NUCLEOPHILIC SUBSTITUTION REACTION OF CHLOROQUINOLINES WITH 1,2,4-TRIAZOLE. I. SYNTHESIS OF 4-(1*H*-1,2,4-TRIAZOL-1-YL)QUINOLINES

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Abstract
Synthesis of 4-(1H-1,2,4-triazol-1-yl)quinolines by the reaction of 4-chloroquinolines with 1,2,4-triazole was studied under neutral, acidic and basic reaction conditions. Significant role of the acid and base catalysis as well as substituent effects on the reactivity of 4-chloroquinolines in these reactions are reported. As a result of this study one can choose the best reaction conditions for the preparation of the title compounds according to the substituents on the quinoline ring.

INTRODUCTION

A lot of work concerning both synthetic and mechanistic aspects of the reactions of 2- and 4-chloroquinolines with various nucleophilic reagents have been published (1). Differences in behaviour of 2- and 4-chloro group in these reactions, furthermore, solvent and substituent effects in case of both charged anionic nucleophilic agents (alkoxide ions) and uncharged reagents (amines, thiols) have been thoroughly investigated, and the existence of acid catalysis caused by the protonation of quinoline ring nitrogen atom in the latter case is well documented (2).

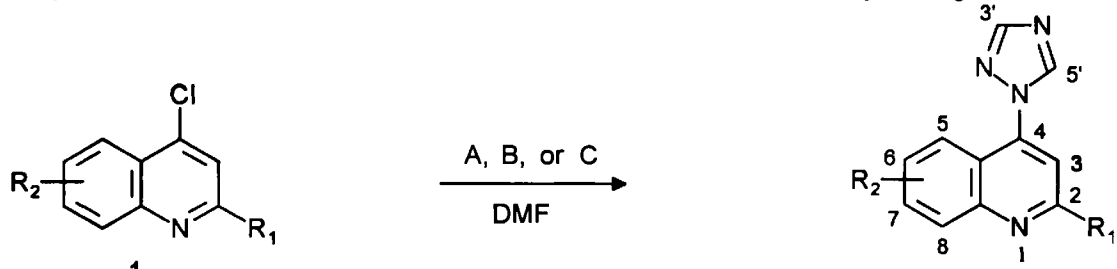
Since aminoquinolines are of special interest due to their different kinds of biological activity, reactions of chloroquinolines with a wide variety of aliphatic, aromatic and heteroaromatic amines have been investigated (1). However, nitrogen-heterocycles containing -NH- moiety have been given little attention as nucleophilic agents in these reactions. As the sole example we have found in the literature, 4-chloroquinolines are reported to give 4-imidazolylquinolines when heated with imidazole or its derivatives at 200 °C for 24 hrs (3).

Our interest in the synthesis of new 2- or 4-(1H-1,2,4-triazol-1-yl)quinolines possessing antiinflammatory and fungicidal activity (4) prompted us to investigate the reaction of 2- and 4-chloroquinolines with 1H-1,2,4-triazole in detail. The primary aim of our work was to find the best reaction conditions for the preparation of the products. On the other hand, we hoped to get further contributions to the present knowledge on the nucleophilic displacement reactions of chloroquinolines using such an N-nucleophilic agent which can react depending on the reaction conditions both as a neutral reagent and as an anion, since its -NH- moiety can readily be deprotonated by means of a strong base. Comparative study on the reactivity of chloroquinolines toward N-nucleophilic reagents under neutral, acidic and basic reaction conditions has not been reported so far.

RESULTS AND DISCUSSION

In this paper we report on the results related to the nucleophilic substitution reaction of 4-chloroquinolines with 1,2,4-triazole. The substituents of the quinoline ring were selected from both electron-releasing (alkyl) and mild (Cl) or strong (NO_2, CCl_3, CF_3) electron-withdrawing groups. With respect to the known characteristic features of the nucleophilic displacement reactions of 4-chloroquinolines (1, 2) three general methods were used in our

investigations. Accordingly, 4-chloroquinolines were treated with 1,2,4-triazole (method A), or with 1,2,4-triazole in the presence of hydrochloric acid (method B), or with the sodium salt of 1,2,4-triazole (method C). Dimethylformamide was used as a solvent in all cases. The reaction temperature was chosen in accordance with the reactivity of the substrate, and the course of the reactions was monitored by tlc or gc.



