SYNTHESIS OF BIS- AND TRIS-1,8-NAPHTHALIMIDES BRIDGED BY N-N BOND

Tao Xu, Jianhua Su, Kongchang Chen and He Tian*
Institute of Fine Chemicals, East China University of Science and Technology
Shanghai 200237, P. R. China

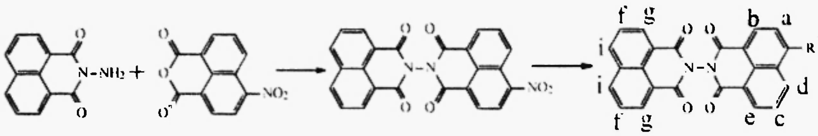
ABSTRACT: Convenient synthesis of some novel 4-alkylamino substituted bis- or tris-1,8-naphthalimides bridged by N-N bond are reported. 400 MHz NMR shows that the number of peaks and chemical shift of aromatic H are closely associated with the peri-effect of different 4-amino substituents.

INTRODUCTION

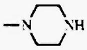
Naphthalimides constitute a very versatile class of compounds, which have been used in a large variety of areas. Their most recent applications have been oriented toward the field of photochemistry because of their special photophysical properties and high charge generation. Much work has been done to develop supramolecular system based on naphthalimides in order to mimic and comprehend the essential feature of bacterial photosynthetic reaction center (1-5). In the Intramolecular Charge Transfer(ICT) process of these systems, aromatic imides act not only as electron donor, but also as electron acceptor. However, femtosecond-scale ultrafast photoswitchable molecules require the donor and acceptor be bridged by the spacer as short as possible and the molecule be kept in "rod-like" configuration so that the ICT can be considerably accelerated (1).

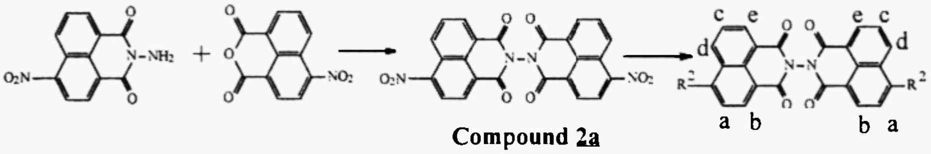
We therefore report, here, the synthesis of some novel bis- or tris-naphthalimides in which the spacer between two naphthalimides is, simply, an N-N bond. Their structures are shown in Scheme 1 and Scheme 2. These compounds are proposed as good candidates for the potential photoswitchable molecules. On the other hand, electroluminescence (EL) of bis-1,8-naphthalimides is also observed in our previous work (6). Compared with the corresponding monomer 1,8-

naphthalimides, bis-1,8-naphthalimides exhibit higher luminous efficiency and stability. In addition, spin-coating is a more economic way to manufacture "sandwich" structure EL device, but the luminous materials should be soluble enough. The solubility of 1c and 1d attains above 10^{-2}mol/L(r.t. in $CHCl_3$), which suffices the requirement of spin-coating.



Compound 1a

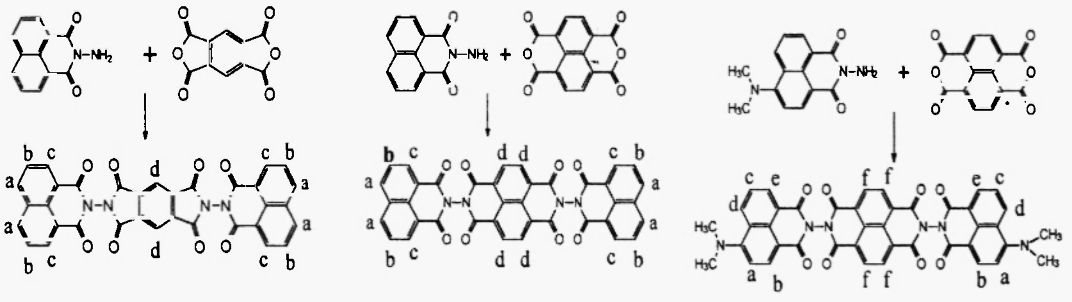
Compound	1b	1c	1d	1e	1f	1g	1h
$-R^1$	$-NH_2$	$-N(CH_3)_2$	$-NH(CH_2)_3CH_3$	$-NH(CH_2)_7CH_3$	$-NHCH_2CH_2OH$	$-NHCH_2CH_2NH_2$	



Compound 2a

Compound	2b	2c
$-R^2$	$-NH_2$	$-N(CH_3)_2$

Scheme 1 Chemical Structures of Bis-1,8-naphthalimides



Compound 3a **Compound 3b** **Compound 3c**

Scheme 2 Chemical Structure of Tris-naphthalimides

It is also reported that substituted bis-1,8-naphthalimides have been shown to demonstrate anticancer activity (7) and very promising antiviral agents with selectivity in vitro activity against the human immunodeficiency virus, HIV-1 (8).

