), and antibreast-cancer activities [3]. On the other hand, the quinoline skeleton is found in a large number of naturally occurring and synthetic biologically active heterocyclic compounds. Notably, bicyclic N,O-acetals are present in a number of natural products, such as quinocarcin, tetrazomine, and the bioxalomycins, showing good antitumor or antimicrobial activity [4].

We have earlier demonstrated an efficient synthesis of indole-fused pentacyclic tetrahydroquinoline, tetrahydroisoquinoline, and benzoxazocin skeletons *via* addition of indoline-2-thiones (=1,3-dihydro-2*H*-indole-2-thione) as bis-nucleophiles to quinolinium and isoquinolinium salts [5]. In the context of our interest in exploring convenient accesses to heterocyclic systems [6], we wish to report a tandem process for the construction of heterotetracyclic naphthooxazocines. The reaction generally involves the initial addition of naphthalenols **1** to quinolinium salts **2** to form an enamine intermediate which can be trapped by intramolecular cyclization of naphthalenols (*Scheme 1*).

Result and Discussion. – Initially, we set out to investigate solvent, base, time, and temperature effects in the reaction of *N*-methylquinolinium iodide (**2a**; $R^1 = Me$, $R^2 =$

Scheme 1. *Synthesis of Naphthooxazocine Derivatives* **3a**–**3i**



R^1 = Me, Et, Bn, *p*-Br–$C_6H_4CH_2$
R^2, R^3 = H, Me
R^4, R^5 = H, OH
X = Br, I

$R^3 = H$, $X = I$) and naphthalen-2-ol (**1a**; $R^4 = R^5 = H$) as simple model substrates (*Table 1*). The results showed that the presence of a base is required to achieve the synthesis of the desired product **3a**. The effect of temperature was studied by carrying out the model reaction at room temperature (23°) and in refluxing solvents. It was observed that the yield increased as the reaction temperature was raised. The effect of solvent was studied, with MeCN providing the highest yields and short reaction times. Considering the reaction time, the amount of substrates, and the yield, the best optimized condition is achieved with Cs_2CO_3 (1 equiv.), quinolinium salt (1 equiv.), and naphthalenol (2 equiv.) in MeCN (5 ml) at 80° for 10 h (*Table 1*).

Table 1. *Optimization of the Conditions of the Model Reaction* **1a** + **2a** → **3a**

Base	Solvent	T [°]	Time [h]	Ratio **1**/**2**	Yield[a]) [%]
K_2CO_3	MeCN	r.t.	72	1 : 1	trace
K_2CO_3	$CHCl_3$	r.t.	72	1 : 1	–
K_2CO_3	toluene	r.t.	24	1 : 1	–
K_2CO_3	DMF	r.t.	24	1 : 1	–
K_2CO_3	MeCN	80	10	1 : 1	27
K_2CO_3	MeOH	70	10	1 : 1	22
K_2CO_3	toluene	110	10	1 : 1	12
Cs_2CO_3	MeCN	80	10	1 : 1	33
Cs_2CO_3	MeCN	80	10	1 : 2	57
Cs_2CO_3	**MeCN**	**80**	**10**	**2 : 1**	**80**

[a]) Yield of isolated product **3a**.

The ^{1}H- and ^{13}C-NMR, and 2D-NMR (^{1}H,^{1}H-COSY, HMQC, and HMBC) spectra and elemental analysis (CHN) of the product clearly indicated the formation of **3a**. The ^{1}H-NMR spectrum of **3a** showed the bridgehead N,O-acetal H_a atom (see *Fig.*) as a *m* at δ(H) 5.59–5.61, the bridgehead H_b as a *m* at δ(H) 4.74–4.76, and H_c and H_d as two *ddd* (J = 12.5, 2.5, and 2.5 Hz) at δ(H) 2.20 and 2.39. The ^{1}H-decoupled ^{13}C-NMR spectrum of **3a** revealed 20 distinct resonances in agreement with the proposed structure. ^{13}C-DEPT Experiments indicated the presence of a resonance at δ(C) 26.5

readily recognized as the CH_2 group (C(15)), signals at δ(C) 83.5 (C(6)), 29.7 (C(14)), and 37.2 (MeN), ten distinct resonances for aromatic CH groups, and six signals for quaternary C-atoms. Further evidence for the bridged structure was given by the HMBC spectrum, in which the correlations were in agreement with the suggested structure. Some key HMBCs are shown in the *Figure*.

