Monatshefte für Chemie 137, 1211–1217 (2006)
DOI 10.1007/s00706-006-0513-1

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

An Efficient Microwave-Assisted Synthesis of Structurally Diverse Styrylquinolines

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Received October 21, 2005; accepted (revised) November 11, 2005
Published online August 24, 2006 © Springer-Verlag 2006

Summary. Aromatic aldehydes undergo condensation with quinaldines under microwave irradiation to afford structurally diverse styrylquinolines in high yields under solvent-free conditions. A comparison with the conventional method clearly indicates the advantages of the new protocol.

Keywords. Heterocycles; Aldehydes; Microwave irradiation; Solid phase synthesis; Styrylquinolines.

Introduction

Quinoline is an important heterocycle contained in various classes of pharmacological agents that can play an important role in biochemical processes [1]. In particular, styrylquinolines having therapeutic activity against HIV integrase have been reported recently [2–5] and FZ41 is an example of such a compound under preclinical development [6].

Several methods are available for the synthesis of styrylquinolines. However, they are low yielding and time consuming. Furthermore, due to side-reactions and large volumes of organic solvents these protocols produce significant quantities of chemical waste. Known methods for the direct introduction of alkyl substituent into the quinoline cycle depend on the reactions of parent heterocycles or their *N*-oxides with organometallic compounds [7–9], reaction of chloro-derivatives with active methylene compound [11–13], or with *Wittig* reagents [14]. However, most often styrylquinolines are obtained in the reaction of an appropriate quinaldine with aldehydes in acetic anhydride (Scheme 1). Protocols described for this reaction require, however, long times and a large excess of aldehyde. The purification of the resulting reaction mixture poses also a problem [15].

Microwave assisted organic synthesis (MAOS) is an attractive alternative for traditional organic synthesis [16–18]. Especially, the use of surface active catalysts

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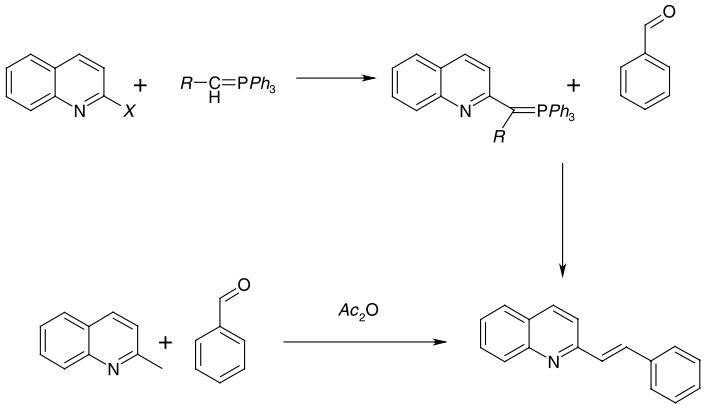
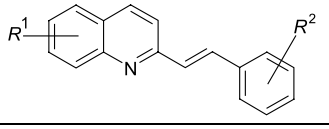


Scheme 1

in dry media (also called solvent-free conditions) is highly interesting because of mild conditions and good selectivity. Neat synthesis is another interesting technique in MAOS. This facilitates to obtain the desired product with minimal amounts of by-products and almost without solvents. In this study, a known route to styrylquinolines has been significantly improved by utilizing microwave irradiation to provide an efficient and rapid path to structurally diversified series of these compounds.

