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SYNTHESIS OF NEW 4-(4,5-DIPHENYL-1H-IMIDAZOL-2-YL)TETRAZOLO[1,5-*a*]QUINOLINES FROM TETRAZOLO[1,5-*a*]QUINOLINES

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Some new 4,5-diphenyl-1H-imidazole derivatives were synthesized in good yields by treating various tetrazolo[1,5-a]quinolines with benzil and ammonium acetate in glacial acetic acid.

Keywords: ammonium acetate, benzil, 4,5-diphenylimidazole, tetrazolo[1,5-*a*]quinoline, 1,5-hydrogen shift.

Quinolines and their derivatives form an important class of pharmacologically active synthetic compounds. The quinoline nucleus can also be frequently recognized in the structure of numerous naturally occurring alkaloids. They have been associated with a broad spectrum of biological activities [1]. The fusion of quinoline to the tetrazole ring is known to increase the biological activity [2].

The imidazoles are common components of a large number of natural products and pharmacologically active molecules [3-10]. The prominence of this moiety makes an improved method of their preparation highly valuable. The biological importance of the imidazole ring system has made it a common structure in numerous synthetic compounds, such as fungicides [11-14], herbicides [15, 16], plant growth regulators [17], and therapeutic agents [18-22]. In recent years, substituted imidazoles have been used as components of provided ionic liquids [23] that have a new approach to "Green Chemistry".

By considering all the above aspects, we wish to report a straightforward and convenient synthesis of new 4,5-diphenyl-1H-imidazole derivatives containing a highly bioactive tetrazole moiety as a development of our ongoing research work [24-26]. The key intermediate tetrazolo[1,5-*a*]quinoline-4-carbaldehydes **2a-i** were prepared by the reaction of 2-chloroquinoline-3-carbaldehyde derivatives **1a-i** with sodium azide in DMSO/AcOH mixture [27] as shown in Scheme 1. The reaction of compounds **2a-i** with benzil **3** and ammonium acetate in the molar ratio of 1:2:4 in glacial acetic acid at reflux conditions afforded the corresponding 4,5-diphenyl-1H-imidazoles **4a-i** in moderate to good yields (Table 1). The IR spectra of compounds **4a-i** showed absorption due to the (N–H) stretch in the range 3329-3365 cm^{-1} (Table 1). In the ^1H NMR spectra of the title compounds **4a-i**, the NH proton has been observed at about 12 ppm, which confirms the formation of the imidazole ring (Table 2).

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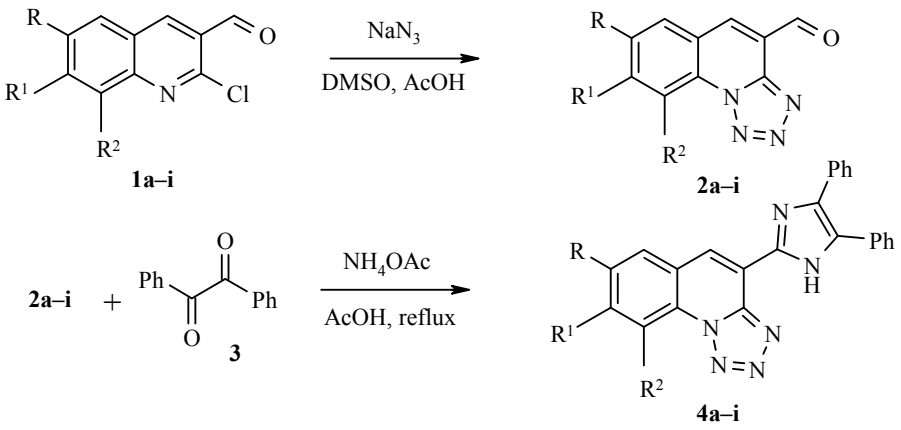
Scheme 1



a R = R^1 = R^2 = H; **b** R = Me, R^1 = R^2 = H; **c** R = R^2 = H, R^1 = Me; **d** R = R^1 = H, R^2 = Me; **e** R^1 = R^2 = H, R = OMe; **f** R = R^2 = H, R^1 = OMe; **g** R = R^1 = H, R^2 = OMe; **h** R^1 = R^2 = H, R = OEt; **i** R = R^1 = H, R^2 = Et

