Studies on 2-Methyl- and 2-Phenyl-4-arylmethylene-2-imidazolin-5-ones and Related Compounds

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Compounds 4-arylmethylene-2-methyl-2-oxazolin-5-ones and 4-arylmethylene-2-styryl-2-oxazolin-5-ones react with primary aromatic amines in the presence of anhydrous zinc chloride to give the corresponding 4-arylmethylene-2-methyl-2-imidazolin-5-ones and 4-arylmethylene-2-styryl-2-imidazolin-5-ones (**5**) respectively. Treatment of **5** with phosphorus pentasulfide gives the corresponding 2-imidazoline-5-thiones. Reaction of 4-arylmethylene-2-phenyl-2-oxazolin-5-ones with hydroxylamine hydrochloride gives the corresponding imidazolinones which was reacted with alkyl halides and acid chlorides to give the corresponding ethers and esters respectively. Structures of the resulting products have been characterized on the basis of elemental analysis, IR, and UV data.

It has been reported[1] that 4-benzylidene-2-methyl-2-oxazolin-5-one reacts with aniline to give 4-benzylidene-1-phenyl-2-methyl-2-imidazol-in-5-one. Recently,[2] under the influence of acetic acid and sodium acetate, 4-arylmethylene-2-phenyl-2-oxazolin-5-ones and primary amines have been reported to yield directly the corresponding imidazolin-5-ones.

The present investigation is mainly concerned with the study of the reaction of 4-arylmethylene-2-methyl-2-oxazlin-5-ones (**1**) and 4-arylmethylene-2-styryl-2-oxazolin-5-ones (**2**) with primary amines, under different conditions, and the study of their behavior with 4-arylmethylene-2-phenyl-2-oxazolin-5-ones (**7**).

1a and **1b** react with aniline in acetic acid and sodium acetate to give *N*-phenyl-2-acetamido-3-arylacrylamides (**3**), instead of the expected 2-imidazolin-5-ones. This can be explained by the fact that the stabilization of the imidazolinone ring by the 2-phenyl group is higher than by the 2-methyl group because the former has three double bonds in conjugation with the ring system than the later. However, when the reaction was carried out in the presence of anhydrous zinc chloride, the corresponding 4-arylmethylene-2-methyl-2-imidazolin-5-ones (**4a—h**) were obtained.

On the other hand, it was previously mentioned[3] that **2a** reacted with primary amines in a benzene solution to give the corresponding α-cinnamido-*N*-substituted cinnamamide. However, when the reaction was carried out in the presence of anhydrous zinc chloride or in acetic acid with sodium acetate gave the corresponding 4-arylmethylene-2-styryl-2-imidazolin-5-ones (**5a—n**). Also, **5a**, **5e**, **5f**, **5h**, **5l**, and **5n** were obtained either by refluxing a mixture of **1a** and **1b** with appropriate amine and aldehyde in acetic acid and sodium acetate or by heating a mixture of **4** and aldehyde in the presence of anhydrous zinc chloride.

Consequently, it can be suggested that transformation of **1** to **5** in acetic acid and sodium acetate must go through an intermediate (**2**) which simultaneously reacted with amines, under reaction condition used to the final products (**5**) according to Scheme 1.

The identity of the imidazolinones (**5**) obtained by any one of these methods was established by TLC (using a benzene–ethanol mixture in the ratio 19:1 respectively) and mixed melting-point determination.

The IR spectra of **2** showed a carbonyl frequency at 1800—1790 cm^{-1} and an unresolved band at 1640—1620 cm^{-1} (due to the C=N and CH=CH). The structural assignment for the products (**4** and **5**) was supported by the IR and UV spectra. The IR spectra of **4** and **5** showed a stretching frequency at 1715—1700 cm^{-1} characteristic of the C=O group and the other band at 1630—1620 cm^{-1} attributed to the C=N stretch in compound **4**, in addition to the unresolved band in compound **5** at 1650—1630 cm^{-1} (due to C=N and CH=CH).

