Synthesis of New Heterocycles: Condensation of 2-Methyl-4*H*-naphth-[1,2-*d*][1,3]oxazin-4-one with Schiff Bases and Formation of 3-Aryl-2-styrylbenzo[*h*]quinazolin-4(3*H*)-ones

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Synopsis. Condensation of 2-Methyl-4*H*-naphth[1,2-*d*][1,3]oxazin-4-one (**2**) with Schiff bases (**3**) in acetic acid has resulted in 3-aryl-2-styrylbenzo[*h*]quinazolin-4(3*H*)-ones (**4**), characterized by spectral and analytical methods.

As a part of our work on the role of Schiff bases in heterocyclizations[1-8] and with a view to prepare hitherto unreported benzo[*h*]quinazolinones, the condensation of 2-methyl-4*H*-naphth[1,2-*d*][1,3]-oxazin-4-one with Schiff bases has been undertaken and the results are presented below.

The reaction of 1-amino-2-naphthalenecarboxylic acid (**1**)[9] with acetic anhydride under refluxing conditions yielded a colourless crystalline compound with mp 178°, identified as 2-methyl-4*H*-naphth[1,2-*d*][1,3]-oxazin-4-one on the basis of spectral and analytical values. Unlike the lactone bond of 2-methyl-3,1-benzoxazin-4-one,[10] which is vulnerable and is readily hydrolyzed to *N*-acetylanthranilic acid in contact with traces of moisture or on prolonged exposure to atmosphere, the lactone bond of **2** was found to be quite stable.

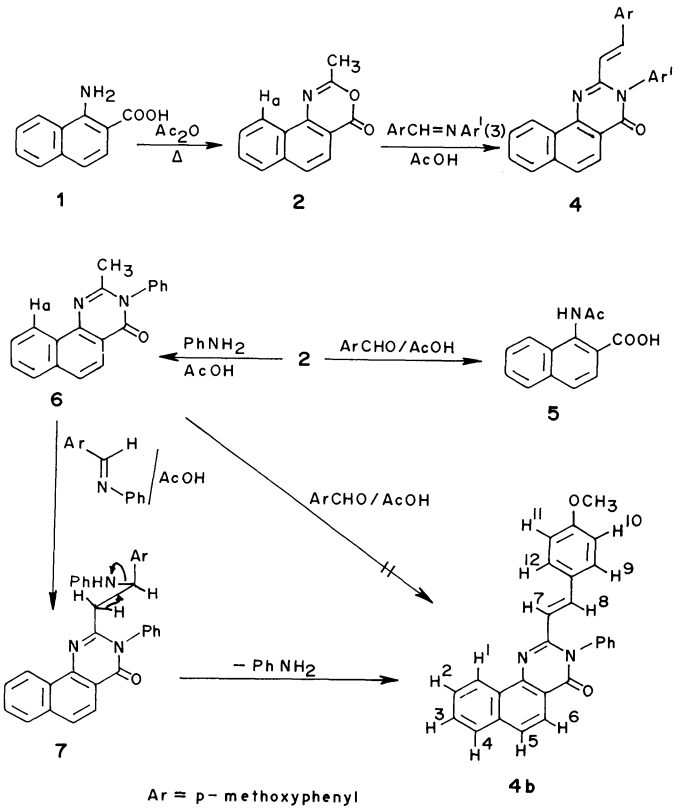
Condensation of compound **2** with an equimolar proportion of *N*-(*p*-methoxybenzylidene)aniline (**3**, Ar=*p*-methoxyphenyl; Ar'=phenyl) in acetic acid medium at steam bath temperature resulted in a yellow crystalline compound, mp 186° in high yield, characterized on the basis of its microanalytical, mass, IR, and ^{1}H-NMR spectral data as 2-(*p*-methoxystyryl)-3-phenylbenzo[*h*]quinazolin-4(3*H*)-one [**4b**; MS: M^+ at *m/z* 404, IR (KBr): $\nu_{C=O}$ at 1670 cm^{-1}, ^{1}H-NMR ($CDCl_3$): δ 3.7 (*s*, 3H, OCH_3) 6.3 (*d*, 1H, H-7, $J_{7,8}$=15 Hz), 6.7—8.0 (*m*, 14H, H-2 to H-6, H-9 to H-12 and five protons of 3-phenyl), 8.2 (*d*, 1H, H-8, $J_{8,7}$=15 Hz) and 9.1—9.3 (*m*, 1H, H-1)]. The *J* value (15 Hz) of the two olefinic protons (H-7 and H-8) suggested the preferred trans-geometry of the exocyclic double bond. Thus, it is apparent that **4b** is formed by styrylation of 2-methyl group and replacement of ring oxygen in **2** by *N*-phenyl moiety in one step.