TABLE 1. Physical and Spectral Characteristics of Compounds **4a-h**

Compound	Found, % / Calculated, %			mp, °C	Yield, %*	IR (KBr, ν_{max}, cm^{-1}) N–H	MS, *m/z* (*m*+1)
	C	H	N				
4a	74.45 / 74.21	4.24 / 4.15	21.52 / 21.64	244-246	84	3365	389.2
4b	74.42 / 74.61	4.35 / 4.51	20.90 / 20.88	282-284	76	3343	403.2
4c	74.50 / 74.61	4.43 / 4.51	20.74 / 20.88	264-266	81	3366	403.2
4d	74.71 / 74.61	4.42 / 4.51	20.69 / 20.88	246-248	71	3350	403.2
4e	71.54 / 71.76	4.21 / 4.34	20.14 / 20.08	266-268	68	3330	419.2
4f	71.45 / 71.76	4.42 / 4.34	20.25 / 20.08	256-258	77	3332	419.2
4g	71.87 / 71.76	4.49 / 4.34	20.24 / 20.08	278-280	63	3329	419.2
4h	72.35 / 72.21	4.85 / 4.66	19.21 / 19.43	242-244	76	3344	433.2
4i	74.74 / 74.98	4.61 / 4.84	20.37 / 20.18	218-220	88	3352	417.2

* Isolated yields.

