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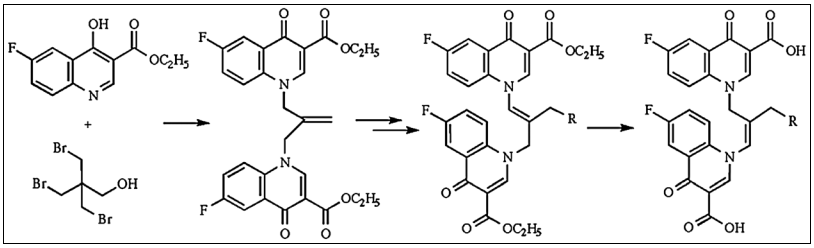
Received May 17, 2012
DOI 10.1002/jhet.1861
Published online 16 May 2014 in Wiley Online Library (wileyonlinelibrary.com).



The reaction of the 4-hydroxyquinoline-3-carboxylate **6** with pentaerythritol tribromide gave the 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) **11**, whose reaction with bromine afforded the 1,1′-(2-bromo-2-bromomethylpropane-1,3-diyl)di(4-quinolone-3-carboxylate) **12**. Compound **12** was transformed into the (*Z*)-1,1′-(2-acetoxymethylpropene-1,3-diyl)di(4-quinolone-3-carboxylate) **13** or (*E*)-1,1′-[2-(imidazol-1-ylmethyl)propene-1,3-diyl]di(4-quinolone-3-carboxylate) **14**. Hydrolysis of the dimer (*Z*)-**13** or (*E*)-**14** with potassium hydroxide provided the (*E*)-1,1′-(2-hydroxymethylpropene-1,3-diyl)di(4-quinolone-3-carboxylic acid) **15** or (*Z*)-1,1′-[2-(imidazol-1-ylmethyl)propene-1,3-diyl]di(4-quinolone-3-carboxylic acid) **16**, respectively. The nuclear Overhauser effect (NOE) spectral data supported that those hydrolysis resulted in the geometrical conversion of (*Z*)-**13** into (*E*)-**15** or (*E*)-**14** into (*Z*)-**16**.

J. Heterocyclic Chem., **51**, 1720 (2014).

INTRODUCTION

In previous papers [1–9], we reported the synthesis and biological activities of the 1-alkyl-4-oxopyridazino[3,4-*b*]quinoxalines **1** as candidates of antibacterial quinolone analogs (Chart 1), some of which showed good antibacterial, antifungal, and/or algicidal activities [3–6]. To search for biologically active compounds, we have then changed the target ring system from 4-oxopyridazino[3,4-*b*]quinoxaline to 4-oxoquinoline such as quinolone antibacterials. Concerning the antibacterial quinolones and new quinolones, many research groups and pharmaceutical companies have developed the excellent antibacterial agents by the modification of the substituents at the N1, C7, and/or C8 positions of the quinolone skeleton. Nowadays, typical new quinolones such as levofloxacin [10], enoxacin [11], ciprofloxacin [12,13], sparfloxacin [14], and some others have clinically been used all over the world. Because quinolone antibacterials are known to interact with the DNA gyrase, various activities have been expected for quinolone derivatives. For example, the 4-quinolone-3-carboxamides **2** [15] and **3** [16] were reported to exhibit antiviral activities. The recent review on 4-quinolones involving new quinolones introduces the synthesis and modification together with the antibacterial and antitumor activities [17].

Recently, we undertook the structural modification of ordinary new quinolones (Chart 1), whose basic moiety at the 7-position was shifted to the N1-side chain, leading to the synthesis of the 1-(pyridin-4-ylalkenyl)-4-quinolone-3-carboxylates **4** [18]. As the result, one of compounds **4** (X═H, R^1═R^2═C_2H_5) was found to possess antimalarial activity, whose potency was regarded as an effective level, whereas the 7-chloro derivatives of compounds **4** (X═Cl) did not exhibit the antimalarial activity. The subsequent shift of the N1-pyridyl moiety to the C3-side chain produced one more class of the antimalarial 4-quinolones **5** [19].

In continuation of the aforementioned works, we further tried the transformation of the N1-moiety in the structural modification of 4-quinolones. Namely, we attempted the conversion of the 4-hydroxyquinoline-3-carboxylate **6** into the 4-quinolone-3-carboxylate **7** (Scheme 1) using pentaerythritol tribromide so as to provide various quinolone analogs **8** possessing two kinds of bases A and B in the N1-moiety. However, the 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) **11** was unexpectedly obtained instead of compound **7** as shown in Scheme 2. This paper describes the synthesis of novel 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) **11** and