1 A: 1,2,4-triazole; B: 1,2,4-triazole, HCl; C: 1,2,4-triazole-Na 2

Most of the reactions went smoothly to completion, but in some cases the reaction was incomplete or no reaction occurred at all under any of the reaction conditions used. Except for these few cases, the yields are very good, and the products can be prepared easily and in high purity by pouring the reaction mixture into water followed by recrystallization of the precipitated crude product from a suitable solvent or solvent mixture.

Table 1. Preparation of 4-(1H-1,2,4-Triazol-1-yl)quinolines (2a - 2u)

Compound	R_1	R_2	Method	Temperature (°C)	Time[a] (h)	Yield[b] (%)	mp (°C) /Cryst. solvent/	$k \cdot 10^5$ /l·mol^{-1}·sec^{-1}/
2a	H	H	A	100	1	65.8	147 - 148	
			A	80	4	66.5	/ethanol/	
			B	80	1	69.1		
			C	100	20	65.4		8.80
2b	H	7-CH_3	A	80	3	69.0	179 - 180	
			B	80	1	78.6	/ethanol/	
			C	100	30	65.2		3.94
2c	H	8-CH_3	A	100	3	75.2	145 - 146	
			B	80	1.5	79.0	/ethanol/	
			C	100	40	73.0		3.65
2d	H	7-CF_3	A	80	5	73.0	100 - 101	
			B	80	1	78.6	/ethanol -	
			C	100	1	77.1	hexane/	196.1
			C	80	5	80.9		40.7
2e	H	8-CF_3	A	100	>50	-	146 - 147	
			B	80	25	65.8	/ethanol/	
			C	100	1	81.7		187.0
			C	90				89.7
			C	80				39.9
2f	H	6-NO_2	A	80	3	65.8	247 - 248	
			B	80	1	67.5	/acetic acid/	
			C	60	1	79.2		159.5

Table1 (continued)

Com-pound	R_1	R_2	Method	Temperature (°C)	Time[a] (h)	Yield[b] (%)	mp (°C) /Cryst. solvent/	k 10^5 /l·mol^{-1}·sec^{-1}/
2g	H	7-NO_2	A	80	5	81.0	245 - 246	
			B	80	1	81.7	/acetic acid/	
			C	70				84.7
			C	60	6	82.8		28.5
			C	100				(1567)[d]
2h	H	8-NO_2	A	100	3	85.8	206 - 207	
			A	80	14	86.2	/acetic acid/	
			B	80	2	81.7		
			C	70				104.0
			C	60	3	81.9		36.9
			C	100				(1668)[d]
2i	CH_3	H	A	100	2	62.6	94 - 96	
			B	80	2	57.0	/ethanol -	
			C	100	40	51.3	water/	3.32
2j	CH_3	6-CH_3	A	100	2	57.1	164 - 165	
			B	80	3	67.2	/ethanol/	
			C	100	50	54.4		1.49
2k	CH_3	8-CH_3	A	100	5	60.0	98 - 100	
			B	80	4	61.3	/ethanol -	
			C	100	>50	48.2[c]	water/	1.30
2l	CH_3	8-*i*-Pr	A	100	13	77.3	82 - 83	
			B	80	7	75.7	/ethanol/	
			C	100	>50	35.7[c]		0.73
2m	CH_3	6-Cl	A	100	3	77.0	177 - 178	
			B	80	3	84.0	/chloroform -	
			C	100	8	85.5	ethanol/	32.4
2n	CH_3	7-Cl	A	100	2	71.2	182 - 183	
			B	80	1	84.0	/chloroform -	
			C	100	5	84.2	ethanol/	37.5
2o	CH_3	8-Cl	A	100	10	74.0	143 - 144	
			B	80	13	71.2	/chloroform -	
			C	100	8	84.0	ethanol/	32.0
2p	CH_3	6,8-Cl_2	A	100	38	73.0	226 - 227	
			B	80	14	82.1	/DMSO -	
			C	100	1	79.6	ethanol/	111.3
			C	80	5	83.2		
2r	CH_3	7-CF_3	A	100	4	60.5	77 - 78	
			B	80	1.5	61.9	/hexane/	
			C	100	4	77.8		43.3
2s	CH_3	8-CF_3	A	100	>50	-	162 - 163	
			B	100	35	60.0	/chloroform -	
			C	100	4	75.0	ethanol/	43.2
2t	CCl_3	8-CH_3	A	100	>50	-	89 - 90	
			B	100	>50	-	/ethanol/	
			C	100	1	70.0		181.4