However, satisfactory purification in preparation of some similar compounds should be performed with chromatography on silica gel (1). Therefore, we, through orthogonal tests with regards to reaction temperature, time and solvent effect, pursue an efficient method to prepare the N-N bond bridged bis- and tris-naphthalimides with high purity, yield and excellent repeatability.

RESULTS AND DISCUSSION

Referring to some others' works (9, 10), we found that the imidation reaction of N-amino-1,8-naphthalimide with 4-nitro-1,8-naphthalic anhydride is greatly improved in protic solvent ethanol. But in acetic acid, the reaction could be inhibited. In aprotic solvents such as DMF, the reaction is lead to substitution and to give very complex brown products including 4-(N-1,8-naphthalimide)amino-1,8-naphthalic anhydride.

The nitro group on 4-position could be substituted by different amines with considerably satisfactory purity and yield in aprotic solvent DMF (11). But DMSO could increase the complexity in products. The optimized temperature should be controlled at about 110℃ for 2.5 h. However, in protic solvent, the naphthalic anhydride without an electrophilic nitro group at 4-position can not react with the sterically hindered N-amino-1,8-naphthalimide resulting from the four C=O groups because the imidation ability of naphthalic anhydride is drastically weaken in the absence of nitro group. For example, the reaction of N-amino-4-dimethylamino-1,8-naphthalimidet with 1,8:4,5-naphthalenetetracarboxylic anhydride does not occurs in ethanol. Pyridine and quinoline are selected to be the appropriate solvents for this reaction.

The study by 400 MHz ^{1}H-NMR shows that bis- and tris- naphthalimides substituted by amino or different alkylamino groups will result in different peak number in downfield region, which is on behalf of the aromatic hydrogens. For instance, as for the mono-substituted bis-naphthalimide, seven peaks appear in downfield region for the compounds substituted by amino and prim. amino group. But there appear five peaks in the downfield region of the compounds substituted by sec. amino group. We also discover that the chemical shift of H_a is 6.9 ppm in amino and prim. amino substituted compounds e.g. **1b**, **1d**, **1e**, **1f**, **1g** . But this value shifts from 6.9 ppm to above 7.5 ppm for sec. amino substituted compounds, e.g. **1c**, **1h**, **2c**, **3c**. This is an interesting phenomenon, because in general, the electrophobic ability of sec. amino group is greater than that of amino and prim. amino groups, therefore, δ values of H_a for compounds substituted by sec. amino group theoretically seem to be less than that of amino or prim. amino substituted compounds.

We assume that the steric interaction between one of the alkyl group of the sec. amino substituent and the hydrogen at the 5-position (peri-effect) should be taken account to elucidate this contradiction. Any steric interaction, which causes lack of planarity of the 4-amino group with the ring, inhibits the charge transfer from nitrogen to ring (12). Thus, in **1c** and **3c**, the electron density of H_a is reduced and lead to the overlap in chemical shift of H_a and H_c; H_b, H_d, and H_e. A critical example is **1h**, in which the degree of peri-effect is located between that of prim. and sec. amino groups, because the cyclic piperazine relaxes the steric hinderance between peri-H and the alkyl on the nitrogen atom. In **1h**, δ of H_a and H_c are separated, but δ of H_d and H_e overlap completely, which are separated in the bis-naphthalimides substituted by amino and prim. amino substituents, even δ of H_a+H_c and H_d+H_e for **1h** partly overlap, also.

EXPERIMENTAL

^{1}H-NMR, MS and elemental analysis were performed on Bruker AM-400(400MHz), HP5989A and MOD-1101, respectively.

N-(4-Nitro-1,8-naphthalimido)-1,8-naphthalimide (1a). A solution of 4-nitro-1, 8-naphthalic anhydride (2.00 g, 8.23 mmol) and N-amino-1, 8-naphthalimide(1.74 g, 8.20 mmol) in absolute ethanol(50 ml) was heated to reflux for 4 h to afford white precipitate, which was collected by filtration while hot and washed with hot acetic acid several times to give 1a as a white solid (3.20 g, yield 90%). Recrystalization from 1, 4-dioxane gave analytical sample of 1a, mp>310℃.