This reaction has been extended to eleven other Schiff bases and the product obtained in each case has been characterized as corresponding 3-aryl-2-styrylbenzo[*h*]-quinazolin-4(3*H*)-one (**4a—l**, Scheme 1, Table 1) by analogy, spectral and microanalytical data.

To understand the mechanism of formation of **4**, the reactions of **2** with *p*-methoxybenzaldehyde and separately with aniline have been carried out under identical conditions of the Schiff base reaction. The former reaction resulted in the formation of 1-acetamido-2-naphthalenecarboxylic acid (**5**)[11] characterized by comparing with an authentic sample prepared from 1-amino-2-naphthalenecarboxylic acid and acetic anhydride and spectral data. Compound **5** must have been formed by the addition of elements of water obviously from solvent to the oxazinone ring followed by ring opening.

Oxazinone **2** with aniline gave a compound with mp 192°, characterized as 2-methyl-3-phenylbenzo[*h*]-quinazolin-4(3*H*)-one(**6**) by spectral data [MS: M^+ at *m/z* 286; IR (KBr): $\nu_{C=O}$ at 1675 cm^{-1}, ^{1}H-NMR ($CDCl_3$+DMSO-d_6): δ 2.3 (*s*, 3H, CH_3), 7.4—8.2 (*m*, 9H, aromatic) and 9.0 (*m*, 1H, H_a)] and microanalytical data. Reaction of **6** with *p*-methoxybenzaldehyde in hot acetic acid did not result in the styrylated product **4b**. However, **6** could be converted into **4b** on treatment with **3** (Ar=*p*-methoxyphenyl, Ar'=phenyl) under identical conditions. This result emphasises the superiority of Schiff bases over aldehydes in the styrylation of an active methyl group. Facile styrylation with Schiff base may be possibly due to better leaving ability of the arylamino moiety compared to hydroxyl, from the possible 2-[2-aryl-2-(arylamino)-ethyl]-3-phenyl benzo[*h*]quinazolin-4(3*H*)-one intermediate (**7**).

Based on these results, the formation of **4** from **2** and Schiff base (**3**) is explained on the basis of initial nucleophilic attack by active methyl group through the enamine tautomer. Its attack on the electrophilic carbon of azomethine function and subsequent transformations were described earlier.[7]



Scheme 1.

TABLE 1. CHARACTERIZATION DATA OF 3-ARYL-2-STYRYLBENZO[*h*]QUINAZOLIN-4(3*H*)-ONES (**4**)

Compd	Ar	Ar′	Mp θ_m/°C	Crystallized from	Yield/%	Mol. formula	C% Found	C% Calcd	H% Found	H% Calcd	N% Found	N% Calcd
4a	C_6H_5	C_6H_5	232	MeOH	80	$C_{26}H_{18}N_2O$	83.13	83.42	4.74	4.81	7.50	7.48
4b	4-$MeOC_6H_4$	C_6H_5	186	MeOH	75	$C_{27}H_{20}N_2O_2$	80.86	80.19	4.92	4.95	6.96	6.93
4c	4-MeC_6H_4	C_6H_5	218	MeOH	74	$C_{27}H_{20}N_2O$	83.65	83.51	5.32	5.15	7.18	7.21
4d	2-$NO_2C_6H_4$	C_6H_5	252	MeOH–CH_2Cl_2	70	$C_{26}H_{17}N_3O_3$	73.98	74.46	4.20	4.06	10.10	10.02
4e	4-ClC_6H_4	C_6H_5	230	MeOH–CH_2Cl_2	76	$C_{26}H_{17}N_2OCl$	77.02	76.37	4.26	4.16	6.90	6.86
4f	C_6H_5	4-$MeOC_6H_4$	233	C_6H_6–MeOH	78	$C_{27}H_{20}N_2O_2$	80.54	80.19	4.88	4.95	6.88	6.93
4g	C_6H_5	4-MeC_6H_4	220	MeOH	82	$C_{27}H_{20}N_2O$	83.14	83.51	5.24	5.15	7.26	7.21
4h	C_6H_5	4-ClC_6H_4	234	C_6H_6–MeOH	81	$C_{26}H_{17}N_2OCl$	76.52	76.37	4.02	4.16	6.90	6.84
4i	4-$MeOC_6H_4$	4-$MeOC_6H_4$	198	C_6H_6–MeOH	76	$C_{28}H_{22}N_2O_3$	77.63	77.42	5.12	5.07	6.38	6.45
4j	4-MeC_6H_4	4-$MeOC_6H_4$	191	MeOH–CH_2Cl_2	73	$C_{28}H_{22}N_2O_2$	80.12	80.38	5.20	5.26	6.76	6.69
4k	4-MeC_6H_4	4-MeC_6H_4	200	MeOH	75	$C_{28}H_{22}N_2O$	83.44	83.58	5.42	5.47	7.05	6.96
4l	4-ClC_6H_4	4-ClC_6H_4	253	MeOH–CH_2Cl_2	70	$C_{26}H_{16}N_2OCl_2$	70.87	70.43	3.68	3.61	6.50	6.33