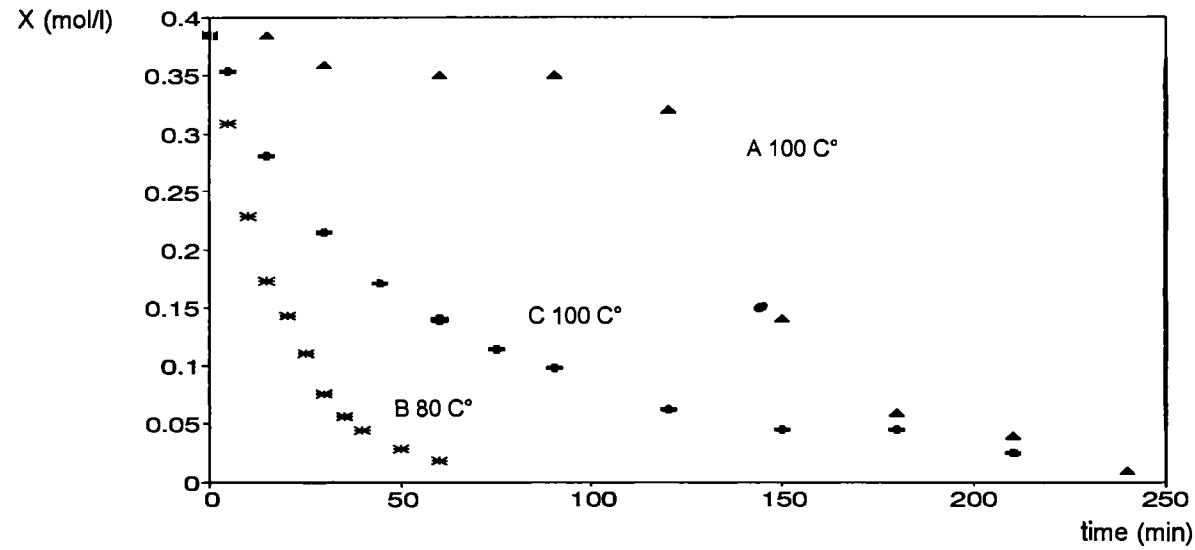
Table1 (continued)

Com-pound	R_1	R_2	Method	Temperature (°C)	Time[a] (h)	Yield[b] (%)	mp (°C) /Cryst. solvent/	k 10^5 /l·mol^{-1}·sec^{-1}/
2u	CCl_3	8-CF_3	A	100	>50	-	136 - 137	
			B	100	>50	-	/ethanol/	
			C	25	14	86.2		11.5

a) Time required to the consumption of the starting chloroquinoline (tic); b) Yield of recrystallized product; c) Separation from the starting material was performed by column chromatography; d) The values in parentheses were calculated by Arrhenius equation

All experimental data of prime importance are assembled in Table 1. There are a number of interesting points emerging from these data on the reactivity of differently substituted 4-chloroquinolines toward 1,2,4-triazole both in neutral or acidic and in basic reaction conditions. First of all, comparing the reaction time data (required for the consumption of the starting chloroquinoline at the same temperature) in methods A and B for each 4-chloroquinoline, it is apparent that the reactions are subjected to acid catalysis except for 2-trichloromethylquinolines. It seems that 4-chloroquinolines even in the presence of a strong electron-withdrawing group (NO_2, CF_3) on the carbocyclic ring are able to compete successfully for the protons initially added to the reaction mixture with 1,2,4-triazole (basic pK_a=2.2 (5)). However, the strong electron-withdrawing CCl_3 group at the 2-position prevents the protonation of the quinoline ring nitrogen and hence the substitution reaction as well. A similar effect of 2-CF_3 and 2-CO_2Et groups has been described (6) in piperidinodechlorination (7) of 4-chloroquinolines, but in the reported case the inhibition of acid catalysis does not prevent the reaction probably due to the high nucleophilicity of piperidine. It is essential to note here, that the successful reactions according to method A are apparently susceptible to autocatalysis, as can be seen on Figure 1 for the reaction of 1r.