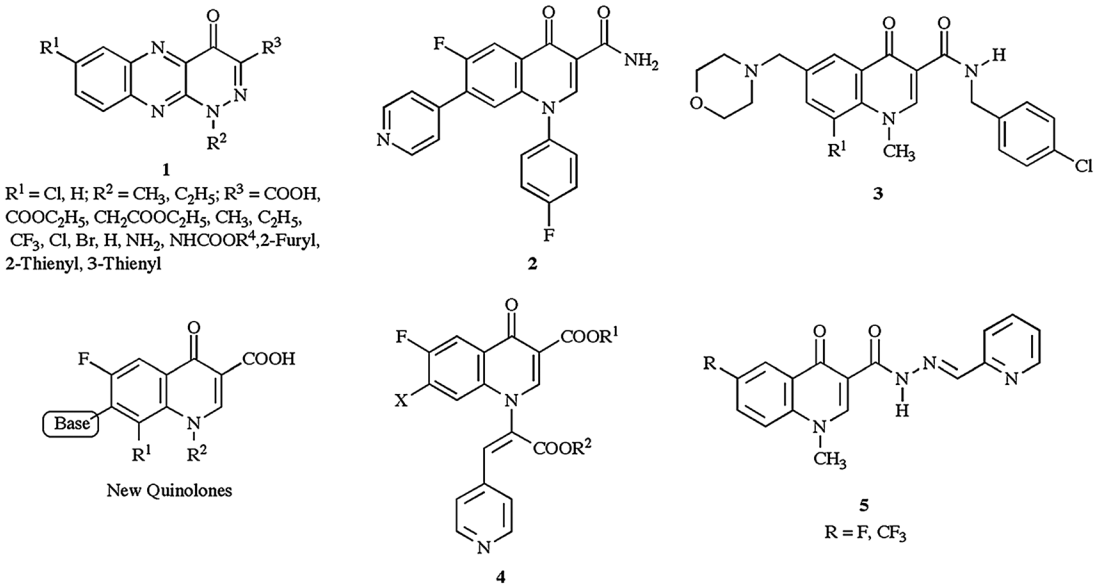


Chart 1

its transformation into the dibromo, imidazolyl, acetoxy, and hydroxy derivatives **12–16**.

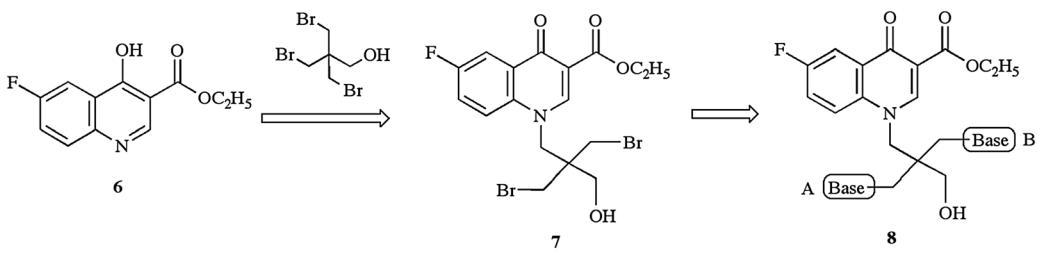
RESULTS AND DISCUSSION

Synthesis of the 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) 11 and related dimers 12–16. The reaction of the 4-hydroxyquinoline-3-carboxylate **6** with pentaerythritol tribromide in the presence of potassium carbonate gave the 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) **11**, presumably via intermediates **7**, **9**, and **10** (Scheme 2). The electron withdrawing 4-quinolone ring [20] would activate the bromomethyl carbon of an intermediate **7**, whose facile reaction with the second 4-quinolone-3-carboxylate **6** formed an intermediate **9**. The presence of two 4-quinolone rings in an intermediate **9** might further activate the bromomethyl carbon [20] to form an oxetane intermediate **10** [21], whose ring cleavage was postulated to afford the dimer **11** with elimination of formaldehyde [22]. The reaction of the dimer **11** with bromine provided the 1,1′-(2-bromo-2-bromomethylpropane-1,3-diyl)di(4-quinolone-3-carboxylate) **12**, whose reaction with sodium acetate or imidazole produced the (*Z*)-1,1′-(2-acetoxymethylpropene-1,3-diyl)di(4-quinolone-3-carboxylate) **13** or (*E*)-1,1′-[2-(imidazol-1-ylmethyl)propene-1,3-diyl]di(4-quinolone-3-carboxylate) **14**, respectively. The hydrolysis of the dimer **13** or **14** with potassium hydroxide provided the (*E*)-1,1′-(2-hydroxymethylpropene-1,3-diyl)di(4-quinolone-3-carboxylic acid) **15** or (*Z*)-1,1′-[2-(imidazol-1-ylmethyl) propene-1,3-diyl]di(4-quinolone-3-carboxylic acid) **16**, respectively.