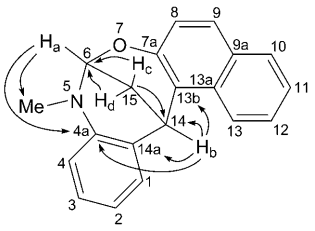


Figure. *Key HMBCs of compound* **3a**

In view of the success of the above reaction, we explored the scope of this promising transformation by varying the structure of the naphthalenol **1** and *N*-alkylquinolinium salt **2** (*Table 2*). The reaction proceeded smoothly under the previously optimized mild conditions, and no undesirable side reactions were observed. The same methano-bridged N,O-acetal structure as for **3a** was assumed for the other derivatives **3b** – **3i** on account of their NMR spectroscopic similarities. This outcome is in agreement with the relative topicity observed in our previously reported nucleophilic additions of **2** [5].

Table 2. *Synthesis of Naphthoxazocine Derivatives* **3** *from Naphthalenols* **1** *and* N-*Alkylquinolinium Salts* **2** (see *Scheme 1*)

R^1	R^2	R^3	R^4	R^5	Product	Yield [%][a])
Me	H	H	H	H	**3a**	80
Et	H	H	H	H	**3b**	82
4-Br–$C_6H_4CH_2$	H	H	H	H	**3c**	58
Bn	H	H	H	H	**3d**	56
Me	Me	H	H	H	**3e**	67
Me	H	Me	H	H	**3f**	73
Me	H	H	H	OH	**3g**	84
Me	H	H	OH	H	**3h**	90
Me	H	Me	OH	H	**3i**	75

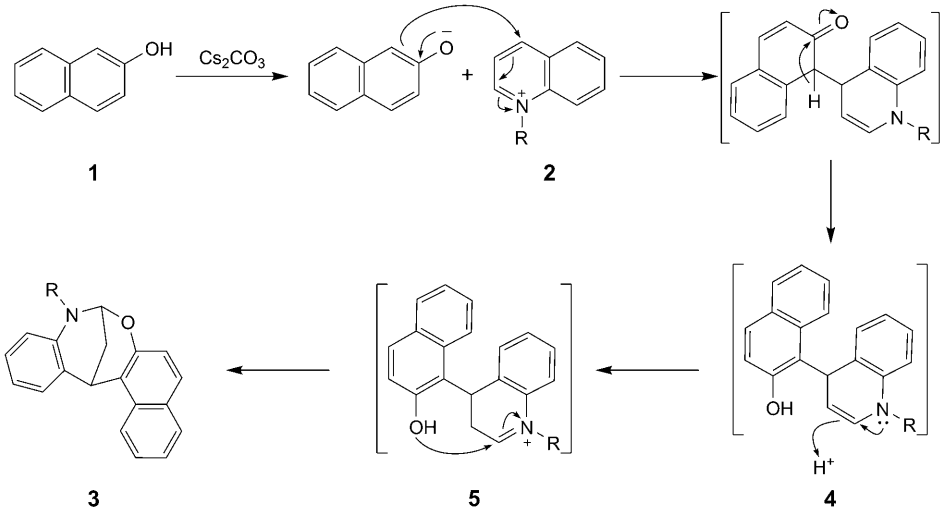
[a]) Yield of isolated product.

Next, we investigated the scope of the analogous reaction of naphthalenols with isoquinolinium salts under the optimized reaction conditions, but no reaction was observed, and the starting isoquinolinium salts and naphthalenols remained unchanged.

