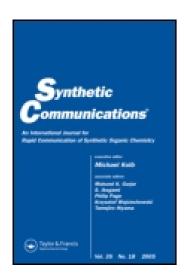
This article was downloaded by: [Ams/Girona*barri Lib]

On: 14 October 2014, At: 01:45 Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer

House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

N-METHYL-3,4-DIHYDRO-[3,1]OXAZINOACRIDINE, A USEFUL INTERMEDIATE IN THE SYNTHESIS OF POLYSUBSTITUTED ACRIDINES

Franck Charmantray ^a , Martine Demeunynck ^b , Abderrahim Wardani ^c & Jean Lhomme ^a Université Joseph Fourier , Laboratoire de Chimie Bioorganique, LEDSS, Grenoble, cedex 9, 38041, France

^b Université Joseph Fourier, Laboratoire de Chimie Bioorganique, LEDSS, Grenoble, cedex 9, 38041, France

Published online: 09 Nov 2006.

To cite this article: Franck Charmantray, Martine Demeunynck, Abderrahim Wardani & Jean Lhomme (2001) N-METHYL-3,4-DIHYDRO-[3,1]OXAZINOACRIDINE, A USEFUL INTERMEDIATE IN THE SYNTHESIS OF POLYSUBSTITUTED ACRIDINES, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:13, 2001-2009, DOI: 10.1081/SCC-100104417

To link to this article: http://dx.doi.org/10.1081/SCC-100104417

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

^c Département de Chimie , Université Chouaib Doukkali, Faculté des Sciences , El Jadida, Maroc

N-METHYL-3,4-DIHYDRO-[3,1]OXAZINO-ACRIDINE, A USEFUL INTERMEDIATE IN THE SYNTHESIS OF POLYSUBSTITUTED ACRIDINES

Franck Charmantray, Martine Demeunynck, Abderrahim Wardani, and Jean Lhomme

¹Laboratoire de Chimie Bioorganique, LEDSS, Université Joseph Fourier, 38041 Grenoble, cedex 9, France ²Université Chouaib Doukkali, Faculté des Sciences, Département de Chimie, El Jadida, Maroc

ABSTRACT

3,4-Dihydro-4-methyl-1*H*-[3,1]oxazinoacridine was prepared in four steps from 3-aminoacridine. DDQ induced opening of the dihydrooxazine ring yielded the 3-methylamino-4-formyl derivative. The same strategy was applied to 11-aminobenzo-[b][1,7]phenanthroline.

Polysubstituted acridines constitute a large family of compounds of biological interest (antitumor, antimalarial agents ...). In most cases, the substituents are introduced in an early stage of the synthesis, prior to the formation of the acridine ring. In the course of a program dedicated to the search for new antitumor agents, we applied electrophilic aromatic substitution to introduce various substituents onto the acridine ring. ¹⁻⁴ The reactions were regioselective. 3-Aminoacridine (1) or 3,6-diaminoacridine

^{*}Corresponding author.

2002

CHARMANTRAY ET AL.

(proflavine) were shown to react at positions 4 or 4 and 5, ortho to the amino groups. No reaction products corresponding to substitution in the 2 (and 7) position could be detected. We took advantage of this reactivity and regioselectivity to prepare a new heterocycle, 10-aminobenzo[b][1,7]-phenanthroline (2), from proflavine.⁵

Reaction of the amino-heterocycles 1 and 2 with formaldehyde was also studied. Depending on the stoichiometry in formaldehyde and on the nature of the acid used as the solvent, various types of molecules were obtained: Tröger's bases, tetrahydroquinazoline and dihydro-[3,1]oxazine derivatives.^{6,7} We report here the synthesis of the N-methyl analogues of dihydro-[3,1]oxazine (9 and 10), prepared from 3-methylaminoacridine 7 and 10-methylaminobenzo[b][1,7]phenanthroline 8 and show that DDQ induced ring cleavage yields the corresponding aldehydes in good yields.