Table 1. Styrylquinolines obtained according to different protocols

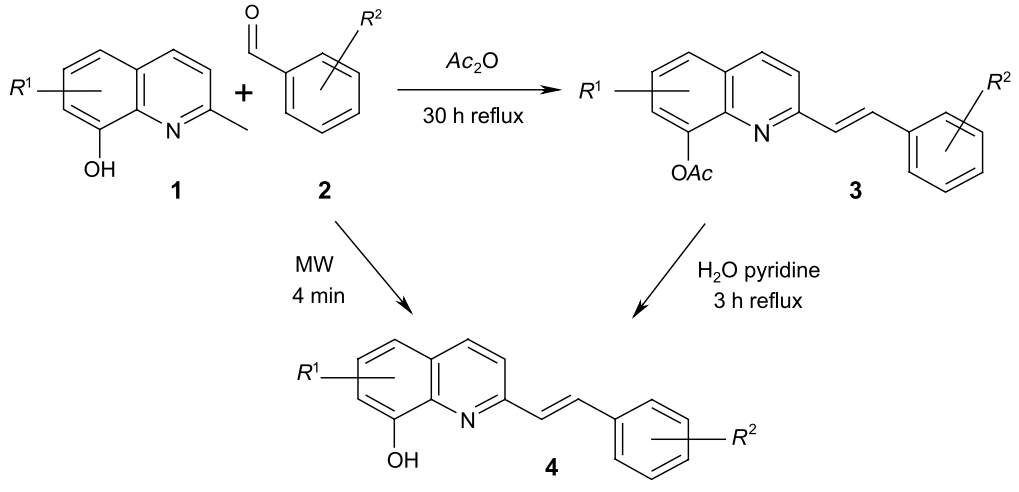
			Mp/°C	Yield/%/time/min	
				Conventional procedure B	Microwave procedure A
4a	8-COOH	2-Cl	187–190	35/300	75/4
4b	8-COOH	2-OH	225–230	32/300	73/4
4c	8-COOH	3-Br	170–175	–	65/4
4d	6-COOH	2-O*Me*	246–249	42/300	59/4
4e	5-COOH	2-OH	338–345 (dec)	–	70/4
4f	5-COOH	3-Cl	238–240	50/300	72/4
4g	6-COOH	2-OH	292–295	61/300	75/4
4h	7-COOH	3-Cl	325	34/300	30/4
4i	5-COOH	2-Br	310	–	76/4
4j	5-COOH	2-O*Me*	241–243	55/300	75/4
4k	5-COOH	3-O*Me*	256–260	60/300	80/4
4l	7-COOH	2-O*Me*	260	–	63/4
4m	7-COOH	2-OH	325–332 (dec)	51/300	62/4
4n	5-COOH 8-COOH	2-O*Me*	283–288	–	82/4
4o	6-COOH	4-O*Me*	279–282	–	78/4
4p	5-COOH 8-COOH	3-Cl	238–240	–	75/4
4q	6-COOH	2-Br	276–278	–	75/4

Results and Discussion

The reactions described herein were performed in open glass tubes using neat reactants under solvent-free conditions. We obtained good results and high yields in a microwave reactor. An illustrative group of synthesized compounds is listed in Table 1. The MW-accelerated reaction compares advantageously to the previously reported process in acetic anhydride, which in fact needs a final hydrolysis as a second step (Scheme 2).

Thus, the MW protocol provides an efficient replacement for a traditional two step synthesis. Under conventional conditions longer time of heating was required to achieve satisfactory yield, and side reactions yielded significant amounts of by-products. Thus it had an effect on purity of isolated product and use of solvent.

As the method described in literature involves a two step process this cannot be used as a reference. Thus, we performed neat synthesis in an oil bath. This process needed a 6 fold excess of the reacting aldehyde in comparison to a 2 fold excess required under MW irradiation. Generally, the results are also much better under MW conditions, *i.e.*, the reaction proceeds much more quickly and the yields are higher. This means that the MW protocol is not only environmentally benign but also a much more economical process. Table 2 shows the solvent volumes required to obtain 0.01 mol of pure product including both the reaction and purification step.



Scheme 2

Table 2. The volumes of solvents required to obtain 0.01 mol of pure product

Method / Solvents	Conventional heat source, V/cm^3		MAOS V/cm^3
	Acetic anhydride	Neat	
Acetic anhydride	5	–	–
Pyridine	7	–	–
Diethyl ether	50	40	20
*Et*OH	50	50	50
Dichloromethane	20	–	–

In conclusion, we have developed an efficient and facile one-step synthesis of structurally diverse styrylquinolines. This method provides a simple and environmentally friendly alternative for the known procedure. A comparison with the conventional method clearly indicates the advantages of the MAOS synthesis that is not only faster but also improves the yields. As the general procedures are based on mixing of neat reactants the problems associated with waste disposal of reagent excess and solvents can be easily minimized.