A plausible reaction mechanism to account for the formation of naphthooxazocines **3** is proposed in *Scheme 2*. C(1)-Atom of the naphthalenolate attacks C(4) of the quinolinium salt. The resulting enamine **4** can in turn be reactivated *via* iminium intermediate **5** which then undergoes a second nucleophilic addition. Intramolecular

nucleophilic cyclization by the O-atom gives the desired product **3**. The excessive amount of naphthalenol may act as a proton source for the transformation of enamine **4** to iminium ion **5**.

Scheme 2. *A Plausible Mechanism for the Formation of* **3a**–**3i**



Conclusions. – We reported a highly efficient method for the synthesis of bridged polycyclic naphthooxazocines. This method offers several advantages such as high conversions, high selectivity, and straightforward starting from easily accessible starting materials, which makes it a useful and attractive strategy for the preparation of polycyclic naphthooxazocines in a single-step operation.

We gratefully acknowledge financial support from the Research Council of Sharif University of Technology and the *Islamic Development Bank* (IDB) for financial backing to purchase a 500 MHz NMR spectrometer.

Experimental Part

General. Commercially available materials were purchased from *Sigma–Aldrich* and *Merck* and were used without any additional purification. TLC: silica gel *60* F_{254} (SiO_2) plates from *Merck*. M.p.: *Büchi-B-540* melting-point apparatus; in sealed capillaries; uncorrected. ^{1}H- and ^{13}C-NMR and DEPT Spectra: *Bruker-Avance-DRX-500* spectrometer; in $CDCl_3$ and (D_6)DMSO at r.t.; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. Elemental analyse: *Perkin-Elmer-2004(II)* CHN analyzer.

Polycyclic Naphtooxazocines **3a**–**3i**: *General Procedure.* A mixture of a naphthalenol **1** (2 mmol), quinolinium salt **2** (1 mmol), and Cs_2CO_3 (1 mmol) in MeCN (5 ml) was heated at 80° for 10 h (TLC monitoring). After completion of the reaction, the solvent was evaporated, and the residue was separated by flash column chromatography (FC) (SiO_2, petroleum ether/AcOEt 6 : 1): pure **3** as a light yellow solid.

*5,14-Dihydro-5-methyl-6,14-methano-6*H*-benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3a**): White solid. M.p. 106–109°. ^{1}H-NMR: 8.38 (*d*, *J* = 8.5, 1 H); 7.77 (*d*, *J* = 8.0, 1 H); 7.56–7.62 (*m*, 3 H); 7.35 (*t*, *J* = 8.0, 1 H); 7.14 (*d*, *J* = 8.5, 1 H); 7.11 (*t*, *J* = 8.0, 1 H); 6.70–6.75 (*m*, 2 H); 5.59–5.61 (*m*, 1 H); 4.74–4.76 (*m*, 1 H); 3.25 (*s*, 3 H); 2.39 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H); 2.20 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C-NMR: 150.2

(C); 143.0 (C); 132.3 (C); 129.7 (C); 129.1 (CH); 128.4 (CH); 127.7 (CH); 127.3 (CH); 127.0 (C); 126.8 (CH); 123.4 (CH); 122.3 (CH); 119.3 (CH); 118.4 (C); 117.6 (CH); 110.8 (CH); 83.5 (CH); 37.2 (Me); 29.7 (CH); 26.5 (CH_2). Anal. calc. for $C_{20}H_{17}NO$ (287.36): C 83.59, H 5.96, N 4.87; found: C 83.40, H 6.00, N 4.81.