RESULTS AND DISCUSSION

The N-methylamino heterocycles were obtained in three steps from the amino derivatives. The reaction with *para*-toluenesulfonyl chloride in pyridine afforded the *para*-toluenesulfonamides **3** and **4**, which were alkylated with methyl iodide in the presence of potassium carbonate to give **5** and **6** in excellent yields. Hydrolysis of the *para*-toluenesulfonamide in sulfuric acid afforded **7** and **8** in quantitative yield. The reaction with formaldehyde was performed in methanesulfonic acid for **8** or 12 N hydrochloric acid for **7**. In both solvents, the reactions proceeded smoothly to give the N-methyl-dihydro-[3,1]oxazines **9** and **10** in good yields (78% and 97% respectively). These compounds were characterized by nmr spectroscopy and mass spectrometry. In the ¹H nmr spectra of **9** and **10**, the two methylenes of the dihydrooxazine rings appeared as two singlets at 5.47 and 5.43 ppm respectively for ArCH₂O, and 4.72 and 4.73 ppm for NCH₂O.

The N-methyl-dihydro-[3,1]oxazine ring in **9** or **10** was shown to be stable in basic conditions (1 N aqueous sodium hydroxide) and to decompose in strong acidic medium (6 N hydrochloric acid). No reaction occurred with

$$X = Y = H$$

$$Y = H$$

$$X = Y = H$$

$$X = Y = H$$

$$X = Y = H$$

$$Y = H$$

$$X = Y = H$$

$$Y =$$

REPRINTS

i) TsCl, py, 0°C; ii) K_2CO_3 , then Mel in excess, DMF, r.t; iii) H_2SO_4 , r.t; iv) $(HCHO)_n$, $MeSO_3H$ or 12N HCl, r.t.

Figure 1.

lithium aluminium hydride, in conditions where the N-unsubstituted analogues were readily cleaved to the corresponding amino-alcohols. Cleavage could be achieved by oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), which is known to oxidize benzyl positions. To our knowledge, this reagent has never been used to open heterocyclic rings such as dihydrooxazines. Different reaction conditions were tested.

As depicted in Figure 2, compound 9 was reacted at room temperature with DDQ in dioxane. The reaction was followed by hplc. When all the starting dihydrooxazine 9 had reacted, the black solid that was formed in solution was separated and vigorously stirred in hot water to achieve hydrolysis of the hemiacetal intermediate. The aldehyde 11 was thus obtained in good yield (70%). The reaction of 10 with DDQ was performed in methanol. The reaction proceeds smoothly at room temperature. In these conditions, it was possible to isolate the acetal intermediate 12 in 95% yield. Formation of the aldehyde 13 was obtained by acidic hydrolysis of 12 (quantitative yield) or in a one-pot reaction from 10 in 85% yield.

CONCLUSION

We designed an efficient strategy to prepare polycyclic N-methyl-dihydro-[3,1]oxazine derivatives. The two compounds described in this



2004

CHARMANTRAY ET AL.

9
$$\stackrel{i}{\longrightarrow}$$
 $\stackrel{N}{\longrightarrow}$ $\stackrel{N}{\longrightarrow}$ $\stackrel{Me}{\longrightarrow}$ $\stackrel{iii}{\longrightarrow}$ $\stackrel{N}{\longrightarrow}$ $\stackrel{N}{\longrightarrow}$ $\stackrel{N}{\longrightarrow}$ $\stackrel{Me}{\longrightarrow}$ $\stackrel{12}{\longrightarrow}$ $\stackrel{13}{\longrightarrow}$ $\stackrel{13}{\longrightarrow}$

i) DDQ, dioxane, r.t, 3 h; ii) DDQ, MeOH, r.t, 1 h; iii) 2N HCl, r.t, 1 h

Figure 2.

paper have been tested as anticancer agents. They display significant cytotoxicity on L1210 (IC $_{50}$ 2 μ M and 1.3 μ M for **9** and **10** repectively). The dihydrooxazine ring was shown to react with DDQ in a regioselective way to afford the corresponding aldehyde. It is to our knowledge the first example of oxidative ring opening achieved by DDQ producing an *ortho*-amino substituted heteroaromatic aldehyde. These type of compounds should be very useful to prepare a large variety of polysubstituted derivatives.

EXPERIMENTAL

Melting points (uncorrected) were determined using the capillary tube. Unless mentioned otherwise 1H NMR spectra were taken at 200 MHz on Bruker AC 200 spectrometer. DMSO-d₆ or CDCl₃ were used as solvent and TMS as an internal standard. The chemical shifts are reported in ppm, in δ units. The mass spectra were recorded on a Varian Mat 311 and AET MS 30 instruments. Thin layer chromatography (tlc) was carried out on "Merck Kieselgel $60F_{254}$ " plates and scanned under ultraviolet light at 254 nm and 365 nm. Column chromatography was carried out with silica gel "Merk Kieselgel 60".