Figure 1: Concentration vs. time for 4-chloro-2-methyl-7-trifluoromethylquinoline (1r) in the general methods A,B and C



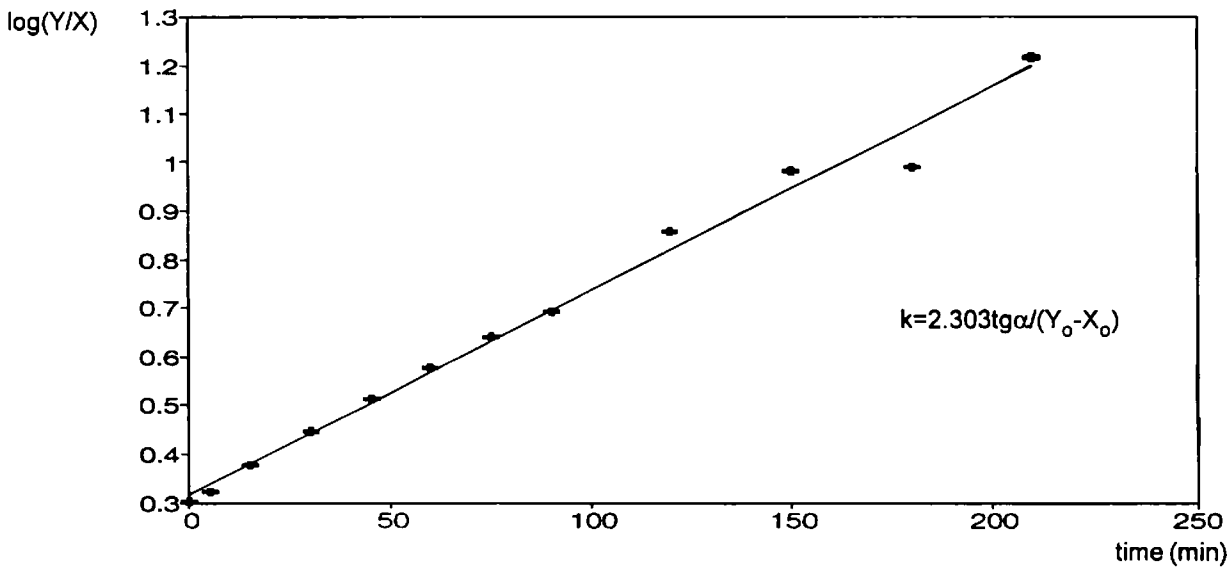
In case of acid catalytic (method B) and autocatalytic (method A) conditions the rate constants could not be determined because the reaction follows a complex kinetic due to increase of hydrochloric acid concentration as the reaction proceeds. Consequently, the reactivity of differently substituted 4-chloroquinolines in these

conditions may be characterized only qualitatively by comparison of the reaction time data required to the consumption of the starting 4-chloroquinoline at the same temperature.

These comparisons show, that 4-chloroquinolines having widely different substituents at 6- and 7-positions (1a, 1b, 1d, 1f, 1g) possess nearly the same reactivity under the reaction conditions of method A or B. This significant, though qualitative, regularity can be understood by taking into consideration that in these conditions substituents exert their effect on the reactivity in two opposing ways. Electron-withdrawing groups, though, increase the electron defficiency at the site of displacement, but at the same time lower the basicity of the substrate and hence the concentration of the reactive quinolinium ion in the reaction mixture. An electron-releasing group exerts the opposite effect on both fields. It seems, that in case of 6- and 7-substituents the opposing factors nearly balance each other. In case of 2- and 8-substituents an additional factor should be taken into consideration. This factor, the steric inhibition of solvation has been held responsible for the rate-depressing effect of 8-Me and 8-*t*-Bu substituents in piperidino- and methoxydechlorination of 4-chloroquinolines (8). This effect should apparently operate in our case, since all the 8-substituted 4-chloroquinolines show lower reactivity than the 6-substituted isomers in spite of the fact, that the substituents at these two positions should exert similar polar effects. Furthermore, the introduction of the bulky isopropyl group instead of methyl to the 8-position, or a methyl group instead of hydrogen to the 2-position causes an additional fall in reactivity.

In case of method C, when 4-chloroquinolines were treated with the sodium salt of 1,2,4-triazole, the absence of the obscure autocatalytic effect provided opportunity for easy determination of the rate constants. It was carried out by gc determination of the 4-chloroquinoline concentration during the reaction (Figure 1). As expected (9), the reaction follows second order kinetic because the second order diagrams were found to be linear in the investigated ranges (Figure 2) and the rate constants independent of the initial reactant concentrations. The second-order rate constants (Table 1) are useful for precise characterization of the reactivity of 4-chloroquinolines toward triazole anion.