*5-Ethyl-5,14-dihydro-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3b**): White solid. M.p. 112–114°. ^{1}H-NMR: 8.39 (*d*, *J* = 8.5, 1 H); 7.78 (*d*, *J* = 8.0, 1 H); 7.59–7.64 (*m*, 3 H); 7.38 (*t*, *J* = 7.5, 1 H); 7.16 (*d*, *J* = 9.0, 1 H); 7.11 (*t*, *J* = 7.5, 1 H); 6.72–6.77 (*m*, 2 H); 5.66–5.68 (*m*, 1 H); 4.73–4.75 (*m*, 1 H); 3.87–3.94 (*m*, 1 H); 3.54–3.61 (*m*, 1 H); 2.42 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H); 2.17 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H); 1.28 (*t*, *J* = 7.5, 3 H). ^{13}C-NMR: 150.0 (C); 141.7 (C); 132.4 (C); 129.7 (C); 129.2 (CH); 128.4 (CH); 127.7 (CH); 127.6 (CH); 127.2 (C); 126.8 (CH); 123.4 (CH); 122.4 (CH); 119.4 (CH); 118.2 (C); 117.3 (CH); 110.8 (CH); 82.4 (CH); 44.2 (CH_2); 29.9 (CH); 26.6 (CH_2); 13.4 (Me). Anal. calc. for $C_{21}H_{19}NO$ (301.38): C 83.69, H 6.35, N 4.65; found: C 83.51, H 6.20, N 4.61.

*5-(4-Bromobenzyl)-5,14-dihydro-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3c**): Yellow solid. M.p. 185–187°. ^{1}H-NMR: 8.39 (*d*, *J* = 8.5, 1 H); 7.78 (*d*, *J* = 8.0, 1 H); 7.59–7.65 (*m*, 3 H); 7.42 (*d*, *J* = 8.5, 1 H); 7.37 (*t*, *J* = 8.0, 1 H); 7.10–7.13 (*m*, 3 H); 6.96 (*t*, *J* = 7.5, 1 H); 6.73 (*t*, *J* = 7.5, 1 H); 6.49 (*d*, *J* = 8.0, 1 H); 5.65–5.67 (*m*, 1 H); 4.98 (*d*, *J* = 17.5, 1 H); 4.79–4.81 (*m*, 1 H); 4.69 (*d*, *J* = 17.5, 1 H); 2.48 (*ddd*, *J* = 12.5, 3.0, 3.0, 1 H); 2.28 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C-NMR: 149.8 (C); 142.0 (C); 137.8 (C); 132.4 (C); 132.1 (CH); 129.8 (C); 129.2 (C); 128.7 (CH); 128.5 (CH); 127.7 (CH); 127.5 (CH); 127.1 (C); 126.9 (CH); 123.6 (CH); 122.3 (CH); 121.0 (C); 119.3 (CH); 118.2 (CH); 118.1 (C); 111.4 (CH); 82.5 (CH); 52.9 (CH_2); 29.7 (CH); 26.7 (CH_2). Anal. calc. for $C_{26}H_{20}BrNO$ (442.34): C 70.60, H 4.56, N 3.17; found: C 70.55, H 4.51, N 3.16.

*5-Benzyl-5,14-dihydro-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3d**): Yellow solid. M.p. 121–123°. ^{1}H-NMR: 8.43 (*d*, *J* = 8.5, 1 H); 7.81 (*d*, *J* = 8.0, 1 H); 7.62–7.68 (*m*, 3 H); 7.28–7.41 (*m*, 6 H), 7.18 (*d*, *J* = 9.0, 1 H); 6.99 (*t*, *J* = 8.5, 1 H); 6.74 (*t*, *J* = 7.5, 1 H); 6.59 (*d*, *J* = 8.0, 1 H); 5.05 (*d*, *J* = 17.0, 1 H); 4.83 (*m*, 1 H); 4.78 (*d*, *J* = 17.0, 1 H); 2.49 (*ddd*, *J* = 12.5, 3.0, 3.0, 1 H); 2.31 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C-NMR: 150.0 (C); 142.4 (C); 138.7 (C); 132.4 (C); 129.8 (C); 129.2 (CH); 129.1 (CH); 128.6 (CH); 127.7 (CH); 127.4 (CH); 127.3 (CH); 127.0 (C); 126.9 (CH); 126.7 (CH); 123.6 (CH); 122.4 (CH); 119.4 (CH); 118.1 (C); 117.9 (CH); 111.6 (CH); 82.3 (CH); 53.2 (CH_2); 29.8 (CH); 26.7 (CH_2). Anal. calc. for $C_{26}H_{21}NO$ (363.45): C 85.92, H 5.82, N 3.85; found: C 85.81, H 5.75, N 3.82.