N-(4-Amino-1,8-naphthalimido)-1,8-naphthalimide (1b) could be prepared by reduction of **1a** with SnCl$_2$ in HCl and ethanol solution (pH = 2). Yield 78%. Recrystallization from acetic acid gave analytical sample of 1b, mp>310℃.

N-(4-Dimethylamino-1,8-naphthalimido)-1,8-naphthalimide (1c). Solution of 1a(0.50 g, 1.14 mmol), 33% dimethylamine aqueous solution(6 ml, 0.44 mol) and CuSO$_4$(0.2 g) in DMF(25 ml) was heated at 110℃ for 2.5 h to give orange solid, which was collected by filtration and washed by hot acetic acid till only one point on the TLC, affording analytical sample of 1c(0.40g, 80%), mp>310℃. Procedure similar to that for 1b was used to prepare compound **1d**, **1e**, **1f**, **1g** and **1h**.

N-(4-n-Butylamino-1,8-naphthalimido)-1,8-naphthlimide (1d). Yield 74%, mp>310℃.

N-(4-n-Octylamino-1,8-naphthalimido)-1,8-naphthlimide (1e). Yield 71%, mp> 310℃.

N-(4-Ethanolamino-1,8-naphthalimido)-1,8-naphthlimide (1f). Yield 67%, mp> 310℃.

N-(4-(1, 2-Ethyldiamino)-1,8-naphthalimido)-1,8-naphthlimide (1g). Yield 74%, mp> 310℃.

N-(4-Piperazine-1,8-naphthalimido)-1,8-naphthalimide (1h). Yield 82%, mp> 310℃.

N-(4-Nitro-1,8-naphthalimido)-4-nitro-1,8-naphthalimide (2a) could be prepared by similar procedure to that for 1a but N-amino-4-nitro-1,8-naphthalimide is used instead of N-amino-1,8-naphalimide, yield 70%, mp>310℃.

4-Amino-N-(4-amino-1,8-naphthalimido)-1,8-naphthalimide (2b) was prepared similarly to 1b.

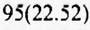
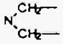
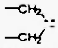
4-Dimethylamino-N-(4-dimethylamino-1,8-naphthalimido)-1,8-naphthalimide (2c) could be prepared by the procedure similar to that for 1c, except that 2c was recrystallized from chlorobenzene. Yield 70%, mp>310℃.

1,2-(N-1,8-Naphthalimido):4,5-(N-1,8-naphthalimido)-pyromellitic diimide (3a). Solution of N-amino-1, 8-naphthaliimide (1.10 g, 5.2 mmol), pyromellitic anhydride (0.5 g, 2.3 mmol) in 70 ml pyridine was heated to reflux for 23 h. The mixture was poured into 100 ml ice water to give pale yellow precipitate, which was collected by filtration and washed by hot K$_2$CO$_3$ (pH = 9-10) and HCl solution (pH = 3-4) sequentially. Washing by hot THF gave 3a (0.9 g, yield 60%) mp>310℃. Under argon atmosphere, 3b and 3c were prepared similarly to 3a, but solvent for 3b was quinoline instead of pyridine.

1,8-(N-1,8-Naphthalimido):4,5-(N-1,8-naphthalimido)-naphthalic diimide (3b). Yield 50%, mp>310℃.

1,8-(N-(4-Dimethylamino-1,8-naphthalimido)):4,5-(N-(4-dimethylamino-1,8-naphthalimido))-naphthalic diimide (3c), mp>310℃.