Experimental

Melting points were measured on a Boetius apparatus. ^{1}H NMR spectra were recorded on a Bruker DRX 500, elemental analysis (C, H) were performed on a EuroVector 3018 apparatus and were in good agreement with calculated values. In some cases the styrylquinolines included water molecules to form stable crystals, which has also been reported previously [19, 20]. 8-Hydroxyquinaldine and aldehydes were obtained from Aldrich and used without further purification. Solvents such as diethyl ether, ethanol, and pyridine were obtained from POCh in analytical grade. Acetic anhydride was dried with Na and fractionally distilled [21]. Suitable quinaldic acids were synthesized according to procedures described earlier in literature [22]. Reactions were performed in a laboratory microwave reactor RM 800PC ensuring a concentrated microwave field CMF from Plazmatronika. The oven was operated at 70% power (560 W) in a two step mode with interval (2 min–30 s–2 min). During all experiments temperature control (170–175°C) was provided.

Procedure A. The appropriate quinaldine derivative (10 mmol) was mixed thoroughly with 2 equiv aldehyde, put in an open vessel and exposed to microwave irradiation for 4 min. Then the reaction mixture was allowed to cool down, 5 cm^3 ether were added, and the resulting solids were filtered off, washed with 20 cm^3 warm ether, and crystallized.

Procedure B. The appropriate quinaldine derivative (10 mmol) was mixed thoroughly with 6 equiv aldehyde and heated under inert gas atmosphere (N_2) during 5 h at 170–175°C. The mixture was then cooled down, diethyl ether was added, and the precipitate was filtered off. The solid was washed with hot diethyl ether and crystallized or chromatographed.

2-[2-(2-Chlorophenyl)vinyl]quinoline-8-carboxylic acid (**4a**, $C_{18}H_{12}ClNO_2$)
Yellow solid, yield 75%, mp 187–190°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.42$–7.48 (m, 2H), 7.54–7.6 (m, 1H), 7.7 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 7.8 (t, $J = 7.5$ Hz, $1H_{arom}$), 8.06–8.14 (m, 3H), 8.34 (d, $J = 8.1$ Hz, $1H_{quin}$), 8.58 (d, $J = 7.2$ Hz, $1H_{quin}$), 8.71 (d, $J = 8.7$ Hz, $1H_{quin}$), 16.4 (bs, 1H) ppm.

2-[2-(2-Hydroxyphenyl)vinyl]quinoline-8-carboxylic acid (**4b**, $C_{18}H_{13}NO_3$)
Brick red solid, yield 73%, mp 225–230°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 6.9$ (t, $J = 7.4$ Hz, $1H_{arom}$), 6.98 (d, $J = 8.4$ Hz, $1H_{arom}$), 7.24 (t, $J = 6.9$ Hz, $1H_{arom}$), 7.6 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 7.74–7.82 (m, 2H), 8.06 (s, 1H), 8.11 (d, $J = 6.9$ Hz, $1H_{arom}$), 8.32 (d, $J = 8.3$ Hz, $1H_{quin}$), 8.58 (d, $J = 7.2$ Hz, $1H_{quin}$), 8.66 (d, $J = 8.7$ Hz, $1H_{quin}$), 10.2 (bs, 1H) ppm.

2-[2-(3-Bromophenyl)vinyl]quinoline-8-carboxylic acid (**4c,** $C_{18}H_{14}BrNO_3$)
Beige solid, yield 65%, mp 170–175°C; ^{1}H NMR (500 MHz, *DMSO*-d_6,): $\delta = 6.88$ (t, $J = 7.9$ Hz, $1H_{arom}$), 6.96 (d, $J = 7.9$ Hz, $1H_{arom}$), 7.10 (d, $J = 8.7$ Hz, $1H_{quin}$), 7.18 (t, $J = 7.7$ Hz, $1H_{arom}$), 7.32–7.4 (m, 2H), 7.54 ($J = 16.4$ Hz, $1H_{vinyl}$), 7.64 (d, $J = 7.8$ Hz, $1H_{quin}$), 7.81 (d, $J = 8.6$ Hz, $1H_{quin}$), 8.11 (d, $J = 16.4$ Hz, $1H_{vinyl}$), 8.27 (d, $J = 8.6$ Hz, $1H_{quin}$) ppm.