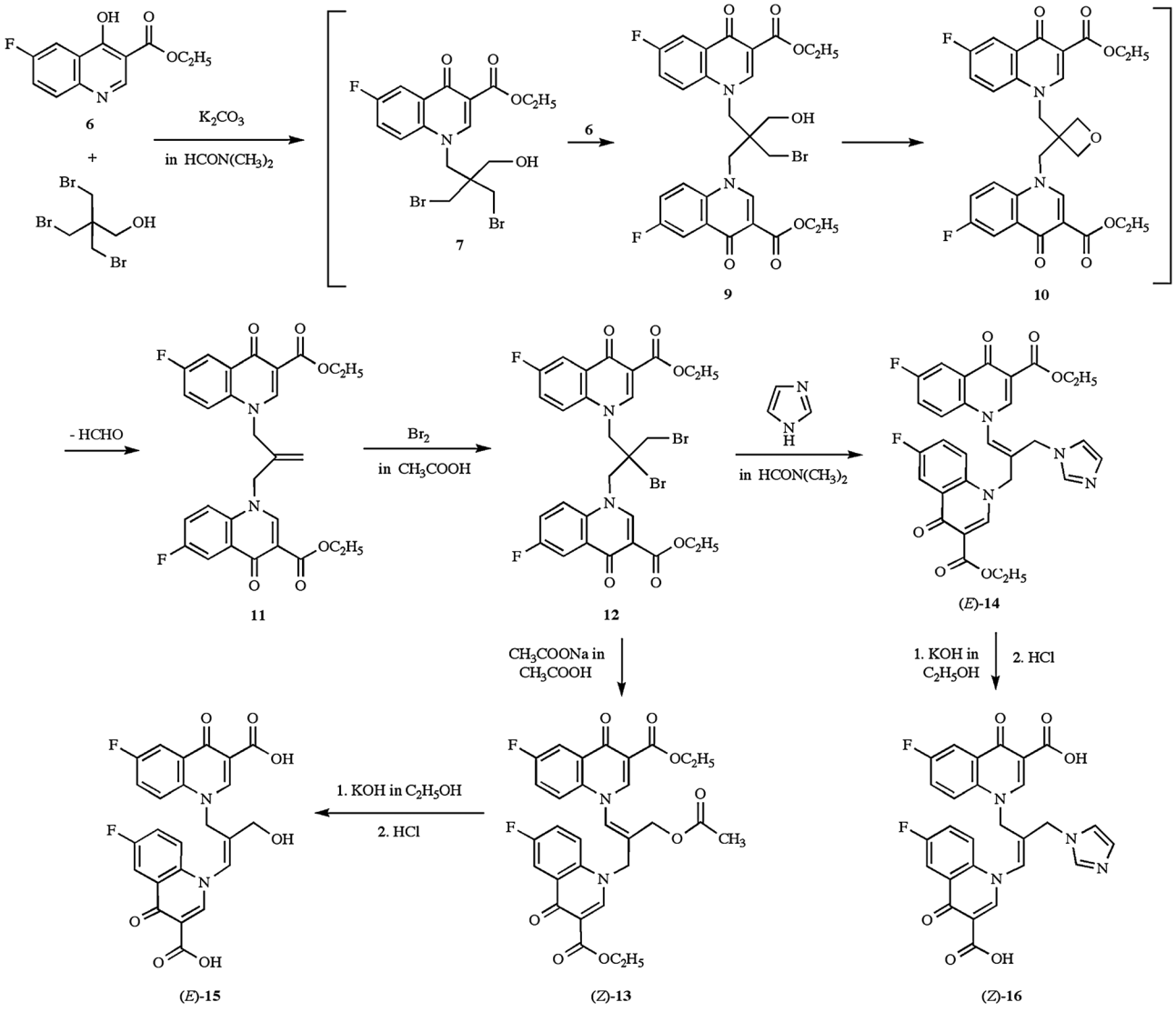
The structure of novel 1,1′-(2-methylenepropane-1,3-diyl)di(4-quinolone-3-carboxylate) **11** and the dimers **12–16** in Scheme 2 was assigned by the analytical and spectral data. Most of dimers were hygroscopic and found to absorb moisture gradually while the microanalyses were carried out. Accordingly, the hydrate numbers in the molecular formulae were not constant for all compounds.

NMR spectral data. The dimers **11** and **12** were found to have a symmetrical structure from the NMR spectral data. In the dimer **11**, the methylene proton signal (4H, δ 5.16) was observed in a lower magnetic field than the vinilic proton signal (2H, δ 4.64), which was confirmed by the

Scheme 1



Scheme 2



nuclear Overhauser effect (NOE) spectral data (Table 1, Chart 2). The vinylic protons suspicious of shielding (δ 4.64) would exist in the position above the quinolone ring to result in the anisotropy effect. The dimer **11** includes the 1-allyl-4-quinolone moiety, and the dimers **14–16** involve both the 1-allyl-4-quinolone and 1-vinyl-4-quinolone moieties (Chart 3). On the basis of the 2-H (δ 8.65) and 8-H (δ 7.86) proton signals of the dimer **11** having the 1-allyl-4-quinolone moiety, the 2-H and 8-H proton signals of the dimers **14–16** were aasigned as follows; 2-H (δ 8.67–8.59) and 8-H (δ 7.88–7.78) in the 1-allyl-4-quinolone moiety; 2-H (δ 8.55–8.32) and 8-H (δ 7.72–7.30) in the 1-vinyl-4-quinolone moiety [23]. Namely, the 2-H and 8-H proton signals of the 1-allyl-4-quinolone moiety were observed in lower magnetic fields than those of the 1-vinyl-4-quinolone moiety. The data of the chemical shifts (Charts 2 and 3) and NOE (Table 1) exhibited the geometry of the dimers **13–16** as **13** (*Z*-form), **14** (*E*-form), **15** (*E*-form), and **16** (*Z*-form). The crucial NOE data are as follows: the dimer **13** [from δ 5.91 (radiation) to δ 7.28 (NOE); from δ 4.53 (radiation) to δ 9.02, 7.70 (NOE)]; the dimer **14** [from δ 8.31 (radiation) to δ 7.48, 4.82 (NOE); from δ 4.82 (radiation) to δ 8.31 (NOE)]; the dimer **15** [from δ 7.15 (radiation) to δ 4.25 (NOE); from δ 4.25 (radiation) to δ 7.15 (NOE)]; the dimer **16** [from δ 5.33 (radiation) to δ 7.26 (NOE)].