Synthesis of N-Methylamino Heterocycles 7 and 8

3-(para-Toluenesulfonylamino)acridine 3

Para-toluenesulfonyl chloride (6 g, 31 mmol) dissolved in pyridine (30 mL) was added dropwise to a solution of 3-aminoacridine 1 (3 g,

15 mmol) in pyridine (100 mL) cooled at 0°C. After 4h stirring at room temperature, compound 3 was precipitated by pouring the solution into a large volume of ether-hexane (1–1 mixture). After filtration, 3 was dissolved in the minimum of methanol and crystallized by adding diethylether. Compound 3 was obtained in 85% yield (9.15 g, 26 mmol).

REPRINTS

Mp $185-190^{\circ}$ C; ¹H nmr (DMSO-d₆) δ 11.8 (1H, s, NH), 9.80 (1H, s, H-9), 9.20–8.90 (3H, m, H-1, H-5 and H-8), 8.65 (1H, m, H-6), 8.63 (2H, m, Ts-H), 8.58 (1H, d, H-4), 8.38 (1H, m, H-7), 8.25 (1H, m, H-2), 8.20 (2H, m, Ts-H), 2.40 (3H, s, CH₃); ms (EI) m/z 348 (M^+); Anal. Calcd. for C₂₀H₁₆N₂O₂S: C-68.70, H-4.67, N-7.74, Found: C-68.95, H-4.63, N-8.04.

(para-Toluenesulfonylamino) Benzo[b][1,7]phenanthroline 4

The same procedure was used starting from 2 (1 g, 4 mmol). Compound 4 (1.5 g, 3.76 mmol) was obtained in 92% yield.

¹H nmr (DMSO-d₆, 60 MHz) δ 11.4 (1H, s, NH), 9.5 (1H, dd, J = 8.2 and J = 1.7 Hz, H-1), 9.0 (1H, dd, J = 4.4 and J = 1.7 Hz, H-3), 8.9 (1H, s, H-7), 8.1 (1H, d, J=9.2 Hz, H-6), 7.9–7.2 (9H, m, H-8, H-5, H-2, H-9, H-11 and TsH), 2.2 (3H, s, TsCH₃); ms (EI) m/z 399 (M⁺); Anal. Calcd. for C₂₃H₁₇N₃O₂S: C-69.15, H-4.29, N-10.52, S-8.03 Found: C-69.35, H-4.41, N-10.71, S-7.86.

3-(N-Methyl-N-para-toluenesulfonylamino) Acridine 5

Compound 3 (0.5 g, 1.4 mmol) was dissolved in DMF (20 mL) in the presence of potassium carbonate (6 mmol). Methyl iodide (4.5 mmol) was added and the solution was stirred at room temperature for 1 h. Salts were removed by filtration and the solvent was evaporated under reduced pressure to dryness. The residue was purified by column chromatography on silica gel. Compound 5 was eluted with ethyl acetate, and was obtained in 85% yield (0.44 g, 1.2 mmol).

Mp 160° C; ¹H nmr (DMSO-d₆) δ 8.70 (1H, s, H-9), 8.07 (1H, m, H-5), 7.94 (1H, m, H-8), 7.91 (1H, d, J=9 Hz, H-1), 7.77 (1H, dd, J=9 and $2.2 \,\mathrm{Hz}$, H-2), 7.71 (1H, m, H-6), 7.52 (1H, d, J= $2.2 \,\mathrm{Hz}$, H-4), 7.47 (1H, m, H-7), 7.38 (2H, d, J = 8 Hz, Ts-H), 7.12 (2H, d, J = 8 Hz, Ts-H), 3.26 (3H, s, NCH₃), 2.31 (3H, s, TsCH₃); ms (Cl, NH₃, isobutane) m/z 363 (M + 1)⁺; Anal. Calcd. for C₂₁H₁₈N₂O₂S, 0.25 H₂O: C-68.74, H-5.08, N-7.63, Found: C-68.60, H-5.07, N-7.47.