Table 1: MS, ^{1}H-NMR and elemental analysis data for compounds studied

Sample	MS (EI.70eV) M/Z(%)	^{1}H-NMR δppm in d_6-DMSO except 3a. 3b.3c in D_2SO_4	Elemental analysis
1a	(M+1)$^+$438(13.3). (M)$^+$437(50.6). (M-NO)$^+$407(25.84). (M-NO$_2$)$^+$392(10.94). 225(15.62). 195(16.67)	8.93(H$_a$, d. J_{ab}=8.25Hz. 1H). 8.83(H$_b$+H$_d$, J_{ba}= 8.25Hz. J_{dc}=7.06Hz.m. 2H). 8.25(H$_c$. t. J_{cd}=7.08Hz. J_{ce}=8.10Hz). 8.05(H$_f$.t. 2H). 8.70(H$_e$+2H$_g$+2H$_i$. m. 5H)	Calcd. for $C_{24}H_{11}N_3O_6$: C. 65.90: H. 2.52: N. 9.61 Found: C. 65.69: H. 2.50: N. 9.46
1b	(M+1)$^+$408(18.13). (M)$^+$ 407(65.35). 362(15.80). 295(20.20)	6.90(H$_a$. d. J_{ab}=8.52Hz. 1H). 8.28 (H$_b$. d. J_{ba} = 8.52Hz. 1H). 7.78(H$_c$.t. J_{cd}=7.3Hz. J_{ce}=8.32Hz. 1H). 8.56(H$_d$. d. J_{dc}=7.31Hz. J_{de}=1.01Hz.1H). 8.78(H$_e$.d. J_{ec}=8.32Hz. J_{ed}=1.01Hz. 1H). 8.63(2H$_g$+2H$_i$. m. 4H). 8.00(2H$_f$. t. J_{fg}= 8.01Hz. J_{fi}=7.61Hz. 2H)	Calcd. For $C_{24}H_{13}O_4N_3$: C.70.76: H. 3.19: N. 10.32 Found: C. 70.56: H. 3.20: N. 10.48
1c	(M)$^+$435(13.8). 198(2.37).180(2.2). 28(100)	7.92(H$_a$+H$_c$. m. 2H). 8.18(2H$_f$. t.2H). 8.57(H$_b$+H$_d$+H$_e$. d. 3H). 8.70(2H$_i$. d.2H). 8.84(2H$_g$. d. 2H)	Calcd. For $C_{26}H_{17}O_4N_3$: C. 71.72: H. 3.91: N. 9.66 Found:C.71.56: H.4.02: N. 9.78
1d	(M+1)$^+$464(22.62). (M)$^+$ 463(62.50). (M-CH$_2$CH$_2$CH$_3$)$^+$420(100). 223(13.94). 195(14.12). 182(78.30)	6.90(H$_a$. d. J_{ab}=8.96Hz. 1H). 8.38(H$_b$. d. J_{ba}=8.97Hz. 1H). 7.80(H$_c$. t.J_{cd}=7.60Hz. J_{ce}=8.20Hz. 1H). 8.56(H$_d$. d. J_{dc}=7.57Hz. J_{de}=0.70Hz. 1H). 8.88(H$_e$. d. J_{ec}=8.20Hz. J_{ed}=0.70Hz. 1H), 8.63(2H$_g$+2H$_i$. m. 4H), 8.00(2H$_f$. t. J_{fg}=7.62Hz.J_{fi}=7.98Hz. 2H), 0.9(-CH$_3$ t. 3H), 1.45(CH$_2$-CH$_3$.m. 2H), 3.50(NH-CH$_2$-. m. 2H), 1.73(NH-CH$_2$-CH$_2$. m. 2H)	Calcd. For $C_{28}H_{21}O_4N_3$: C. 72.57: H. 4.54: N. 9.07 Found: C. 72.52: H. 4.56: N. 9.21
1e	(M+1)$^+$520(32.65). (M)$^+$519(70.74). (M-(CH$_2$)$_5$CH$_3$)$^+$434(11.25). (M-(CH$_2$)$_6$CH$_3$+1)$^+$421. 407(14.72). 182(100)	6.90(H$_a$, d. J_{ab}=8.83Hz. 1H), 8.30(H$_b$, d.J_{ba}=8.85Hz. 1H). 7.82(H$_c$. t. J_{cd}=7.6Hz.J_{ce}=8.22Hz. 1H). 8.52(H$_d$, d. J_{dc}=7.30Hz. 1H). 8.85(H$_e$, d. J_{ec}=8.23Hz. 1H), 8.63 (2H$_g$+2H$_i$. m. 4H), 8.00(2H$_f$. t. J_{fg}=7.61Hz, j_{fi}=7.90Hz. 2H). 0.9(-CH$_3$, t. 3H). 1.45(CH$_3$-(CH$_2$)$_5$-, m. 10H), 3.50 (NH-CH$_2$-, m.2H).1.75(NH-CH$_2$-CH$_2$, m. 2H)	Calcd. For $C_{32}H_{29}O_4N_3$: C, 73.99; H, 5.59; N. 8.09 Found: C, 73.63: H. 5.56: N. 8.28
1f	(M)$^+$451(20.98). (M-1)$^+$450(66.06), (M-OH)$^+$434(12.03). (M-CH$_2$-OH)$^+$420(30.80). (M-CH$_2$-OH-1)$^+$419(100)	6.90(H$_a$, d, J_{ab}=8.81Hz. 1H), 8.35(H$_b$, d, J_{ba}=8.68Hz, 1H). 7.80(H$_c$, t. J_{cd}=6.96Hz. J_{ce}=7.93Hz, 1H), 8.56(H$_d$, d. J_{dc}=7.19Hz. 1H), 8.90(H$_e$, d. J_{ec}=8.02Hz, 1H), 8.70 (2H$_g$+2H$_i$, m, 4H), 8.00(2H$_f$, t. J_{fg}=7.81Hz, j_{fi}=7.98Hz, 2H). 3.55(NH-CH$_2$-, t, 2H). 3.75(-CH$_2$-OH, t. 2H)	Calcd. For $C_{26}H_{17}O_5N_3$: C. 69.18; H, 3.77; N, 9.31 Found: C, 69.47; H, 3.72; N. 9.23