Table 2 shows the carbon chemical shifts of our typical quinolone dimers **11**, **13**, and **14** assigned by the heteronuclear multiple bond connectivity (HMBC) and heteronuclear multiple quantum coherence (HMQC) spectral data.

Interpretation for the isomerization of the (*E*)-isomer and (*Z*)-isomer into (*Z*)-isomer and (*E*)-isomer. In the transformation of the dibromodimer **12** into the dimer (*Z*)-

Table 1

NOE correlation of compounds **11**, (*Z*)-**13**, (*E*)-**14**, (*E*)-**15**, and (*Z*)-**16**.

Compound	Radiation (δ)	NOE (δ) (%)
11	8,65	5.16 (1.1)
	5.16	8.65 (0.73), 7.86 (2.2)
(*Z*)-**13**	**5.91**[a]	9.46 (5.7), 8.34 (6.1), **7.28**[a] (2.2), 4.53 (0.69)
	4.53[a]	**9.02**[a] (1.9), **7.70**[a] (0.61), 5.91 (0.39)
(*E*)-**14**	**8.31**[a]	**7.48**[a] (0.23), 7.02[a] (0.29), **4.82**[a] (0.16)
	7.48	4.82 (0.37)
	6.80	7.02 (0.94)
	6.79	7.30 (0.30)
	5.18	7.88 (0.57), 7.48 (0.41), 7.02 (1.2)
	4.82[a]	**8.31**[a] (0.70), 7.48 (1.7), 7.02 (1.2)
(*E*)-**15**	8.59	5.47 (3.4)
	8.36	7.15 (1.4)
	7.15[a]	8.36 (1.8), 7.52 (3.5), **4.25**[a] (1.4)
	5.65	4.25 (2.0)
	5.47	8.59 (1.8), 7.84 (8.7), 4.25 (1.5)
	4.25[a]	**7.15**[a] (4.9), 5.65 (1.5), 5.47 (0.77)
(*Z*)-**16**	7.98	7.78 (1.5)
	5.54	8.60 (0.84), 7.78 (3.2)
	5.33[a]	9.37 (1.7), 7.98 (2.2), **7.26**[a] (0.90), 5.54 (0.23)

[a]Bold letter values in radiation and NOE columns mean the crucial NOE to support the (*E*) or (*Z*) isomer.

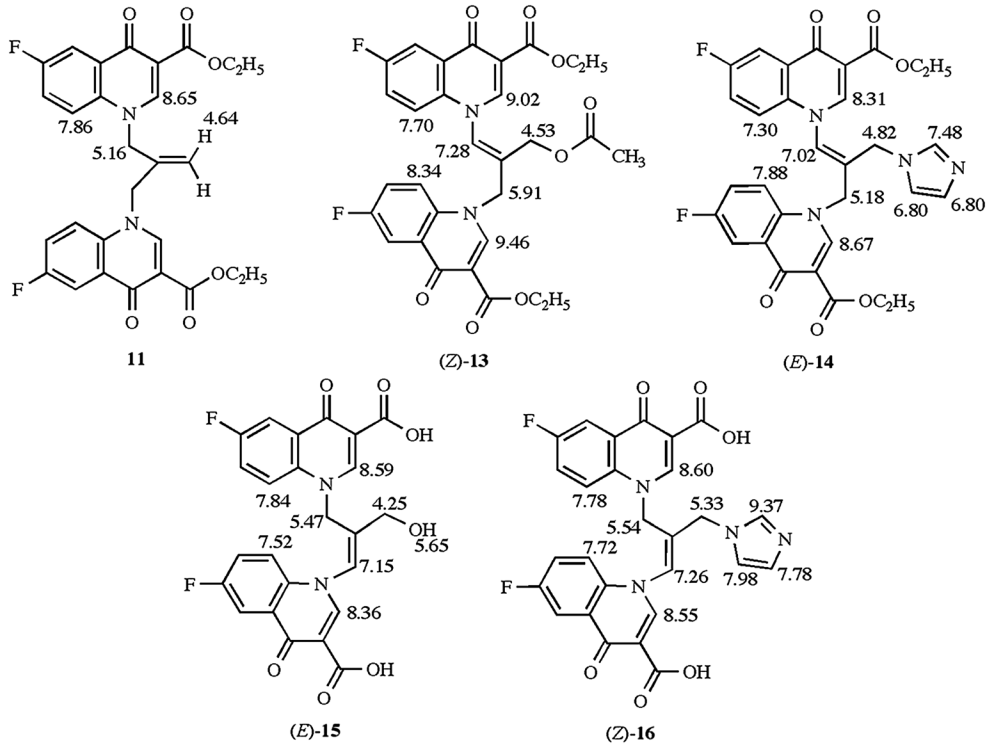
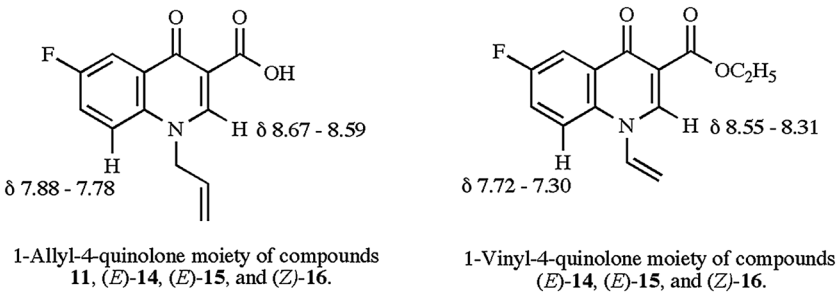