Scheme 2

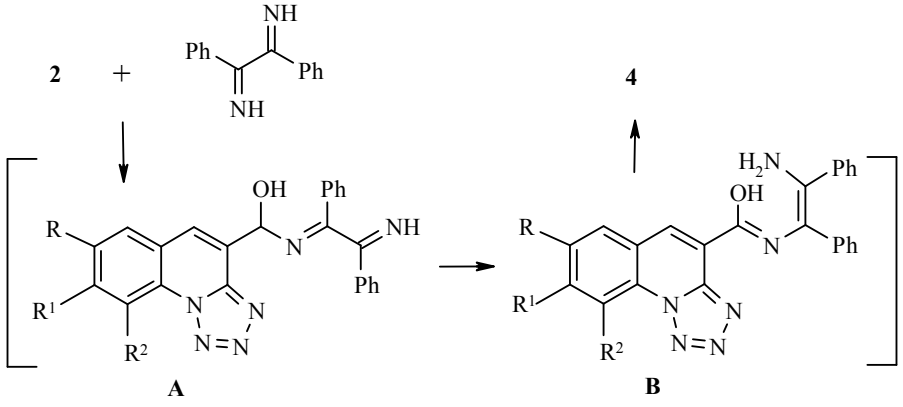


TABLE 2. ^{1}H NMR Spectra of Compounds **2e,h,i** and **4a-i**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)*
2e	3.63 (3H, s, OCH_3); 7.84-7.94 (2H, m, H Ar); 8.54 (1H, s, H Ar); 8.64 (1H, d, *J* = 10.0, H Ar); 10.72 (1H, s, CHO)
2h	1.24 (3H, t, *J* = 6.0, $OCH_2C\underline{H}_3$); 3.68 (2H, q, *J* = 6.0, $OC\underline{H}_2CH_3$); 7.70-7.82 (2H, m, H Ar); 8.57 (1H, s, H Ar); 8.70 (1H, s, H Ar); 10.75 (1H, s, CHO)
2i	1.36 (3H, t, *J* = 8.0, $CH_2C\underline{H}_3$); 2.89 (2H, q, *J* = 8.0, $C\underline{H}_2CH_3$); 7.59-7.78 (2H, m, H Ar); 8.52 (1H, s, H Ar); 8.64 (1H, s, H Ar); 10.54 (1H, s, CHO)
4a	7.28-7.58 (10H, m, H Ar); 7.85 (1H, t, *J* = 7.6, H Ar); 7.97 (1H, t, *J* = 7.6, H Ar); 8.38 (1H, d, *J* = 8.0, H Ar); 8.66 (1H, d, *J* = 8.0, H Ar); 8.87 (1H, s, H Ar); 12.66 (1H, s, NH)
4b	2.55 (3H, s, CH_3); 7.25-7.78 (10H, m, H Ar); 8.02 (1H, d, *J* = 8.0, H Ar); 8.18-8.32 (3H, m, H Ar); 12.52 (1H, s, NH)
4c	2.40 (3H, s, CH_3); 7.48-7.92 (10H, m, H Ar); 8.13 (1H, d, *J* = 8.0, H Ar); 8.21-8.48 (3H, m, H Ar); 12.11 (1H, s, NH)
4d	2.51 (3H, s, CH_3); 7.32-7.68 (10H, m, H Ar); 8.08-8.32 (4H, m, H Ar); 12.01 (1H, s, NH)
4e	3.90 (3H, s, OCH_3); 7.01-7.38 (10H, m, H Ar); 8.11 (1H, d, *J* = 8.0, H Ar); 8.20-8.54 (3H, m, H Ar); 12.48 (1H, s, NH)
4f	3.82 (3H, s, OCH_3); 7.18-7.64 (10H, m, H Ar); 7.97 (1H, d, *J* = 8.0, H Ar); 8.21-8.43 (3H, m, H Ar); 12.10 (1H, s, NH)
4g	3.78 (3H, s, OCH_3); 6.88-7.21 (10H, m, H Ar); 7.78-8.03 (4H, m, H Ar); 12.45 (1H, s, NH)
4h	1.34 (3H, t, *J* = 8.0, $OCH_2C\underline{H}_3$); 4.32 (2H, q, *J* = 8.0, $OC\underline{H}_2CH_3$); 6.82-7.25 (10H, m, H Ar); 7.55-7.97 (4H, m, H Ar); 12.25 (1H, s, NH)
4i	1.42 (3H, t, *J* = 8.0, $OCH_2C\underline{H}_3$); 3.36 (2H, q, *J* = 8.0, $OC\underline{H}_2CH_3$); 7.21-7.57 (10H, m, H Ar); 8.04-8.25 (4H, m, H Ar); 12.24 (1H, s, NH)

* $CDCl_3$, 200 MHz (compounds **2e,h,i**), DMSO-d_6, 400 MHz (compounds **4a-i**).

As a plausible mechanism (Scheme 2) underlying the formation of the imidazole, the initially formed benzildiimine would attack the aldehyde function of compound **2**, giving rise to the intermediate **A**. The latter would undergo a 1,5-hydrogen shift to give the intermediate **B,** which would further cyclize to 4-(4,5-diphenyl-1H-imidazol-2-yl)tetrazolo[1,5-*a*]quinoline **4**.

EXPERIMENTAL

All chemicals and solvents were purchased from Merck (Darmstadt, Germany), Spectrochem (Mumbai, India), Lancaster (Ward Hill, MA, USA), and S. D. Fine-chem (India). Melting points were determined in open capillaries on Kumar's melting point apparatus (India) and are uncorrected. IR spectra were recorded on a JASCO FT-IR 4100 spectrometer (Japan) using KBr discs. ^{1}H NMR spectra were recorded on Varian Mercury Plus (400 MHz) and Bruker AC200 (200 MHz) spectrometers. Mass spectra (ESI) were recorded on Waters Micromass Quattro II spectrometer. Elemental analyses were performed on CHNS analyzer Flash 1112, Thermo Finnigan. The progress of the reactions was monitored by TLC on Merck silica plates. Solvents were commercially available materials of reagent grade.

Synthesis of Tetrazolo[1,5-*a*]quinoline-4-carbaldehyde Derivatives 2a-i (General Method). All the compounds were prepared by a reported method, and some of the compounds are well characterized in the literature [2, 27-31].

Synthesis of 4-(4,5-Diphenyl-1H-imidazol-2-yl)tetrazolo[1,5-*a*]quinoline Derivatives 4a-i (General Method). A mixture of tetrazolo[1,5-*a*]quinoline-4-carbaldehyde **2** (10 mmol), benzil **3** (20 mmol), and ammonium acetate (40 mmol) was refluxed in glacial acetic acid. The progress of the reaction was monitored

on TLC. After completion of the reaction, the reaction mixture was poured on crushed ice. The solid obtained was extracted with CH_2Cl_2 (2×50 ml) and washed with water (2×10 ml) and brine (2×20 ml). The separated organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The obtained crude product was purified by column chromatography on silica gel, using CH_2Cl_2–MeOH, 8:2, as eluent.

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