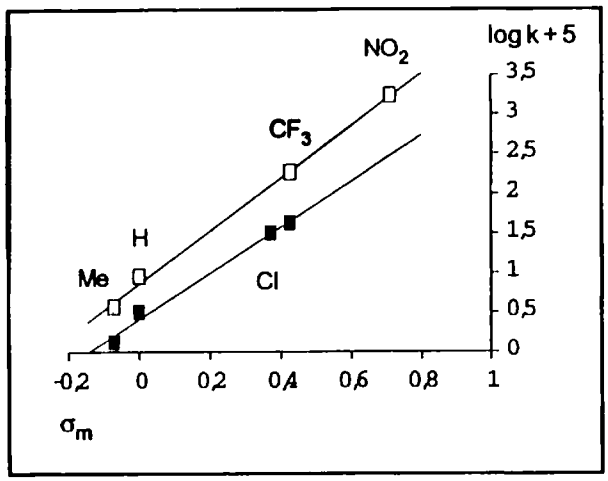
Figure 2: Determination of the rate constant for 4-chloro-2-methyl-7-trifluormethylquinoline (1r) in method C



The influence of the substituents on the reactivity of the substrate under the reaction conditions of method C can be clearly interpreted on the basis of the known electronic theory of substituent effects in aromatic systems. Accordingly, our experimental data show that a methyl group having inductive electron-releasing effect, at all the positions investigated exerts a slight deactivating effect. Conversely, all the electron-withdrawing groups (Cl, CF_3, CCl_3, NO_2) facilitate the substitution reaction. It was found that the reactivity data (log k) at 100 °C for the differently substituted 4-chloroquinolines correlate well with the known (10) Hammett's σ parameters of the substituents. The correlation was found to be much better with σ_m than with σ_p in case of both 7- and 8-substituted derivatives (Figure 3). Furthermore, the comparison of the reactivity data (k) at 60 °C for 6-, 7- and 8-nitro compounds (1f, 1g, 1h) shows the much stronger activating effect of the nitro group at the "conjugative" (2) 6-position than at the "non-conjugative" 7-position. The much weaker effect of the nitro group at the other "conjugative" 8-position can probably be attributed to the steric inhibition of resonance, which is a well known effect in the substitution reactions of nitrochlorobenzenes having a substituent ortho to the nitro group (11). It should be noted here, that our observations concerning the substituent effects on the reactivity of 4-chloroquinolines toward triazole anion are on the whole consistent with the reported results of the kinetic study on methoxydechlorination (12); however, the effect of the nitro group at different positions of the quinoline ring has not been investigated so far.

Figure 3: Correlation of reactivity data (log k) with Hammett's σ parameters for the reaction of 4-chloroquinolines with the sodium salt of 1,2,4-triazole at 100 °C

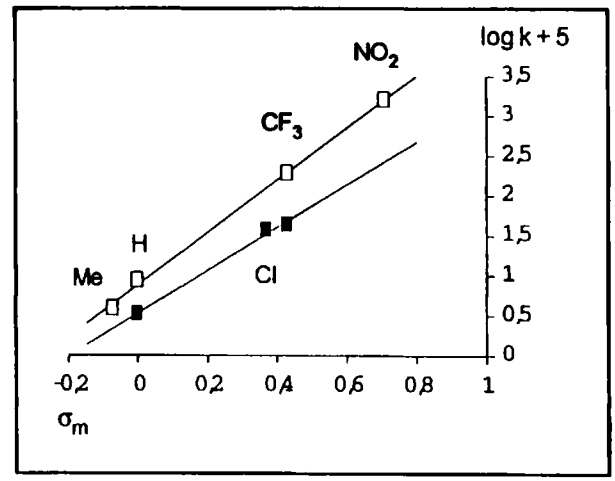
4-chloro-8-substituted quinolines



For 2-unsubstituted series (□): log k= 3.32 σ_m - 4.17 (r= 0.999)

For 2-Me series (■): log k= 2.90 σ_m - 4.59 (r= 0.993)

4-chloro-7-substituted quinolines



For 2-unsubstituted series (□): log k= 3.27 σ_m - 4.12 (r= 0.999)

For 2-Me series (■): log k= 2.68 σ_m - 4.48 (r=0.997)

To summarize our observations with respect to preparative efficacy of the three general methods described here, we can say that acid catalysis is generally effective with the exception of 2-trichloromethylquinolines, but 4-chloroquinolines having only strong electron-withdrawing substituents react usually faster and give better yields when treated with the sodium salt of 1,2,4-triazole. As a result of our investigation one can choose the best reaction conditions for the preparation of the title products according to the substituent(s) on the quinoline ring.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Büchi apparatus and are uncorrected. The ^{1}H-nmr spectra were recorded on a Varian Gemini-200 instrument at 200 MHz in DMSO-d_6 solution using TMS as internal standard and chemical shifts are expressed in ppm. Mass spectra were scanned on a VG TRIO-2 spectrometer in EI mode at 70 eV.