Chart 2. Selected NMR spectral data for compounds **11**, (*Z*)-**13**, (*E*)-**14**, (*E*)-**15**, and (*Z*)-**16**.

13 or (*E*)-**14**, the antiperiplanar position of two quinolone rings would be favored for the elimination of hydrogen bromide leading to the formation of an intermediate **17** (Scheme 3). The allyl bromide residue of an intermediate **17** then underwent substitution with acetate or imidazole to give the dimer (*Z*)-**13** or (*E*)-**14**, respectively.



1-Allyl-4-quinolone moiety of compounds **11**, (*E*)-**14**, (*E*)-**15**, and (*Z*)-**16**.

1-Vinyl-4-quinolone moiety of compounds (*E*)-**14**, (*E*)-**15**, and (*Z*)-**16**.

Chart 3. Chemical shifts of 2-H and 8-H protons for compounds **11**, (*E*)-**14** (*E*)-**15**, and (*Z*)-**16**.

Concerning the (*E*)/(*Z*) isomerization in the respective conversion of the dimer (*Z*)-**13** or (*E*)-**14** into the dimer (*E*)-**15** or (*Z*)-**16**, there would be some attracting interaction such as stacking (arene–arene or arene–π interaction) between two quinolone rings of anion intermediates (Scheme 3) [24,25]. Successive treatment of anion intermediates **18** with hydrochloric acid afforded the dimer (*E*)-**15** or (*Z*)-**16**.

Antimalarial screening data. The dimers **11–16** were evaluated for the *in vitro* antimalarial activity, and the IC_{50} was 54–100 μM to *Plasmodium falciparum*. These values were regarded as not effective level.

CONCLUSION

The reaction of the 4-hydroxyquinoline-3-carboxylate **6** with pentaerythritol tribromide gave the 1,1′-dimer **11**, which was converted into the dibromodimer **12** (Scheme 2). The reaction of the dibromodimer **12** with sodium acetate or imidazole effected the β-elimination of hydrogen bromide to afford the dimer (*Z*)-**13** or (*E*)-**14**, respectively, maintaining two quinolone rings in the *trans* position (Scheme 3). Subsequent treatment of the dimer (*Z*)-**13** or (*E*)-**14** with potassium hydroxide resulted in the geometry conversion into the dimer (*E*)-**15** or (*Z*)-**16**, respectively, sustaining two quinolone rings in the *cis* position. These results suggest the formation of an anion intermediate **18** and then spontaneous stacking between two quinolone rings.