*5,14-Dihydro-5,6-dimethyl-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3e**): White solid. M.p. 150–152°. ^{1}H-NMR: 8.33 (*d*, *J* = 8.5, 1 H); 7.75 (*d*, *J* = 7.5, 1 H); 7.61 (*d*, *J* = 8.5, 1 H); 7.53–7.57 (*m*, 2 H); 7.33 (*t*, *J* = 8.5, 1 H); 7.11 (*d*, *J* = 8.5, 1 H); 7.07 (*t*, *J* = 8.5, 1 H); 6.71 (*t*, *J* = 7.5, 1 H); 6.67 (*d*, *J* = 8.0, 1 H); 4.65 (*dd*, *J* = 3.5, 2.5, 1 H); 3.10 (*s*, 3 H); 2.36 (*dd*, *J* = 12.5, 3.5, 1 H); 2.24 (*dd*, *J* = 12.5, 2.5, 1 H); 1.89 (*s*, 3 H). ^{13}C-NMR: 150.7 (C); 144.7 (C); 132.6 (C); 129.8 (C); 129.0 (CH); 128.5 (CH); 128.2 (C); 127.5 (CH); 126.78 (CH); 126.75 (CH); 123.4 (CH); 122.5 (CH); 119.5 (CH); 117.4 (CH); 117.1 (C); 111.8 (CH); 85.5 (C); 35.3 (CH_2); 31.9 (Me); 31.6 (CH); 26.2 (Me). Anal. calc. for $C_{21}H_{19}NO$ (301.38): C 83.69, H 6.38. N 4.65; found: C 83.52, H 6.30, N 4.65.

*5,14-Dihydro-2,5-dimethyl-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocine* (**3f**): White solid. M.p. 154–156°. ^{1}H-NMR: 8.37 (*d*, *J* = 8.5, 1 H); 7.60 (*d*, *J* = 8.5, 1 H); 7.59–7.62 (*m*, 2 H); 7.33–7.36 (*m*, 2 H); 7.12 (*d*, *J* = 8.5, 1 H); 6.90 (*d*, *J* = 8.0, 1 H); 6.61 (*d*, *J* = 8.0, 1 H); 5.57–5.59 (*m*, 1 H); 4.69–4.71 (*m*, 1 H); 3.22 (*s*, 3 H); 2.37 (*ddd*, *J* = 12.5, 3.0, 2.5, 1 H); 2.26 (*s*, 3 H); 2.20 (*ddd*, *J* = 12.5, 3.0, 2.5, 1 H). ^{13}C-NMR: 150.3 (C); 140.7 (C); 132.3 (C); 129.7 (C); 129.1 (CH); 128.3 (CH); 128.1 (CH); 128.0 (CH); 127.0 (C); 126.7 (CH); 123.3 (CH); 122.3 (CH); 119.3 (CH); 118.5 (C); 110.9 (CH); 83.7 (CH); 37.2 (Me); 29.6 (CH); 26.6 (CH_2); 20.8 (Me). Anal. calc. for $C_{21}H_{19}NO$ (301.38): C 83.69, H 6.35, N 4.65; found: C 83.62, H 6.30, N 4.64.