Materials: 1H-1,2,4-triazole was purchased from Fluka Chemie AG; 4-chloroquinoline derivatives were prepared according to previously described procedures (13, 14).

Sodium salt of 1H-1,2,4-triazole - Clean sodium (23 g, 1 mol) was dissolved in dry ethanol (500 ml), then 1,2,4-triazole (69 g, 1 mol) was added to this solution, and the reaction mixture was refluxed for 1 hour under nitrogen. The resulting solution was concentrated almost to dryness under reduced pressure, the residue was suspended in diethyl ether (100 ml), then was filtered by suction and dried in a vacuum dessicator over potassium hydroxide pellets. Yield: 76.7 g (84.3 %), mp 308-310 °C.

1H-1,2,4-triazole hydrochloride - 1,2,4-triazole (69 g, 1 mol) was dissolved in concentrated hydrochloric acid (200 ml) and the solution was evaporated to dryness under reduced pressure. The residue was suspended in dry acetone (100 ml) then was filtered by suction and dried in the air. Yield: 92.0 g (87.2 %), mp 168-170 °C.

Preparation of 4-(1H-1,2,4-triazol-1-yl)quinolines (2a - u). General Procedures.

The corresponding 4-chloroquinoline derivative (1) (0.01 mol) was treated in dimethylformamide (10 ml) with 1.38 g (0.02 mol) of 1,2,4-triazole (method A), or with the mixture of 0.69 g (0.01 mol) of 1,2,4-triazole and 1.06 g (0.01 mol) of 1H-1,2,4-triazole hydrochloride (method B), or with 1.82 g (0.02 mol) of sodium salt of 1,2,4-triazole (method C) at a temperature given in Table 1. The reaction mixture was worked up by pouring into water (50 ml) and neutralization with aqueous sodium hydroxide solution (method A and B) or hydrochloric acid solution (method C). The precipitated product was collected, washed with water and dried. The crude product was recrystallized from the solvent or solvent mixture given in Table 1.

Kinetic experiments - The corresponding 4-chloroquinoline derivative (1) (0.01 mol) was dissolved in dimethylformamide (20 ml) and 1.0 g of N-methylformanilide (internal standard) was added to this solution. The mixture was immersed into a constant temperature bath regulated by a thermostat, and the internal temperature was adjusted to the desired value (Table 1). Sodium salt of 1,2,4-triazole (1.82 g, 0.02 mol) was then added and the reaction was followed by gc. The first sample (1 ml) was taken immediately after addition of sodium salt of 1,2,4-triazole. This sample was added into a 25 ml volumetric flask containing 15 ml of ethanol, then the flask was filled up with ethanol to the mark. The initial concentration of the chloroquinoline (X_0) was determined by gc using calibration curve. Further samples (ca. 0.1 ml) were withdrawn at appropriate time intervals, diluted with ethanol, and the actual concentration of the chloroquinoline (X) was calculated on the basis of the peak area of the chloroquinoline and the internal standard.

The calculation of the rate constants was based upon the equation: $\ln(X_0Y/Y_0X)=(Y_0-X_0)kt$, in which X_0 and Y_0 mean the concentration of the chloroquinoline and the sodium salt of 1,2,4-triazole at the zero time ($Y_0=2X_0$), X

and Y mean their concentration in time t ($Y=X_0+X$).

The second order rate constants were determined from the plots log(Y/X) vs. time by the method of least squares (Figure 2) and are given in Table 1.