EXPERIMENTAL

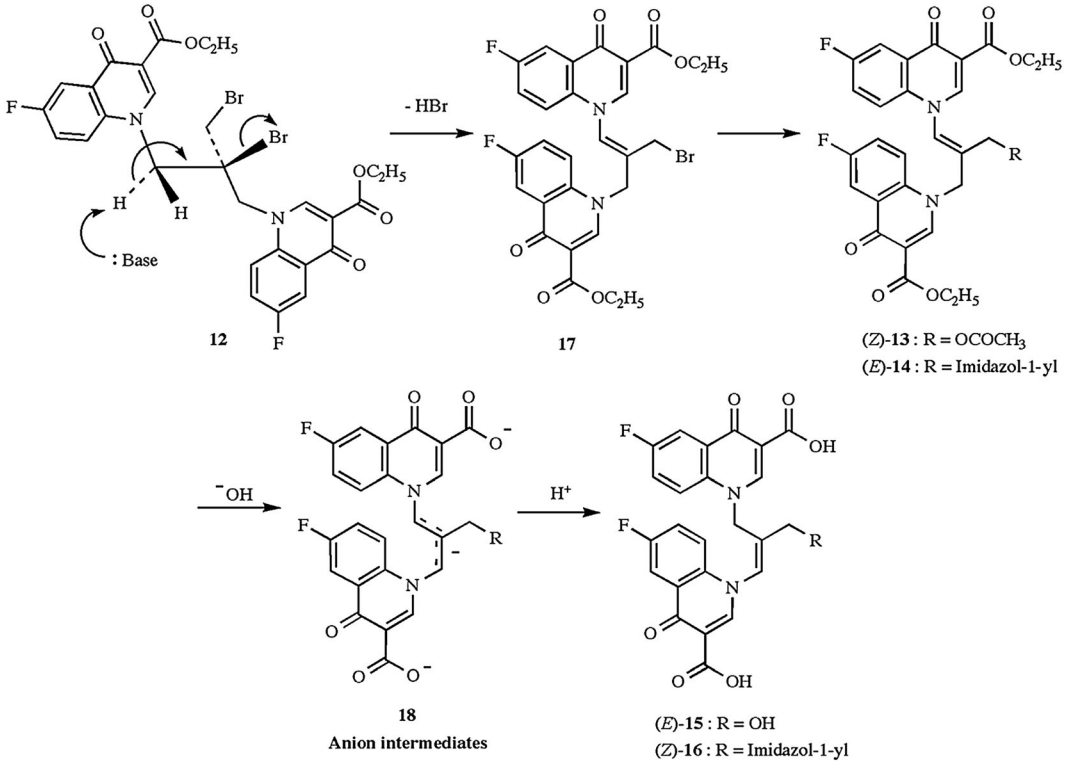
All melting points were determined on a Yazawa (Tokyo) micro melting point BY-2 apparatus and are uncorrected. The IR spectra

Table 2

Carbon chemical shifts for compounds **11**, **13**, and **14**.

		Compound **13**		Compound **14**	
Carbon	Compound **11**	1- Allyl-4-quinolone moiety	1- Vinyl-4-quinolone moiety	1- Allyl-4-quinolone moiety	1- Vinyl-4-quinolone moiety
2-C	149.9	150.6	148.3	150.6	148.1
3-C	109.7	110.3	110.1	110.5	110.2
4-C	172.0	172.4	172.1	172.4	172.4
172	129.9	130.3	129.2	130.4	129.3
5-C	110.8	111.3	111.0	111.3	111.0
6-C	159.3	160.5	158.9	160.5	158.8
7-C	120.9	121.3	121.1	121.1	121.0
8-C	120.7	120.8	120.7	120.6	120.6
8a-C	136.0	136.2	136.1	136.1	136.0
Ester C=O	164.5	164.7	164.3	164.6	164.3
Ester CH_2	59.9	60.3	60.1	60.2	60.1
Ester CH_3	14.3	14.5	14.4	14.5	14.4
Others	139.1 [N1 (=C=)] 112.4 [N1 (=CH_2)] 54.7 (N1-CH_2)	169.8 (Acetyl C=O) 134.2 ([N1 (=C=)] 129.6 (N1-CH=) 58.9 (N1-CH_2) 54.1 (Acetoxy CH_2) 20.3 (Acetyl CH_3)		137.9 (Imidazole 2-C) 135.6 [N1 (=C=)] 129.0 (Imidazole 4-C) 128.3 (Imidazole 5-C) 119.7 (N1-C=) 54.2 (N1-CH_2) 43.3 (Imidazolyl CH_2)	

Scheme 3. Postulated mechanism for the conversion of compounds (*Z*)-**13**, (*E*)-**14** into (*E*)-**15**, (*Z*)-**16**.



(potassium bromide) were recorded with a JASCO (Tokyo) FT/IR-200 spectrophotometer. The NMR spectra were measured with a Varian (Vernon Hills, IL) XL-400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) and Varian INOVA 600 (600 MHz for ^{1}H and 151 MHz for ^{13}C) spectrometers. The chemical shifts are given in the δ scale. The mass spectra (MS) were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer (Waltham, MA) 240B instrument.

Ethyl 6-Fluoro-4-hydroxyquinoline-3-carboxylate (6). This sample was synthesized by a method reported in literatures [26,27], wherein diethyl (4-fluoroanilino)methylenemalonate (obtained from the reaction of 4-fluoroaniline with diethyl ethoxymethylenemalonate) was refluxed in diphenyl ether.

Diethyl 1,1′-(2-Methylenepropane-1,3-diyl)di(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate) (11). A mixture of compound **6** (5.0 g, 21.3 mmol), pentaerythritol tribromide (10.36 g, 31.9 mmol), and potassium carbonate (4.4 g, 31.9 mmol) in *N,N*-dimethylformamide (100 mL) was heated at 120–140°C with stirring for 1 h. The reaction mixture was filtered, and the filtrate was evaporated *in vacuo* to give colorless crystals **11**. Recrystallization from *N,N*-dimethylformamide/ethanol/water afforded colorless needles as monohydrate (5.17 g, 87%); mp 157–158°C; IR: ν cm^{-1} 1720, 1620; MS: *m/z* 522 (M^+); NMR (deuteriodimethyl sulfoxide): 8.65 (s, 2H, 2-H), 7.86 (dd, *J* = 9.0, 4.5 Hz, 2H, 8-H), 7.85 (dd, *J* = 9.0, 3.0 Hz, 2H, 5-H), 7.66 (ddd, *J* = 9.0, 8.0, 3.0 Hz, 2H, 7-H), 5.16 (s, 4H, CH_2), 4.64 (s, 2H, vinylic H), 4.21 (q, *J* = 7.0 Hz, 4H, ester CH_2), 1.26 (t, *J* = 7.0 Hz, 6H, ester CH_3). *Anal*. Calcd. for $C_{28}H_{24}F_2N_2O_6 \cdot H_2O$: C, 62.22; H, 4.85; N, 5.18. Found: C, 62.26; H, 4.60; N, 5.09.

