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Note

Bisazaheterocycles : Part VIII — A new synthesis of 2,2′-bisquinazolinones

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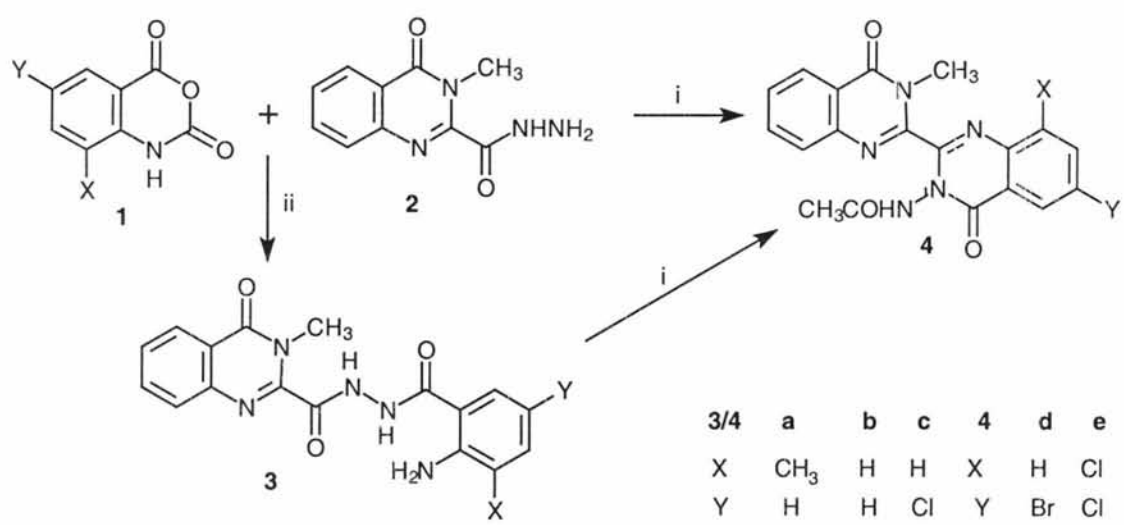
A one step synthesis of 2,2′-bisquinazolin-4(3*H*)-ones **4** from isatoic anhydride **1** and 2-hydrazinocarbonyl-3-methylquinazolin-4(3*H*)-one **2** is reported.

As part of our efforts to develop facile synthetic routes for commercially important azinylquinazolinones, we planned to synthesise 2,2′-bisquinazolinones as heat resistant whitening agents[1]. In our present investigation, isatoic anhydride **1** was reacted with 2-hydrazinocarbonyl-3-methylquinazolin-4(3*H*)-one **2** to isolate 2,2′-bisquinazolin-4(3*H*)-ones (**4**, **Scheme I**) in one step thus providing a facile and new synthesis of **4**. For example, an equimolar mixture of **1a** and **2** on refluxing in acetic acid containing *p*-TSA yielded 3-acetylamino-3-methyl-2,2′-bisquinazolin-4(3*H*)-one **4a** (M^+ at m/z 375). The UV spectrum (λ_{max} at 282, 231 and 208 nm) is similar to that of 2-aryl-3-methyl-quinazolin-4(3*H*)-one spectrum (λ_{max} at 283 and 224 nm). The IR spectrum (KBr) showed a single NH absorption (3317 cm^{-1}) and two carbonyl peaks (1686 and 1724 cm^{-1}). The presence of two carbonyls in the molecule was also confirmed by ^{13}C NMR spectrum (δ_{CO} 159.10 and 160.64). The ^1H NMR spectrum (DMSO-d_6) exhibited three singlets (δ 2.6, 2.65 and 3.8), each integrating for three protons (Ar-CH_3, CO-CH_3 and N-CH_3). The corresponding ^{13}C NMR signals were observed at δ 17.01, 21.3 and 31.82 ppm. The presence of two quinazolin-4(3*H*)-one moieties in **4a** is also evident from the appearance of the two *peri*-protons as doublets at 8.05 (J = 9 Hz) and 8.3 (J = 9 Hz) in the ^1H NMR spectrum, and base peak at m/z 160 (3-methylquinazolin-4(3*H*)-one ion) in EIMS at 70 eV.