2006 CHARMANTRAY ET AL.

10-(N-Methyl-N-*para*-toluenesulfonylamino) benzo[b][1,7]-phenanthroline **6**

The same method was used to prepare **6** from **4** (0.8 g, 2 mmol) in 90% yield after purification.

Mp 218–219°C; ¹H nmr (DMSO-d₆, 60 MHz) δ 9.5 (1H, m, H-1), 9.0 (1H, m, H-3), 8.9 (1H, s, H-7), 8.1 (1H, d, J=9.2 Hz, H-6), 7.9–7.2 (9H, m, H-2, H-5, H-8, H-9, H-11 and Ts-H), 3.4 (3H, s, NCH₃), 2.3 (3H, s, TsCH₃); Anal. Calcd. for C₂₄H₁₉N₃O₂S: C-69.71, H-4.63, N-10.16, S-7.75, Found: C-69.41, H-4.68, N-10.26, S-7.64.

3-Methylaminoacridine 7

Compound 5 (0.2 g, 0.5 mmol) dissolved in sulfuric acid (1 mL) was stirred at room temperature for 90 min. The solution was added dropwise to cold diluted aqueous ammonium hydroxide and compound 7 was extracted with methylene chloride. The solvent was concentrated and compound 7 precipitated by adding diethyl ether, it was obtained in quantitative yield (0.113 g, 0.5 mmol).

Mp 225–227°C; ¹H nmr (DMSO-d₆) δ 8.71 (1H, s, H-9), 7.98 (1H, m, H-5), 7.88 (1H, m, H-8), 7.80 (1H, d, J=9 Hz, H-1), 7.70 (1H, m, H-6), 7.38 (1H, m, H-7), 7.07 (1H, d, J=9 Hz, H-2), 6.85 (1H, s, NH), 6.68 (1H, s, H-4), 2.84 (3H, s, NCH₃); ms (FAB+, NBA) m/z 209 (M+1)⁺; Anal. Calcd. for C₁₄H₁₂N₂: C-79.71, H-5.88, N-13.28, Found: C-79.93, H-5.72, N-13.40.

10-(Methylamino)benzo[b][1,7]phenanthroline 8

The same method was used to prepare $\bf 8$ in quantitative yield starting from $\bf 6$ (0.2 g, 0.48 mmol).

Mp 286°C: 1 H nmr (DMSO-d₆) δ 9.50 (1H, ddd, J=8.2, 1.8 and 0.6 Hz, H-1), 8.93 (1H, dd, J=4.5 and 1.8 Hz, H-3), 8.64 (1H, s, H-7), 8.00 (1H, d, J=9.2 Hz, H-6), 7.81 (1H, d, J=9 Hz, H-8), 7.68 (1H, d, J=9.2 Hz, H-5), 7.64 (1H, dd, J=8.2 and 4.5 Hz, H-2), 7.13 (1H, dd, J=9 and 2.1 Hz, H-9), 6.90 (1H, d, J=2.1 Hz, H-11), 6.58 (1H, m, NH), 2.90 (3H, d, J=4.9 Hz, CH₃); ms (EI) m/z 259 (100, M⁺); Anal. Calcd. for $C_{17}H_{13}N_3$: C-78.74, H-5.05, N-16.21, Found: C-78.53, H-4.92, N-15.94.



Obtention of the N-Methyl-dihydro[3,1]oxazine ring

3,4-Dihydro-4-methyl-1*H*-[3,1]oxazinoacridine 9

Compound 7 (0.64 g, 3.2 mmol) was dissolved in 12 N hydrochloric acid (6 mL) in the presence of paraformaldehyde (0.6 g, 20 mmol). The mixture was stirred at room temperature for 45 min and then basified with diluted aqueous ammonium hydroxide. Compound 9 was extracted with dichloromethane. Concentration of the solvent afforded 9 as a yellow powder in 78% yield (0.62 g, 2.5 mmol).

REPRINTS

Mp 154°C; ¹H nmr (CDCl₃) δ 8.50 (1H, s, H-9), 8.05 (1H, d, J=8.7 Hz, H-5), 7.84 (1H, d, J=8.3 Hz, H-8), 7.72 (1H, d, J=9.2 Hz, H-1), 7.63 (1H, m, H-6), 7.38 (1H, m, H-7), 7.18 (1H, d, J=9.2 Hz, H-2), 5.47 (2H, s, ArCH₂O), 4.72 (2H, s, NCH₂O), 3.00 (3H, s, NCH₃); ms (FAB+, NBA) m/z 251 (M+1)⁺; Anal. Calcd. for C₁₆H₁₄N₂O: C-76.23, H-5.68, N-11.11, Found: C-76.27, H-5.64, N-10.70.