*5,14-Dihydro-5-methyl-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocin-12-ol* (**3g**): White solid. M.p. 140–143°. ^{1}H-NMR: 7.70 (*d*, *J* = 2.5, 1 H); 7.62 (*d*, *J* = 8.5, 1 H); 7.53 (*d*, *J* = 7.5, 1 H); 7.50 (*d*, *J* = 8.5, 1 H); 7.09 (*t*, *J* = 8.0, 1 H); 6.93–6.98 (*m*, 2 H); 6.66–6.70 (*m*, 2 H); 5.80 (*s*, 1 H); 5.57–5.59 (*m*, 1 H); 4.52–4.54 (*m*, 1 H); 3.24 (*s*, 3 H); 2.33 (*ddd*, *J* = 12.5, 3.0, 3.0, 1 H); 2.14 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C NMR: 154.7 (C); 150.8 (C); 143.0 (C); 133.8 (C); 131.0 (CH); 128.2 (CH); 127.7 (CH); 127.3 (CH); 126.8 (C); 125.0 (C); 117.6 (CH); 116.9 (CH); 114.9 (CH); 110.8 (CH); 105.4 (CH); 83.5 (CH); 37.1, 29.8 (CH); 26.5 (CH_2). Anal. calc. for $C_{20}H_{17}NO_2$ (303.35): C 79.19, H 5.65, N 4.62; found: C 79.12, H 5.57, N 4.60.

*5,14-Dihydro-5-methyl-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocin-8-ol* (**3h**): Yellow solid. M.p. 135–138°. ^{1}H-NMR: 8.30 (*d*, *J* = 8.5, 1 H); 7.68 (*d*, *J* = 8.0, 1 H); 7.58 (*d*, *J* = 8.0, 1 H); 7.50 (*t*, *J* = 8.0, 1 H); 7.36 (*t*, *J* = 8.0, 1 H); 7.18 (*s*, 1 H); 7.13 (*t*, *J* = 8.0, 1 H); 6.78 (*t*, *J* = 7.5, 1 H); 6.73 (*d*, *J* = 8.5, 1 H); 6.01 (br. *s*, 1 H); 5.71–5.73 (*m*, 1 H); 4.75–4.77 (*m*, 1 H); 3.23 (*s*, 3 H); 2.38 (*ddd*, *J* = 12.5, 3.0, 3.0, 1 H); 2.23 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C-NMR: 145.5 (C); 142.5 (C); 140.3 (C); 130.3 (C); 127.9 (CH); 127.8 (CH); 127.5 (CH); 126.9 (C); 126.6 (C); 124.3 (CH); 124.2 (CH); 122.2 (CH); 119.3 (C); 118.2 (CH); 111.1 (CH); 108.5 (CH); 84.6 (CH); 37.3 (Me); 29.5 (CH); 26.4 (CH_2). Anal. calc. for $C_{20}H_{17}NO_2$ (303.35): C 79.19, H 5.65, N 4.62; found: C 79.22, H 5.64, N 4.61.

*5,14-Dihydro-2,5-dimethyl-6,14-methano-6*H-*benzo[*d*]naphtho[1,2-*g*][1,3]oxazocin-8-ol* (**3i**): White solid. M.p. 145–147°. ^{1}H-NMR: 8.29 (*d*, *J* = 8.5, 1 H); 7.67 (*d*, *J* = 8.0, 1 H); 7.50 (*t*, *J* = 7.5, 1 H); 7.36 (*s*, 1 H); 7.35 (*t*, *J* = 7.5, 1 H); 7.14 (*s*, 1 H); 6.93 (*d*, *J* = 8.0, 1 H); 6.63 (*d*, *J* = 8.5, 1 H); 6.10 (br. *s*, 1 H); 5.71–5.73 (*m*, 1 H); 4.70–4.72 (*m*, 1 H); 3.23 (*s*, 3 H); 2.38 (*ddd*, *J* = 12.5, 2.5, 3.0, 1 H); 2.28 (*s*, 3 H); 2.24 (*ddd*, *J* = 12.5, 2.5, 2.5, 1 H). ^{13}C-NMR: 145.5 (C); 140.5 (C); 140.2 (C); 130.2 (C); 128.3 (CH); 128.2 (CH); 127.8 (CH); 127.3 (C); 126.9 (C); 126.6 (C); 124.2 (CH); 124.1 (CH); 122.2 (CH); 119.4 (C); 111.2 (CH); 108.4 (CH); 84.8 (CH); 37.4 (Me); 29.4 (CH); 26.6 (CH_2); 20.8 (Me). Anal. calc. for $C_{21}H_{19}NO_2$ (317.38): C 79.47, H 6.03, N 4.41; found: C 79.35, H 6.05, N 4.38.