The above reaction was extended to four other isatoic anhydrides **1** and in each case the corresponding 2,2′-bisquinazolinone **4** was isolated and characterised (**Table I**). When **1a** was reacted with **2** in acetic acid at room temperature, 2-[(2-aminobenzoyl)hydrazinocarbonyl]-3-methylquinazolin-4(3*H*)-one **3a** was obtained [mp 230°C; UV (λ_{max}, nm) : 364, 287 and 209; IR (KBr, cm^{-1}) : 3464, 3408 (NH_2), 3298 (NH), 3156 (NH), 1698 (C=O), 1668 (C=O)]. The diaroyl hydrazine **3a** could easily be converted to **4a** by refluxing in acetic acid containing *p*-TSA, suggesting the intermediacy of **3a** in the formation of **4a**. The mechanism of formation of **4** through **3** is explained by invoking the formation of a benzotriazepinone and its ring contraction by Heindel's type rearrangement



3/4	a	b	c	4	d	e
X	CH_3	H	H	X	H	Cl
Y	H	H	Cl	Y	Br	Cl

i) - AcOH, *p*-TSA, reflux ii) AcOH, Room Temp, stirring

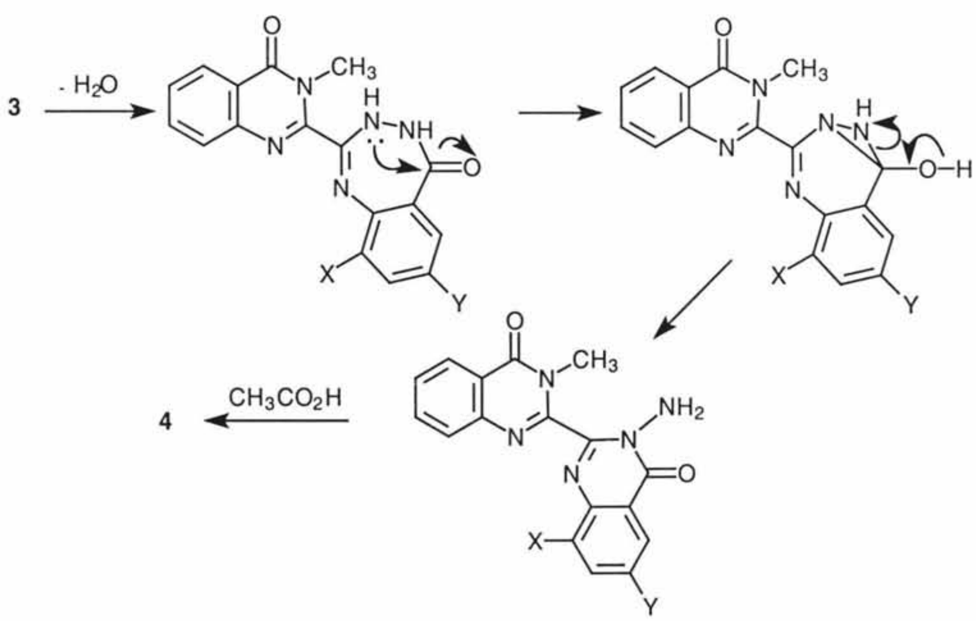
Scheme I

Table I— Characterisation data of compounds **3** and **4**

Compd	X	Y	Yield (%)	m.p. °C	Mass (M^+)	UV (nm)	^1H NMR (δ ppm)
3a	CH_3	H	80	230	—	364 287 209	—
3b	H	H	70	160	338 (+1)	369 288 208	3.9 (s, 3H, N-CH_3), 6.6-7.9 (m, 7H, Ar-H), 8.3 (d, J = 10 Hz, 1H, *peri*- proton), 10.8 (1H, NH)
3c	H	Cl	74	210	—	—	—
4a	CH_3	H	80	290	375	282 231 208	2.6 (s, 3H, ArCH_3), 2.65(s, 3H, $COCH_3$), 3.8 (s, 3H, NCH_3), 8.05 (d, J = 9 Hz, 1H, *peri*-proton), 8.3 (d, J = 9 Hz, 1H, *peri*-proton)
4b	H	H	96	230	—	—	2.7 (s, 3H, $COCH_3$), 4 (s, 3H, NCH_3),7.6 – 7.9 (m, 6H, Ar-H), 8.2 (d, J =7 Hz, 1H, *peri*-proton), 8.4 (d, J = 10 Hz, 1H, *peri*-proton)
4c	H	Cl	87	250	395	—	2.6 (s, 3H, $COCH_3$), 3.75 (s, 3H, NCH_3), 7.6 – 7.9 (m, 5H, Ar-H), 8.15 (s, 1H, *peri*-proton), 8.3 (d, J = 8 Hz, 1H, *peri*-proton)
4d	H	Br	91	230	—	381 281 226	2.6 (s, 3H, $COCH_3$), 3.8 (s, 3H, NCH_3), 7.4 – 7.9 (m, 5H, Ar-H), 8 (s, 1H, *peri*-proton), 8.2 (d, J = 9 Hz, 1H, *peri*-proton)
4e	Cl	Cl	82	265	—	385 288 229	2.65 (s, 3H, $COCH_3$), 4 (s, 3H, NCH_3), 7.6 – 7.9 (m, 4H, Ar-H), 8.3 (s, 1H, *peri*-proton), 8.4 (d, J = 9 Hz, 1H, *peri*-proton)

^{13}C NMR of **4a** : 160.64, 159.1, 154.21, 148.01, 145.9, 135.57, 135.25, 135.82, 128.41, 127.48,126.53, 126.35, 124.14, 121.27, 120.42, 31.82, 21.30, 17.01

^1H NMR spectra of **3b, 4b** and **4e** were recorded in $CDCl_3$; of **4a, 4c** and **4d** were recorded in DMSO-d_6



Scheme II

under acidic conditions followed by amino group acetylation (**Scheme II**).