3,4-Dihydro-4-methyl-1H-[3,1]benzooxazino[5,6-b][1,7]-phenanthroline **10**

Compound 8 (1 g, 3.9 mmol) was dissolved in 5 mL of methanesulfonic acid (98%) in the presence of paraformaldehyde (0.3 g, 10 mmol). The mixture was stirred at room temperature for 10 min and then basified with diluted aqueous ammonium hydroxide. Compound 10 was extracted twice with dichloromethane. Concentration of the solvent afforded 10 as a yellow powder in 97% yield (1.12 g, 3.7 mmol).

Mp 183°C; ¹H nmr (DMSO-d₆, 300 MHz) δ 9.42 (1H, d, J=8.2 Hz, H-13), 8.96 (1H, dd, J=4.4 and 1.6 Hz, H-11), 8.73 (1H, s, H-7), 8.0 (1H, d, J=9.2 Hz, H-8), 7.89 (1H, d, J=9.1 Hz, H-6), 7.71 (1H, d, J=9.2 Hz, H-9), 7.65 (1H, dd, J=8.2 Hz and 4.4 Hz, H-12), 7.36 (1H, d, J=9.1 Hz, H-5), 5.43 (2H, s, ArCH₂O), 4.73 (2H, s, NCH₂O), 3.03 (3H, s, NCH₃); ms (EI) m/z 301 (98, M⁺); Anal. Calcd. for C₁₉H₁₅N₃O: C-75.73, H-5.02, N-13.94, Found: C-75.87, H-5.12, N-13.72.

Oxidative Ring Cleavage

4-Formyl-3-methylaminoacridine 11

A mixture of 9 (1.5 g, 6 mmol) and DDQ (12 mmol) in dioxane was stirred at room temperature for 3 h. The black solid that deposited was

filtered, and suspended in water (2 L). The mixture was stirred at 85°C for 7 h. After cooling to room temperature, dichloromethane was added (1 L) and the solution was stirred overnight. The organic layer was then separated, washed with water, dried over sodium sulfate and concentrated under reduced pressure. Compound 11 was precipitated by adding diethyl ether and was obtained in 70% yield (0.991 g, 4.2 mmol).

Mp 233°C; 1 H nmr (CDCl₃) δ 11.40 (1H, s, CHO), 10.55 (1H, s, NH), 8.37 (1H, s, H-9), 8.05 (1H, d, J = 8.4 Hz, H-5), 7.85 (1H, d, J = 9.0 Hz, H-1), 7.80 (1H, d, J = 8.0 Hz, H-8), 7.70 (1H, m, H-6), 7.40 (1H, m, H-7) 7.08 (1H, d, J = 9.0 Hz, H-2), 3.10 (3H, s, NCH₃); ms (FAB+, glycerol) m/z 237 (M+1)⁺; Anal. Calcd. for $C_{15}H_{12}N_2O$: C-76.25, H-5.12, N-11.86, Found: C-76.21, H-5.16, N-11.68.

Ring Cleavage of 3,4-Dihydro-4-methyl-1*H*-[3,1]benzoxazino[5,6-*b*] [1,7] Phenanthroline 10 in Methanol: Formation of 3,4-Dihydro-1-methoxy-4-methyl-1*H*-[3,1]benzooxazino[5,6-*b*][1,7]phenanthroline 12 and 4-Formyl-3-methylamino-benzo[b][1,7]phenanthroline 13

DDQ (0.2 g, 0.8 mmol) was added to a solution of **10** (0.1 g, 0.33 mmol) dissolved in 50 mL of dried methanol. The reaction was kept at room temperature for 1 h. The insoluble fraction was filtered off and washed with water and methylene chloride. The organic layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel using ethyl acetate as eluent.