2-[2-(2-Methoxyphenyl)vinyl]quinoline-6-carboxylic acid (**4d**, $C_{19}H_{15}NO_3$)
Brown solid, yield 59%, mp 246–249°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.93$ (s, OCH_3), 7.04 (t, $J = 7.5$ Hz, $1H_{arom}$), 7.12 (d, $J = 7.2$ Hz, $1H_{arom}$), 7.4 (t, $J = 8.4$ Hz, $1H_{arom}$), 7.51 (d, $J = 16.4$ Hz,

$1H_{vinyl}$), 7.8 ($J = 7.8$ Hz, $1H_{arom}$), 7.88 (d, $J = 8.6$ Hz, $1H_{quin}$), 8.04–8.21 (m, 3H), 8.53 (d, $J = 8.6$ Hz, $1H_{quin}$), 8.63 (s, 1H) ppm.

2-[2-(2-Hydroxyphenyl)vinyl]quinoline-5-carboxylic acid (**4e**, $C_{18}H_{13}NO_3$)
Red solid, yield 70%, mp 338–345°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 6.9$ (t, $J = 7.5$ Hz, $1H_{arom}$), 7.04 (d, $J = 8.15$ Hz, $1H_{arom}$), 7.3 (t, $J = 7.5$ Hz, $1H_{arom}$), 7.62 (d, $J = 7.75$ Hz, $1H_{arom}$), 7.94 (d, $J = 16.34$ Hz, $1H_{vinyl}$), 8.06 (t, $J = 7.8$ Hz, $1H_{quin}$), 8.32–8.35 (m, 2H), 8.48 (d, $J = 9.13$ Hz, $1H_{arom}$), 8.55 (d, $J = 8.43$ Hz, $1H_{quin}$), 9.61 (d, $J = 9.3$ Hz, $1H_{quin}$), 10.7 (s, 1H), 13.7 (s, 1H) ppm.

2-[2-(3-Chlorophenyl)vinyl]quinoline-5-carboxylic acid (**4f**, $C_{18}H_{12}ClNO_2$)
Yellow solid, yield 72%, mp 238–240°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.4$–7.5 (m, 2H), 7.6 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 7.75 (d, $J = 7.5$ Hz, $1H_{arom}$), 7.82–7.9 (m, 3H), 7.98 (d, $J = 9.0$ Hz, $1H_{arom}$), 8.2–8.28 (m, 2H), 9.3 (d, $J = 9.3$ Hz, $1H_{quin}$), 13.2 (bs, 1H) ppm.

2-[2-(2-Hydroxyphenyl)vinyl]quinoline-6-carboxylic acid (**4g**, $C_{18}H_{13}NO_3$)
Orange solid, yield 75%, mp 292–295°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 6.93$ (t, $J = 7.6$ Hz, $1H_{arom}$), 7.1 (d, $J = 8.1$ Hz, $1H_{arom}$), 7.32 (t, $J = 8.4$ Hz, $1H_{arom}$), 7.61 (d, $J = 7.2$ Hz, $1H_{arom}$), 8.0 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 8.37–8.46 (m, 3H), 8.5 (d, $J = 8.7$ Hz, $1H_{quin}$), 8.82 (s, 1H), 9.0 (d, $J = 9.0$ Hz, $1H_{quin}$), 11 (bs, 1H) ppm.

2-[2-(3-Chlorophenyl)vinyl]quinoline-7-carboxylic acid (**4h**, $C_{18}H_{12}ClNO_2$)
Yellow solid, yield 30%, mp 325°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.4$ (d, $J = 8.2$ Hz $1H_{arom}$), 7.45 (t, $J = 7.8$ Hz, $1H_{arom}$), 7.57 (d, $J = 16.3$ Hz, $1H_{vinyl}$), 7.72 (d, $J = 7.6$ Hz, $1H_{arom}$), 7.8–7.85 (m, 3H), 7.95 (d, $J = 9.0$ Hz, $1H_{quin}$), 8.18–8.21 (m, 2H), 9.26 (d, $J = 9.0$ Hz, $1H_{quin}$) ppm.