IR(KBr): All the compounds showed a carbonyl stretching frequency around 1670 cm^{-1}

4a; MS: M^+ at *m/z*: 374; ^{1}H-NMR ($CDCl_3$): δ 6.5(*d*, 1H, olefinic, *J*=15Hz), 7.3—7.7(*m*, 15H, aromatic), 8.2(*d*, 1H, olefinic, *J*=15Hz), and 9.1—9.2(*m*, 1H, aromatic).

4c; MS: M^+ at *m/z*: 388; ^{1}H-NMR ($CDCl_3$): δ 2.3(*s*, 3H, methyl), 6.4(*d*, 1H, olefinic, *J*=15Hz), 7.1—7.8 (*m*, 14H, aromatic), 8.1(*d*, 1H, olefinic, *J*=15Hz), and 9.2(*m*, 1H, aromatic).

4f; MS: M^+ at *m/z*: 404; ^{1}H-NMR ($CDCl_3$): δ 3.8(*s*, 3H, methoxy), 6.6(*d*, 1H, olefinic, *J*=16Hz), 7.0—7.7(*m*, 14H, aromatic), 8.2(*d*, 1H, olefinic, *J*=16Hz), and 9.2(*m*, 1H, aromatic).

4g; MS: M^+ at *m/z*: 388; ^{1}H-NMR ($CDCl_3$): δ 2.5(*s*, 3H, methyl), 6.5(*d*, 1H, olefinic, *J*=15Hz), 7.2—7.7(*m*, 14H, aromatic), 8.2(*d*, 1H, olefinic, *J*=15Hz), and 9.2(*m*, 1H, aromatic).

4h, **4j**, and **4k**; MS: M^+ at *m/z*: 408, 418, and 402 respectively.

Experimental

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer infracord 377 Spectrophotometer, ^{1}H-NMR spectra on Varian A-60D instrument using TMS as internal standard and mass spectra on a Perkin-Elmer Hitachi RMU-6L instrument.

1-Amino-2-naphthalenecarboxylic Acid (1): An ethanolic solution of potassium hydroxide (0.5 mol in 56 ml) was added to a boiling solution of 2-methyl-1-nitronaphthalene[12] (0.21 mol in 100 ml) during a period of 6 h and the resulting solution heated under reflux for a further period of 6 h. The mixture was steam-distilled to remove ethanol and then filtered. The filtrate was brought to the neutralization point first with strong acetic acid and then with dilute acetic acid. At first there comes down brown, flocculent precipitates which was discarded. The filtrate on further acidification gave light brown precipitates which was filtered after 2 h. The crude amino acid was purified by repeated dissolution in sodium hydroxide and precipitation with acetic acid, mp 198—199°, yield 10.4 g (26%).

2-Methyl-4H-naphth[1,2-d][1,3]oxazin-4-one (2): A mixture of 1-amino-2-naphthalenecarboxylic acid (3.74 g, 0.02 mol) and acetic anhydride (10 ml) was refluxed for 4 h, the resulting solution concentrated to one third and allowed to stand. The compound that separated was filtered, treated with charcoal and recrystallized from pet. ether (60—80°)–benzene, mp 178°, [MS: M^+ at *m/z* 211, IR (KBr): $\nu_{C=O}$ at 1745 cm^{-1}, ^{1}H-NMR ($CDCl_3$): δ 2.55 (*s*, 3H, CH_3) 7.5—8.2 (*m*, 5H, aromatic) and 8.7—8.9 (*m*, 1H, H_a); Found: C, 73.25; H, 4.32; N, 6.68%; $C_{13}H_9NO_2$ requires C, 73.93; H, 4.26; N, 6.64%].

Condensation of 2 with Schiff Bases (3): *General Procedure.* To a solution of **2** (2 m mol) in acetic acid (2 ml) was added the required Schiff base (**3**; 2 m mol) and the reaction mixture heated on a steam bath for half an hour and left aside for few minutes. The crystalline compound that separated in each case was filtered, washed with a few drops of methanol and recrystallized from appropriate solvent. The characterization data of benzo[*h*]quinazolinones (**4**) thus prepared are given in Table 1.

The acetic acid filtrate on dilution with water and processing the resulting solid gave additional quantities of **4**.

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