1g	(M)$^+$450(46.99), (M-CH$_2$-NH$_2$)$^+$420(61.30), 408(70.95), 362(11.30) 182(73.62)	6.90(H$_a$, d, J_{ab}=8.90Hz, 1H), 8.35(H$_b$, d, J_{ba}=8.74Hz, 1H), 7.80(H$_c$, t, J_{cd}=7.28Hz, J_{ce}= 8.32Hz, 1H), 8.56(H$_d$, d, J_{dc}= 7.28Hz. 1H),8.90(H$_e$, d, J_{ec}=8.36Hz, 1H), 8.67 (2H$_g$+2H$_i$, m, 4H), 8.00(2H$_f$, t, J_{fg}=7.54Hz, j_{fi}=7.95Hz,2H), 2.9(-CH$_2$-NH$_2$, t. 2H), 3.50(NH-CH$_2$-,t,2H)	Calcd. For $C_{26}H_{18}O_4N_4$: C,69.33; H,4.00; N,12.44 Found: C, 69.56; H, 4.12; N, 12.29
1h	(M+1)$^+$477(12.76), (M)$^+$476(37.21), (M- $\begin{smallmatrix}\text{—CH}_2\\ \text{—CH}_2\end{smallmatrix}\!\rangle$NH)$^+$433(100). 195(22.52), 180(22.17). 126(34.26)	^{1}H-NMR(in DMSO-d$_6$) δppm 7.45(H$_a$, d, J_{ab}=7.97Hz, 1H),8.55(H$_b$, d. J_{ba}=7.95Hz, 1H), 7.95(H$_c$, m, 1H), 8.05 (2H$_f$, m, 2H), 8.63(H$_d$+H$_e$,m, partly overlap with H$_g$+H$_i$,2H), 8.70(2H$_g$+2H$_i$, m, partly overlap with H$_d$+H$_e$, 4H), 3.05(t,  N$\langle\!\begin{smallmatrix}\text{CH}_2\text{—}\\ \text{CH}_2\text{—}\end{smallmatrix}$, 4H), 2.1(t,  $\begin{smallmatrix}\text{—CH}_2\\ \text{—CH}_2\end{smallmatrix}\!\rangle$, 4H)	Calcd. For $C_{28}H_{20}O_4N_4$: C, 70.59; H, 4.20; N,11.76 Found: C, 71.04; H, 4.33; N, 11.54
2a	(M)$^+$482(100), (M-NO)$^+$ 452(17.14), (M-2NO+1)$^+$ 423(19.72). 225(59.23)	8.25(2H$_c$, J_{cd}=8.19Hz, J_{ce}=8.02Hz, t, 2H), 8.67(2H$_e$, J_{ec}=8.03Hz, d, 2H), 8.83(2H$_b$+2H$_d$,m, 4H), 8.90(2H$_a$, J_{ab}=8.75Hz, d, 2H)	Calcd. for $C_{24}H_{10}N_4O_8$: C, 59.75; H,2.07; N,11.62 Found: C, 59.99; H. 2.17; N, 11.57
2b	(M)$^+$422(20.4). 197(1.93). 28(100)	6.90(2H$_a$, d, J_{ab}=8.53Hz, 2H), 8.26(H$_b$, d, J_{ba} = 8.55Hz, 2H), 7.80(H$_c$, t. J_{cd}=7.52Hz, J_{ce}=8.43Hz, 2H), 8.65(H$_d$, d. J_{dc}=7.68Hz, J_{de}=1.81Hz. 2H), 8.85(H$_e$, d. J_{ec}= 8.39Hz. J_{ed}=1.79Hz. 2H)	Calcd. For $C_{24}H_{14}O_4N_4$: C.68.25: H, 3.32; N, 13.27 Found: C. 68.46; H, 3.75; N. 12.98
2c	(M)$^+$478(46.99). 240(7.41). 223(14.80).196(7.67)	9.20(2H$_a$+2H$_c$. m. 4H), 9.61(2H$_b$, d, 2H). 9.87(2H$_d$+2H$_e$, d. 4H), 4.59(-N(CH$_3$)$_2$. 6H)	Calcd. For $C_{28}H_{22}O_4N_4$: C. 70.29; H,4.60; N.11.72 Found: C. 70.31: H. 4.44;N, 11.80
3a	(M)$^+$ was not observed in EI(70eV)	7.88(4H$_b$, t , 4H) , 8.50(4H$_a$, d. 4H), 8.64 (4H$_c$. d. 4H) .8.98(2H$_d$, s. 2H)	Calcd. For $C_{34}H_{14}O_8N_4$: C, 67.33; H, 2.31; N, 9.24 Found: C, 67.87; H, 2.35: N. 9.17
3b	(M)$^+$ was not observed in EI(70eV)	7.85(4H$_b$, t. 4H). 8.55(4H$_a$, d. 4H), 8.68 (4H$_c$, d. 4H), 8.85 (4H$_d$, s ,4H)	Calcd. for $C_{38}H_{16}N_4O_8$: C, 69.41; H, 2.44; N, 8.54 Found: C, 69.21: H,2.52: N. 8.30
3c	(M)$^+$ was not observed in EI(70eV)	7.85(2H$_a$+2H$_c$. broad. 4H). 8.25(2H$_b$, s, 2H), 8.50(2H$_d$+2H$_e$, broad, 4H). 8.62(4H$_f$, s. 4H), 3.23(N-(CH$_3$)$_2$. s. 12H)	Calcd. for $C_{42}H_{26}N_6O_8$: C.67.92; H, 3.50; N, 11.32 Found: C. 68.06; H. 3.65:N. 11.31