2-[2-(2-Bromophenyl)vinyl]quinoline-5-carboxylic acid (**4i**, $C_{18}H_{12}BrNO_2$)
Brown solid, yield 76%, mp 310°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.34$ (t, $J = 8.4$ Hz, $1H_{arom}$), 7.49 (t, $J = 7.5$ Hz, $1H_{arom}$), 7.58 (d, $J = 16.1$ Hz, $1H_{vinyl}$), 7.74 (d, $J = 7.95$ Hz, $1H_{arom}$), 7.9 (t, $J = 8.1$ Hz, $1H_{quin}$), 7.98 (d, $J = 7.8$ Hz, $1H_{arom}$), 8.06 (d, $J = 9.15$ Hz, $1H_{quin}$), 8.15 (d, $J = 16.13$ Hz, $1H_{vinyl}$), 8.26–8.34 (m, 2H), 8.39 (d, $J = 9.0$ Hz, $1H_{quin}$) ppm.

2-[2-(2-Methoxyphenyl)vinyl]quinoline-5-carboxylic acid (**4j**, $C_{19}H_{15}NO_3$)
Yellow solid, 75%, mp 241–243°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.97$ (s, OCH_3), 7.06–7.18 (m, 2H), 7.47 (t, $J = 6.9$ Hz, $1H_{arom}$), 7.73 (d, $J = 8.4$ Hz, $1H_{arom}$), 8.0–8.14 (m, 3H), 8.29 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 8.41–8.44 (m, 1H), 8.68 (d, $J = 8.4$ Hz, $1H_{quin}$), 9.6 (d, $J = 9.2$ Hz, $1H_{quin}$), 9.72 (d, $J = 9$ Hz, $1H_{quin}$) ppm.

2-[2-(3-Methoxyphenyl)vinyl]quinoline-5-carboxylic acid (**4k**, $C_{19}H_{15}NO_3$)
Yellow solid, 80%, 256–260°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.84$ (s, OCH_3), 6.95 (d, $J = 7.0$ Hz, $1H_{arom}$), 7.33–7.39 (m, 3H), 7.54 (d, $J = 16.35$ Hz, $1H_{vinyl}$), 7.81–7.89 (m, 2H), 8.0 (d, $J = 9.1$ Hz, $1H_{quin}$), 8.2–8.24 (m, 2H), 9.7 (d, $J = 9.0$ Hz, $1H_{quin}$) ppm.

2-[2-(2-Methoxyphenyl)vinyl]quinoline-7-carboxylic acid (**4l**, $C_{19}H_{15}NO_3$)
Yellow solid, yield 63%, mp 260°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.97$ (s, OCH_3), 7.09 (t, $J = 6.0$ Hz, $1H_{arom}$), 7.18 (d, $J = 8.2$ Hz, $1H_{arom}$), 7.5 (t, $J = 8.4$ Hz, $1H_{arom}$), 7.74 (d, $J = 9.1$ Hz, $1H_{arom}$), 8.0 (d, $J = 16.4$ Hz, $1H_{vinyl}$), 8.2 (d, $J = 8.4$ Hz, $1H_{quin}$), 8.27–8.38 (m, 2H), 8.47 (d, $J = 8.9$ Hz, $1H_{quin}$), 8.9–8.94 (m, 2H) ppm.