Acetal derivative 12 was thus isolated in 95% yield (0.106 g, 0.32 mmol). One-pot benzylic oxidation and hydrolysis of the acetal was achieved by acidic treatment of the methanolic solution with 2 N HCl (1 mL), for 1 h, under stirring. The insoluble fraction was filtered off and the filtrate basified with aqueous sodium hydrogenocarbonate. The aqueous solution was extracted with methylene chloride, the organic phase was concentrated and subjected to column chromatography using the same conditions as described above. Compound 13 was isolated as pure product (0.081 g, 0.28 mmol) in 85% global yield.

12. Mp 190–192°C; ¹H nmr (DMSO-d₆, 300 MHz) δ 9.59 (1H, dd, J=8.2 Hz and 1.8 Hz, H-13), 8.93 (1H, dd, J=4.5 Hz and J=1.8 Hz, H-11), 8.41 (1H, s, H-7), 7.87–7.76 (3H, m, H-6, H-8, H-9), 7.57 (1H, dd, J=8.2 Hz and J=4.5 Hz, H-12), 7.17 (1H, d, J=9.2 Hz, H-9), 6.41 (1H, s, H-1), 4.87 (2H, dd, J=8.8 Hz, H-3), 3.83 (3H, s, OCH₃), 3.11 (3H, s, NCH₃); ms (EI) m/z 331 (56, M⁺); Anal. Calcd. for $C_{20}H_{17}N_3O_2$: C-72.49, H-5.17, N-12.68, Found: C-72.22, H-5.01, N-12.59.

POLYSUBSTITUTED ACRIDINES

13. Mp 260° C; 1 H nmr (DMSO-d₆, $300\,\text{MHz}$) δ 11.47 (1H, s, CHO), 10.23 (1H, q, J=5.1Hz, NH), 9.52 (1H, dd, J=8.2 Hz and J=1.7 Hz, H-1), 8.97 (1H, dd, J=4.4 Hz and J=1.7 Hz, H-3), 8.77 (1H, s, H-7), 8.17 (1H, d, J=9.3 Hz, H-6), 8.05 (1H, d, J=9.3 Hz, H-8), 7.77 (1H, d, J=9.3 Hz, H-5), 7.68 (1H, dd, J=8.2 Hz and J=1.7 Hz, H-2), 7.36 (1H, d, J=9.3Hz, H-9), 3.10 (3H, d, J=5.1Hz, NCH₃); ms (EI) m/z 287 (40, M⁺); Anal. Calcd. for $C_{18}H_{13}N_3O$: C-75.25, H-4.56, N-14.62, Found: C-75.03, H-4.67, N-14.49.

REFERENCES

- 1. Wardani, A.; Lhomme, J.; Bigg, D.C.H. and Salez, H. Patent PCT Int APP. WO 9107, 403.
- 2. Duflos, A.; Bigg, D.C.H.; Lhomme, J.; Fixler, N.; Etievant, C. and Demeunynck, M. Patent FR 2712 290A, 1993.
- 3. Lhomme, J.; Bigg, D.C.H.; Duflos, A.; Bonnaud, B.; Demeunynck, M.; Etievant, C. and Kiss, R. Patent PCT Int APP. WO 94 25439.
- Duflos, A.; Bigg, D.C.H.; Lhomme, J.; Bonnaud, B. and Etievant, C. Patent Fr 2716454.
- 5. Wardani, A. and Lhomme, J. Tetrahedron Lett. 1993, 34, 6411.
- 6. Salez, H.; Wardani, A.; Demeunynck, M.; Tatibouët, A. and Lhomme, J. Tetrahedron Lett. **1995**, *36*, 1271.
- 7. Tatibouët, A.; Fixler, N.; Demeunynck, M. and Lhomme, J. Tetrahedron 1997, 53, 2891.
- 8. Fixler, N. PhD Thesis, Grenoble, 1994.
- 9. Oikawa, Y. and Yonemitsu, O. J. Org. Chem. 1977, 42, 1213.
- 10. Oikawa, Y.; Yoshioka, T. and Yonemitsu, O. Tetrahedron Lett. **1982**, 23, 885.
- 11. Xu, Y.-C.; Lebeau, E.; Gillard, J.W. and Attardo, G. Tetrahedron Lett. **1993**, *34*, 3841.

Received in the UK July 17, 2000

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the U.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our Website User Agreement for more details.

Order now!

Reprints of this article can also be ordered at http://www.dekker.com/servlet/product/DOI/101081SCC100104417