Diethyl 1,1′-(2-Bromo-2-bromomethylpropane-1,3-diyl)di(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate) (12). Bromine (2.0 mL, 39.0 mmol) was added to a suspension of compound **11** (5.0 g, 9.6 mmol) in acetic acid (100 mL), and the mixture was heated at 100°C with stirring for 1 h to give a clear solution. After the solution was cooled to room temperature, water (200 mL) was added to the solution to precipitate crystals **12**, which were collected by filtration and washed with saturated sodium bicarbonate solution and sodium thiosulfate solution (5.79 g, 92%). Recrystallization from ethanol provided colorless needles; mp 212–213°C; IR: ν cm^{-1} 1720, 1620; MS: *m/z* 680 (M^+), 682 ($M^+ + 2$), 684 ($M^+ + 4$); NMR (deuteriodimethyl sulfoxide): 8.82 (s, 2H, 2-H), 8.35 (dd, *J* = 9.0, 4.0 Hz, 2H, 8-H), 7.86 (dd, *J* = 9.0, 3.0 Hz, 2H, 5-H), 7.71 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 2H, 7-H), 5.18 (d, *J* = 16.0 Hz, 2H, methylene CH), 5.06 (d, *J* = 16.0 Hz, 2H, methylene CH), 4.19 (q, *J* = 7.0 Hz, 4H, ester CH_2), 4.08 (s, 2H, $BrCH_2$), 1.23 (t, *J* = 7.0 Hz, 6H, ester CH_3). *Anal*. Calcd. for $C_{28}H_{24}Br_2F_2N_2O_6$: C, 49.29; H, 3.55; N, 4.11. Found: C, 49.18; H, 3.85; N, 4.21.

Diethyl (*Z*)-1,1′-(2-Acetoxymethylpropene-1,3-diyl)di(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate) (13). A solution of compound **12** (5.0 g, 7.33 mmol) and anhydrous sodium acetate (1.50 g, 18.3 mmol) in acetic acid (100 mL) was heated at 120°C with stirring for 1 h and then refluxed with stirring for 2 h. Evaporation of the solvent *in vacuo* gave an oily substance, which was crystallized from ethanol/water to afford colorless needles **13** (3.92 g, 92%); mp 223–225 °C; IR: ν cm^{-1} 3440, 1740, 1690, 1620; MS: *m/z* 580 (M^+); NMR (deuteriotrifluoroacetic acid): 2-H [9.46 (s, 1H), 9.02 (s, 1H)], 8-H [8.34 (dd, *J* = 9.0, 4.0 Hz, 1H), 7.70 (dd, *J* = 9.0, 4.0 Hz, 1H)], 5-H [8.20 (dd, *J* = 8.0, 3.0 Hz, 1H), 8.10 (dd, *J* = 8.0, 2.5 Hz, 1H)], 7-H [7.96 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H), 7.71 (ddd, *J* = 9.0, 9.0, 2.5 Hz, 1H)], 7.28 (s, 1H, vinylic H), 5.91 (s, 2H, CH_2), 4.53 (s, 2H, acetoxy CH_2), ester CH_2 [4.49 (q, *J* = 7.0 Hz, 2H), 4.45 (q, *J* = 7.0 Hz, 2H)], 1.86 (s, 3H, acetyl CH_3), ester CH_3 [1.31 (t, *J* = 7.0 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H)]. *Anal*. Calcd. for $C_{30}H_{26}F_2N_2O_8 \cdot 2.5H_2O$: C, 57.60; H, 4.99; N, 4.48. Found: C, 57.95; H, 4.66; N, 4.65.