2-[2-(2-Hydroxyphenyl)vinyl]quinoline-7-carboxylic acid (**4m**, $C_{18}H_{13}NO_3$)
Red solid, yield 62%, mp 325–332°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 6.91$ (t, $J = 7.5$ Hz, $1H_{arom}$), 7.04 (d, $J = 8.15$ Hz, $1H_{arom}$), 7.29 (t, $J = 7.8$ Hz, $1H_{arom}$), 7.62 (d, $J = 7.8$ Hz, $1H_{arom}$), 7.94

(d, $J = 16.35$ Hz, $1H_{vinyl}$), 8.06 (m, 1H), 8.32–8.35 (m, 2H), 8.5 (d, $J = 9.1$ Hz, $1H_{quin}$), 8.55 (d, $J = 8.5$ Hz, $1H_{quin}$), 9.61 (d, $J = 9.3$ Hz, $1H_{quin}$), 10.7 (bs, 1H), 13.7 (bs, 1H) ppm.

2-[2-(2-Methoxyphenyl)vinyl]quinoline-5,8-dicarboxylic acid (**4n**, $C_{20}H_{15}NO_5$)
Orange solid, yield 82%, mp 283–288°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.93$ (s, OCH_3), 7.04 (t, $J = 7.5$ Hz, $1H_{arom}$), 7.12 (d, $J = 8.3$Hz, $1H_{arom}$), 7.4 (t, $J = 6.9$ Hz, $1H_{arom}$), 7.54 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 7.83 (d, $J = 7.7$ Hz, $1H_{arom}$), 8.04 (d, $J = 16.5$ Hz, $1H_{vinyl}$), 8.12 (d, $J = 9.2$ Hz, $1H_{quin}$), 8.27 (d, $J = 7.7$ Hz, $1H_{quin}$), 8.56 (d, $J = 7.7$ Hz, $1H_{quin}$), 9.37 (d, $J = 9.1$ Hz, $1H_{quin}$) ppm.

2-[2-(4-Methoxyphenyl)vinyl]quinoline-6-carboxylic acid (**4o**, $C_{19}H_{15}NO_3$)
Yellow solid, yield 78%, mp 279–282°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 3.81$ (s, OCH_3), 7.02 (d, $J = 8.8$ Hz, $2H_{arom}$), 7.38 (d, $J = 16.3$ Hz, $1H_{vinyl}$), 7.72 (d, $J = 8.8$ Hz, $2H_{arom}$), 7.85–7.92 (m, 2H), 8.02 (d, $J = 8.8$ Hz, $1H_{quin}$), 8.2 (d, $J = 8.75$ Hz, $1H_{quin}$), 8.49–8.61 (m, 2H) ppm.

2-[2-(3-Chlorophenyl)vinyl]quinoline-5,8-dicarboxylic acid (**4p**, $C_{19}H_{12}ClNO_4$)
Light yellow solid, yield 75%, mp 238–240°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.45$–7.55 (m, 2H), 7.74–7.82 (m, 2H), 7.83 (d, $J = 16.3$ Hz, $1H_{vinyl}$), 7.9–8.1 (m, 2H), 8.27 (d, $J = 9.1$ Hz, $1H_{quin}$), 8.32 (d, $J = 7.7$ Hz, $1H_{quin}$), 9.44 (d, $J = 9.15$ Hz, $1H_{quin}$) ppm.

2-[2-(2-Bromophenyl)vinyl]quinoline-6-carboxylic acid (**4q**, $C_{18}H_{12}BrNO_2$)
Beige solid, yield 75%, mp 276–278°C; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 7.34$ (t, $J = 8.7$ Hz, $1H_{arom}$), 7.5 (t, $J = 7.5$ Hz, $1H_{arom}$), 7.57 (d, $J = 16.05$ Hz, $1H_{vinyl}$), 7.74 (d, $J = 7.2$ Hz, $1H_{arom}$), 7.95 (d, $J = 8.6$ Hz, $1H_{arom}$), 8.0 (d, $J = 7.95$ Hz, $1H_{quin}$), 8.1–8.26 (m, 3H), 8.63 (d, $J = 8.6$ Hz, $1H_{quin}$), 8.67 (s, 1H) ppm.

Acknowledgements

We would like to thank for the financial support of Polish State Committee for Scientific Research (KBN) grant No. 4 T09 A 011 27.