Experimental Section

Melting points mentioned were determined in capillaries using Polman digital melting point apparatus (Model No. Mp96) and are uncorrected. UV spectra (in nm) were recorded in methanol on a Shimadzu 1520 ultraviolet-visible spectrophotometer; IR spectra (in cm^{-1}) in KBr pellets on a Shimadzu 435 instrument; and ^1H NMR spectra on a Varian Gemini (200 MHz) spectrophotometer with TMS as internal standard (chemical shifts in δ, ppm). The solvent in which the NMR spectra were recorded is indicated at the appropriate places. Mass spectra were recorded on VG-micro mass 70 - 70H instrument with direct inlet probe.

2 - [(2-Aminoaroyl) hydrazinocarbonyl]-3-methyl-quinazolin-4(3*H*)-one 3: General procedure.

Method A. A mixture of **2** (1 mmole) and isatoic anhydride **1** (1 mmole) was refluxed in pyridine (5 mL) for 9 hr. The reaction mixture was poured in water (20 mL) and the solid separated was filtered, washed with ethanol and recrystallised from methanol to yield **3**. The characterisation data of compounds **3a-e** are given in **Table I**.

Method B. A mixture of **2** (1 mmole) and **1** (1 mmole) in acetic acid (5 mL) was stirred for 9 hr at room temperature. The reaction mixture was poured in ice-cold water (20 mL). Compound **3** was separated out as a solid. It was filtered, dried and recrystallised from methanol.

3-Acetamido-3-methyl-2,2′-bisquinazolin-4(3*H*)-one 4 : General procedure

Method A. Isatoic anhydride **1** (1 mmole) was added to a solution of **2** (1 mmole) in acetic acid (5 mL) containing a pinch of *p*-TSA and the reaction mixture was refluxed for 9 hr. The reaction mixture was then cooled and poured into ice-cold water (20 mL). The product that separated was filtered, washed with ice-cold water (5 mL) and recrystallised from methanol to yield **4**.

Method B. Compound **3** (1 mmole) was added to acetic acid (5 mL) containing a pinch of *p*-TSA and the reaction mixture was refluxed for 9 hr. The cooled reaction mixture was poured in ice-cold water (20 mL). The product that separated was filtred, washed with ice-cold water (5 mL) and recrystallised from methanol to yield **4**. The characterisation data of compounds **4a-e** are given in **Table I**.

Acknowledgement

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References

1 Haginiwa Y H & Yamamoto Y, *Yakugaku Zasshi*, **1974**, 958; *Chem Abstr*, 83, **1975**, 9965.