Diethyl (*E*)-1,1′-[2-(Imidazol-1-ylmethyl)propene-1,3-diyl]di-(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate) (14). A solution of compound **12** (3.0 g, 4.40 mmol) and imidazole (1.50 g, 22.0 mmol) in *N,N*-dimethylformamide (30 mL) was heated at 120–140°C with stirring for 5 h. Evaporation of the solvent *in vacuo* gave an oily residue, which was crystallized from ethanol/water afforded pale yellow needles **14** (1.89 g, 71%); mp 252–253°C; IR: ν cm^{-1} 3440,1720, 1620; MS: *m/z* 588 (M^+); NMR (deuteriodimethyl sulfoxide): 2-H [8.67 (s, 1H), 8.31 (s, 1H)], 8-H [7.88 (dd, *J* = 9.0, 4.5 Hz, 1H), 7.30 (dd, *J* = 9.0, 4.5 Hz, 1H)], 5-H [7.86 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.79 (dd, *J* = 9.0, 3.0 Hz, 1H)], 7-H [7.75 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H), 7.65 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H)], imidazole 2-H [7.48 (s, 1H)], vinylic H [7.02 (s, 1H)], imidazole 4-H, 5-H [6.81 (s, 1H), 6.80 (s, 1H)], CH_2 [5.18 (s, 2H), 4.82 (s, 2H)], ester CH_2 [4.22 (q, *J* = 7.0 Hz, 2H), 4.18 (q, *J* = 7.0 Hz, 2H)], ester CH_3 [1.27 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.0 Hz, 3H)]. *Anal*. Calcd. for $C_{31}H_{26}F_2N_4O_6 \cdot 5/6H_2O$: C, 61.69; H, 4.62; N, 9.28. Found: C, 61.97; H, 4.45; N, 8.93.

(*E*)-1,1′-(2-Hydroxymethylpropene-1,3-diyl)di(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid) (15). A solution of potassium hydroxide (1.66 g, 29.6 mmol) in water (20 mL) was added to a boiling suspension of compound **13** (5.0 g, 8.62 mmol) in ethanol (200 mL)/water (30 mL) to give a clear solution. The solution was refluxed with stirring for 2 h to precipitate colorless crystals of potassium salt. After cooling to room temperature, the colorless crystals were collected by filtration. The crystals were dissolved in water (20 mL), and 1 N hydrochloric acid (30 mL) was added to the solution to precipitate compound **15**, which were collected by filtration and washed with water to give an analytically pure sample (3.62 g, 87%); mp 285°C (decomposed); IR: ν cm^{-1} 1730, 1620; MS: *m/z* 482 (M^+); NMR (deuteriodimethyl sulfoxide): COOH [14.35 (s, 1H), 14.31 (s, 1H)], 2-H [8.59 (s, 1H), 8.36 (s, 1H)], 8-H [7.84 (dd, *J* = 9.0, 4.0 Hz, 1H), 7.52 (dd, *J* = 9.0, 4.5 Hz, 1H)], 5-H [7.78 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.69 (dd, *J* = 9.0, 3.0 Hz, 1H)], 7-H [7.67 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H), 7.58 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H)], 7.15 (s, 1H, vinylic H) , 5.65 (t, *J* = 3.5 Hz, 1H, OH), 5.47 (s, 2H, CH_2), 4.25 (d, *J* = 3.5 Hz, 2H, CH_2). *Anal*. Calcd. for $C_{24}H_{16}F_2N_2O_7$: C, 59.76; H, 3.34; N, 5.87. Found: C, 59.78; H, 3.40; N, 5.85.

(*Z*)-1,1′-[2-(Imidazol-1-ylmethyl)propene-1,3-diyl]di(6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid) (16). A solution of potassium hydroxide (250 mg, 4.46 mmol) in water (5 mL) was added to a boiling suspension of compound **14** (800 mg, 1.32 mmol) in ethanol (50 mL)/water (5 mL), and the solution was refluxed with stirring for 2 h to precipitate colorless crystals of potassium salt. After cooling to room temperature, the colorless crystals were collected by filtration. The crystals were dissolved in water (10 mL), and 1 N hydrochloric acid (6 mL) was added to the solution to precipitate compound **16**, which was collected by filtration and washed with water (460 mg, 66%). Recrystallization from ethanol/water gave colorless needles; mp 262–263°C; IR: ν cm^{-1} 3420, 3060, 1760, 1640; MS: *m/z* 532 (M^+); high resolution MS: Calcd. for $C_{27}H_{18}F_2N_4O_6$: 533.127, found: 533.127; NMR (deuteriodimethyl sulfoxide): 9.37 (dd, *J* = 1.5, 1.5 Hz, 1H, imidazole 2-H), 2-H [8.60 (s, 1H), 8.55 (s, 1H)], 7.98 (dd, *J* = 2.0, 1.5 Hz, imidazole 5-H), 7.78 (dd, *J* = 2.0, 1.5 Hz, imidazole 4-H), 8-H [7.78 (dd, *J* = 8.5, 4.5 Hz, 1H), 7.72 (dd, *J* = 8.5, 4.5 Hz, 1H)], 5-H [7.77 (dd, *J* = 8.5, 3.0 Hz, 1H), 7.60 (dd, *J* = 8.5, 3.0 Hz, 1H)], 7-H [7.62 (ddd, *J* = 8.5, 8.5, 3.0 Hz, 1H), 7.60 (ddd, *J* = 8.5, 8.5, 3.0 Hz, 1H)], 7.26 (s, 1H, vinylic H), 5.54 (s, 2H, CH_2), 5.33 (s, 2H, CH_2). The COOH proton signals were not observed presumably due to the presence of moisture in a solution. *Anal*. Calcd. for $C_{27}H_{18}F_2N_4O_6 \cdot 3H_2O$: C, 55.29; H, 4.12; N, 9.55. Found: C, 55.21; H, 3.73; N, 9.51.

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