References

[1] Mekouar K, Mouscadet JF, Desmaele D, Subra F, Leh H, Savoure D, Auclair C, d'Angelo J (1998) J Med Chem **41**: 2846
[2] Zouhiri F, Danet M, Bernard C, Normand-Bayle M, Mouscadet J-F, Leh H, Thomas CM, Mbemba G, d'Angelo J, Desmaele D (2005) Tetrahedron Lett **46**: 2201
[3] Ouali M, Laboulais C, Leh H, Gill D, Desmaele D, Mekouar Kh, Zouhiri F, Auclair C, d'Angelo J, Mouscadet JF, Le Bret M (2000) J Med Chem **43**: 1949
[4] Polanski J, Zouhiri F, Jeanson L, Desmaële D, d'Angelo J, Mouscadet JF, Gieleciak R, Gasteiger J, Le Bret M (2002) J Med Chem **45**: 4647
[5] Bernard Ch, Zouhiri F, Normand-Bayle M, Danet M, Desmaele D, Leh H, Mouscadet JF, Mbemba G, Thomas C, Bonnenfant M, Le Bret M, d'Angelo J (2004) Bioorg Med Chem Lett **14**: 2473
[6] Pommier Y, Johnson AA, Marchand C (2005) Nat Rev Drug Discov **4**: 236
[7] Ochiai E (1967) Aromatic Amine Oxides, Elsevier, New York
[8] Katritzky AR, Lagowski JM (1971) Chemistry of the heterocyclic N-oxides, Academic Press, New York
[9] Taylor EC, Martin SF (1974) J Am Chem Soc **96**: 8095
[10] Giam CS, Stout JL (1969) J Chem Soc D 142
[11] Ochiai E, Kuniyoshi I (1957) Pharm Bull **5**: 292

[12] Higashino T, Hayashi E (1970) Chem Pharm Bull **18**: 1457
[13] Cooper GG, Rickard RL (1971) J Chem Soc C 772
[14] Taylor EC, Martin SF (1972) J Am Chem Soc **94**: 2874
[15] Phillips JP, Breese R, Barrall EM (1959) J Org Chem **24**: 104
[16] Lidstrom P, Tierney J, Wathey B, Westman J (2001) Tetrahedron **57**: 9225
[17] Caddic S (1995) Tetrahedron **51**: 10403
[18] For more comprehensive reviews see also: a) Loupy A (Ed) (2002) Microwaves in Organic synthesis, Wiley-VCH, Weinheim; b) Hayes BL (2002) Microwave synthesis: chemistry at the speed of light, CEM Publishing, Matthews, NC; c) Varma RS (2002) Advances in Green Chemistry: Chemical Syntheses Using Microwave Irradiation, Astra Zeneca Research Foundation, Kavitha Printers, Bangalore, India; d) Kappe CO, Stadtler A (2005) Microwaves in Organic and Medicinal Chemistry, Wiley-VCH, Weinheim
[19] Musiol R, Niedbala H, Majerz-Maniecka K, Mrowczyk A, Oleksyn B, Polanski J (2005) Annals Pol Chem Soc (in print)
[20] Majerz-Maniecka K, Oleksyn B, Musiol R, Podeszwa B, Polanski J (2005) Joint Meeting on Med Chem Vienna, Austria, June 20–23: PO-136
[21] Dippy JF, Evans RM (1950) J Org Chem **15**: 451
[22] a) Miller V (1890) Chem Ber **23**: 2272; b) Glen WL, Bailey CC (1941) J Am Chem Soc **63**: 639; c) Mills JT, Harris J, Lambounre LJ (1927) J Chem Soc **119**: 1298
[23] Polanski J, Niedbala H, Musiol R, Tabak D, Podeszwa B, Gieleciak R, Bak A, Palka A, Magdziarz T (2004) Acta Poloniae Pharm **61**: 3
[24] Polanski J, Niedbala H, Musiol R, Podeszwa B, Tabak D, Palka A, Mencel A, Mouscadet JF, Gieleciak R, Bak A, Magdziarz, LeBret M (2005) J Med Chem (submitted)
[25] Majerz-Maniecka K, Musiol R, Nitek W, Oleksyn BJ, Mouscadet JF, LeBret M, Polanski J (2006) Bioorg Med Chem Lett **16**: 5