Table 2. ^{1}H-NMR and Mass Spectral Data of Compounds 2a-u

Compound	^{1}H-NMR δ (ppm), J (Hz)	MS[a] m/e (%)
2a	7.74 (td, 1H, J_1=8.3, J_2=6.8, J_3=1.3, 6-H), 7.82 (d, 1H, J=4.6, 3-H), 7.92 (td, 1H, J_1=8.4, J_2=6.8, J_3=1.4, 7-H), 8.14 (dd, 1H, J_1=8.3, J_2=1.4, 5-H), 8.21 (dd, 1H, J_1=8.4, J_2=1.3, 8-H) 8.50 (s, 1H, 3'-H), 9.10 (d, 1H, J=6.4, 2-H), 9.27 (s, 1H, 5'-H).	196 (M^+, 100)
2b	2.57 (s, 3H, 7-CH_3), 7.57 (dd, 1H, J_1=8.5, J_2=1.6, 6-H), 7.72 (d, 1H, J=4.7, 3-H), 8.00 (d, 1H, J=1.7, 8-H), 8.05 (d, 1H, J=8.5, 5-H), 8.45 (s, 1H, 3'-H), 9.05 (d, 1H, J=4.7, 2-H), 9.25 (s, 1H, 5'-H).	210 (M^+, 100)
2c	2.80 (s, 3H, 8-CH_3), 7.60 (dd, 1H, J_1=8.4, J_2=7.1, 6-H), 7.77 (d, 1H, J=7.1, 7-H), 7.82 (d, 1H, J=4.6, 3-H), 7.90 (d, 1H, J=8.4, 5-H), 8.47 (s, 1H, 3'-H), 9.10 (d, 1H, J=4.6, 2-H), 9.23 (s, 1H, 5'-H).	210 (M^+, 100)
2d	7.98 (dd, 1H, J_1=8.5, J_2=1.8, 6-H), 8.03 (d, 1H, J=4.6, 3-H), 8.42 (d, 1H, J=8.5, 5-H), 8.49 (s, 1H, 3'-H), 8.51 (d, 1H, J=1.8, 8-H) 9.25 (d, 1H, J=4.6, 2-H), 9.32 (s, 1H, 5'-H).	264 (M^+, 100)
2e	7.87 (dd, 1H, J_1=8.5, J_2=7.4, 6-H), 8.00 (d, 1H, J=4.7, 3-H), 8.35 (d, 1H, J=7.4, 7-H), 8.45 (d, 1H, J=8.5, 5-H), 8.52 (s, 1H, 3'-H), 9.26 (d, 1H, J=4.7, 2-H), 9.30 (s, 1H, 5'-H).	264 (M^+, 100)
2f	8.10 (d, 1H, J=4.8, 3-H), 8.35 (d, 1H, J=9.4, 8-H), 8.59 (dd, 1H, J_1=9.4, J_2=2.4, 7-H) 8.61 (s, 1H, 3'-H), 9.31 (d, 1H, J=4.8, 2-H), 9.33 (d,1H, J=2.4, 5-H) 9.42 (s, 1H, 5'-H).	241 (M^+, 100)
2g	8.05 (d, 1H, J=4.7, 3-H), 8.45-8.55 (m, 3H, 3'-H + 6-H + 5-H), 8.95 (d, 1H, J=2.0, 8-H), 9.30 (d, 1H, J=4.7. 2-H), 9.33 (s, 1H, 5'-H).	241 (M^+, 100)
2h	7.90 (dd, 1H, J_1=8.9, J_2=8.1, 6-H), 8.05 (d, 1H, J=4.8, 3-H), 8.42 (dd, 1H, J_1=8.1, J_2=1.1, 7-H), 8.50 (dd, 1H, J_1=8.9, J_2=1.1, 5-H), 8.55 (s, 1H, 3'-H), 9.22 (d,1H, J=4.8, 2-H), 9.32 (s, 1H, 5'-H).	241 (M^+, 100)