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Reference and Notes

(1) S. R. Greenfield, W. A. Svec, D. J. Gosztola, and M. R. Wasielewski, *J. Am. Chem. Soc.*, **118**, 6767 (1996).

(2) M. P. Debreczeny, W. A. Svec, E. M. Marsh, and M. R. Wasielewski, *J. Am. Chem. Soc.*, **118**, 8174 (1996).

(3) A. Osuka, R. Ahang, K. Maruyama, T. Ohno, and K. Nozaki, *Bull. Chem. Soc. Jpn.*, **66**, 3773 (1993).

(4) G. P. Wiederrecht, W. A. Svec and M. R. Wasielewski, *J. Am. Chem. Soc.*, **119**, 6199 (1997).

(5) K. Hasharoni, H. Levanon, S. R. Greenfild, D. J. Gosztola, W. A. Svec, and M. R. Wasielewski, *J. Am. Chem. Soc.*, **118**, 10228 (1996).

(6) J. Su, T. Xu, K. Chen, and H. Tian, *Synthetic Metals*, **91**, 249 (1997).

(7) M. F. Brana, J. M.Castellano, M. Moran, M. J.Perez de Vega, C. R. Romerdahl, X-D Qian, P. Bousquet, F. Emling and E. Schlick, *Anti-Cancer Drug Design*, **8**, 257 (1993).

(8) D. Rideout, R. Schinazi, C.D. Pauza, K. Lovelace, L.-C. Chiang, T. Calogeropoulou, M. McCarthy and J. H. Elder, *J. Cell. Biochem.*, **51**, 446 (1993).

(9) R. W. Mikkleton, and J. Parrick, *J. Heterocyclic Chem.*, **22**, 1567 (1985).

(10) R. W. Mikkleton, J. Parrick, E. D. Clarke and P.Wardman, *J. Heterocyclic Chem.*, **23**, 849 (1986).

(11) M. S. Alexiou, J. Tyman, and I. Wilson, *Tetrahedron Lett.*, **22**, 2303 (1981).

(12) M. S. Alexiou, V. Tychopoulos, S. Ghorbanian, J. H. P. Tyman, R. G. Brown, and P. I. Brittain, *J. Chem. Soc Perkin Trans.* 2, 837 (1990).

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