REFERENCES

[1] B. K. Mehta, K. Yanagisawa, M. Shiro, H. Kotsuki, *Org. Lett*. **2003**, *5*, 1605; K. Takeda, Y. Ohtani, *Org. Lett.* **1999**, *1*, 677; J. R. Rodríguez, L. Castedo, J. L. Mascareñas, *Org. Lett.* **2001**, *3*, 1181.

[2] M. Demeunynck, A. Tatibouet, 'Recent Developments in Tröger's Base Chemistry, In Progress in Heterocyclic Chemistry', Vol. 11, Eds. G. W. Gribble, T. L. Gilchrist, Pergamon, Oxford, UK, 1999, p. 1; J.-F. Wang, Y.-X. Liao, P.-Y. Kuo, Y.-H. Gau, D.-Y. Yang, *Synlett* **2006**, *3*, 2791.

[3] J. K. Mishra, K. Samanta, M. Jain, M. Dikshit, G. Panda, *Bioorg. Med. Chem. Lett*. **2010**, *20*, 244; S. Seto, A. Tanioka, M. Ikeda, S. Izawa, *Bioorg. Med. Chem. Lett*. **2005**, *15*, 1485.

[4] M. E. Flanagan, R. M. Williams, *J. Org. Chem*. **1995**, *60*, 6791; K. Fujimoto, T. Oka, M. Morimoto, *Cancer Res.* **1987**, *47*, 1516; T. Sato, F. Hirayama, T. Saito, H. Kaniwa, *J. Antibiot.* **1991**, *44*, 1367; K. Suzuki, T. Sato, M. Morioka, K. Nagai, K. Abe, H. Yamaguchi, T. Saito, Y. Ohmi, K. Susaki, *J. Antibiot*. **1991**, *44*, 479.

[5] F. M. Moghaddam, Z. Mirjafary, H. Saeidian, S. Taheri, M. Doulabi, M. Kiamehr, *Tetrahedron* **2010**, *66*, 134; F. M. Moghaddam, S. Taheri, Z. Mirjafary, H. Saeidian, *Synlett* **2010**, *1*, 123; F. M. Moghaddam, Z. Mirjafary, H. Saeidian, S. Taheri, M. R. Khodabakhshi, *Tetrahedron Lett.* **2010**, *51*, 2704; F. M. Moghaddam, Z. Mirjafary, H. Saeidian, S. Taheri, B. Soltanzadeh, *Tetrahedron* **2010**, *66*, 3678.

[6] F. M. Moghaddam, M. M. Farimani, *Tetrahedron Lett*. **2010**, *51*, 540; F. M. Moghaddam, M. Kiamehr, S. Taheri, Z. Mirjafary, *Helv. Chim. Acta* **2010**, *93*, 964; F. M. Moghaddam, H. Saeidian, Z. Mirjafary, S. Taheri, S. Kheirjou, *Synlett* **2009**, 1047; M. Kiamehr, F. M. Moghaddam, *Tetrahedron Lett.* **2009**, *50*, 6723; D. Enders, H. Saeidian, Z. Mirjafary, D. Iffland, G. Raabe, J. Runsink, *Synlett* **2009**, 2872; F. M. Moghaddam, Z. Mirjafary, H. Saeidian, M. J. Javan, *Synlett* **2008**, 892; F. M. Moghaddam, H. Saeidian, Z. Mirjafary, S. Taheri, *J. Sulfur Chem.* **2006**, *27*, 545.

Received April 7, 2010