2i	2.75 (s, 3H, 2-CH_3), 7.65 (td, 1H, J_1=8.4, J_2=6.9, J_3=1.2, 6-H), 7.75 (s, 1H, 3-H), 7.85 (td, 1H, J_1=8.4, J_2=6.9, J_3=1.3, 7-H), 8.05 (dd, 1H, J_1=8.4, J_2=1.3, 5-H), 8.09 (dd, J_1=8.4, J_2=1.2, 8-H), 8.47 (s, 1H, 3'-H), 9.24 (s, 1H, 5'-H).	210 (M^+, 100)
2j	2.48 (s, 3H, 6-CH_3), 2.75 (s, 3H, 2-CH_3), 7.67 (dd, 1H, J_1=8.5, J_2=1.7, 7-H), 7.71 (s, 1H, 3-H), 7.77 (d, 1H, J=1.7, 5-H), 8.00 (d, 1H, J=8.5, 8-H), 8.45 (s,1H, 3'-H), 9.22 (s, 1H, 5'-H).	244 (M^+, 100)
2k	2.75 (s, 6H, 2-CH_3 + 6-CH_3), 7.50 (dd, 1H, J_1=8.4, J_2=7.1, 6-H), 7.69 (d, 1H, J= 7.1, 7-H), 7.73 (s, 1H, 3-H), 7.80 (d, 1H, J=8.4, 5-H), 8.44 (s, 1H, 3'-H), 9.19 (s, 1H, 5'-H).	224 (M^+, 100)
2l	1.36 (d, 6H, J=7.0, ***CH_3***-CH-***CH_3***), 2.77 (s, 3H, 2-CH_3), 4.38 (m, 1H, J=7.0, CH), 7.58 (dd, 1H, J_1=8.1, J_2=6.8, 6-H), 7.70 (s, 1H, 3-H), 7.73 (d, 1H, J=6.8, 7-H), 7.66 (d,1H, J=8.1, 5-H) 8.44(s, 1H, 3'-H), 9.19 (s, 1H, 5'-H).	252 (M^+, 45), 237 (100)
2m	2.75 (s, 3H, 2-CH_3), 7.85 (s, 1H, 3-H), 7.89 (dd, 1H, J_1=9.1, J_2=2.3, 7-H), 8.10 (d, 1H, J=9.1, 8-H), 8.19 (d, 1H, J=2.3, 5-H), 8.50 (s, 1H, 3'-H), 9.27 (s, 1H, 5'-H).	244 (M^+, 100)
2n	2.77 (s, 3H, 2-CH_3), 7.70 (dd, 1H, J_1=8.0, J_2=2.2, 6-H), 7.80 (s, 1H, 3-H), 8.12 d, 1H, J=2.2, 8-H), 8.16 (d, 1H, J=8.0, 5-H), 8.48 (s, 1H, 3'-H), 9.25 (s,1H, 5'-H).	244 (M^+, 100)
2o	2.77 (s, 3H, 2-CH_3), 7.60 (dd, 1H, J_1=8.50, J_2=7.4, 6-H), 7.85 (s, 1H, 3-H), 8.02 (d, 1H, J=8.5, 5-H), 8.04 (d, 1H, J=7.4, 7-H), 8.47 (s, 1H, 3'-H), 9.23 (s, 1H, 5'-H).	244 (M^+, 100)
2p	2.80 (s, 3H, 2-CH_3), 7.95 (s, 1H, 3-H), 8.17 (m, 2H, 5-H + 7-H), 8.50 (s, 1H, 3'-H), 9.27 (s, 1H, 5'-H).	278 (M^+, 100)
2r	2.80 (s, 3H, 2-CH_3), 7.92 (dd, 1H, J_1=8.8, J_2=1.8, 6-H), 7.97 (s, 1H, 3-H), 8.35 (d, 1H, J=8.5, 5-H), 8.42 (d, 1H, J=1.8, 8-H), 8.50 (s, 1H, 3'-H), 9.30 (s,1H, 5'-H).	278 (M^+, 100)
2s	2.77 (s, 3H, 2-CH_3), 7.77 (dd, 1H, J_1=7.9, J_2=7.0, 6-H), 7.90 (s, 1H, 3-H), 8.27 (d, 1H, J=7.0, 7-H), 8.39 (d, 1H, J=7.9, 5-H), 8.50 (s, 1H, 3'-H), 9.25 (s, 1H, 5'-H).	278 (M^+, 100)
2t	2.85 (s, 3H, 8-CH_3), 7.75 (dd, 1H, J_1=8.4, J_2=6.7, 6-H), 7.90 (d, 1H, J=6.7, 7-H), 7.98 (d, 1H, J=8.4, 5-H), 8.42 (s, 1H, 3-H), 8.51 (s, 1H, 3'-H), 9.34 (s, 1H, 5'-H).	327 (M^+, 35), 292 (100)
2u	8.00 (dd, 1H, J_1=8.4, J_2=7.3, 6-H), 8.46 (d, 1H, J=7.3, 7-H), 8.53 (d, 1H, J=8.4, 5-H), 8.56 (s, 1H, 3'-H), 8.65 (s, 1H, 3-H), 9.40 (s, 1H, 5'-H).	380 (M^+, 15), 345 (100)

The elemental analyses for C, H and N were within +/- 0.4 % of the theoretical values for all of these new compounds.

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