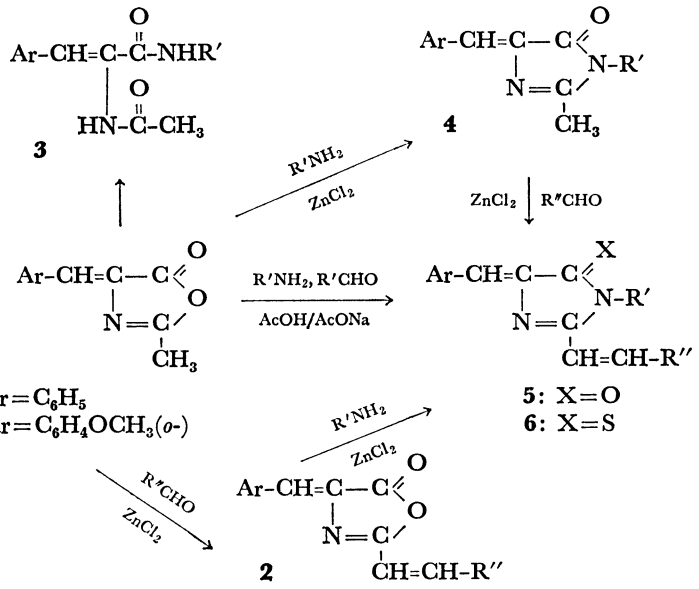
The UV absorption spectra of **4** are characterized by a principal absorption band at 352—378 cm^{-1}, which assigned to n-π^* transition of the carbonyl group perturbed by intramolecular charge transfers from arylmethylene residue to the polarized carbonyl group. This was confirmed through the pronounced red shift to 378 nm observed in **4f** and **4h** which can be attributed to the donating character of the methoxyl group in the arylmethylene residue. The data obtained for **4** showed a hypsochromic shift of about 20—25 nm in comparison with 4-arylmethylene-2-phenyl-2-imidazolin-5-ones.[4]

The UV spectra of **5** were similar to those of **4** and exhibited a principal absorption band at 410—432 nm. The data obtained for **5** showed a bathochromic shift of about 55—60 nm and 30—40 nm when compared with that of **4** and 4-arylmethylene-2-phenyl-2-imidazolin-5-ones respectively.[4]

Treatment of **5a**, **5e**, **5h**, **5i**, and **5j** with phosphorus pentasulfide in dry pyridine produced the corresponding 4-arylmethylene-2-styryl-2-imidazoline-5-thione (**6a**, **6e**, **6h**, **6i**, and **6j**).

The IR spectra of **6** showed absorption bands within the range 1270—1258 cm^{-1} and 1660—1640 cm^{-1} which are characteristic for C=S and –C=N– groupings respectively. The UV spectra of **6a** and **6h** are characterized by two or three absorption bands. The far-UV band is located at longer wavelength than the corresponding one in **5**. This behavior is understandable in view of the higher energy level of the nonbounding electrons in sulfur as compared to the oxygen atom.[5]

Furthermore, the authors have also investigated the hitherto unknown reaction of 4-arylmethylene-2-phenyl-2-oxazolin-5-ones (**7a—c**) and hydroxylamine hydrochloride. Compounds **7a—c** react with hydroxyl-



Ar = C_6H_5	R″
2a:	C_6H_5
b:	$C_6H_4N(CH_3)_2$-*p*
c:	C_6H_4Br-*p*
d:	$C_6H_4NO_2$-*p*

e: Ar = $C_6H_4OCH_3$-*o*, R″ = C_6H_5

3a: Ar = R′ = C_6H_5
b: Ar = $C_6H_4OCH_3$-*o*, R′ = C_6H_5

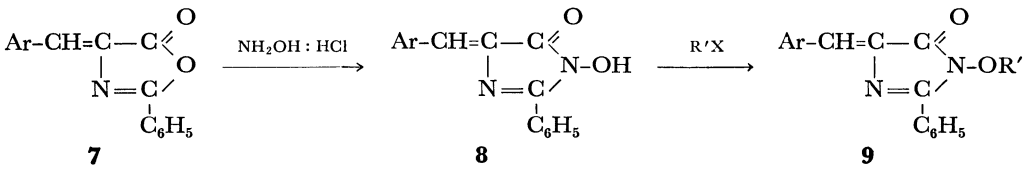
Ar = C_6H_5	R′	R″
5a:	C_6H_5	C_6H_5
b:	$C_6H_4CH_3$-*m*	C_6H_5
c:	$C_6H_4OCH_3$-*p*	C_6H_5
d:	C_6H_4OH-*p*	C_6H_5
e:	C_6H_5	$C_6H_4N(CH_3)_2$-*p*
f:	C_6H_5	$C_6H_4OCH_3$-*o*
g:	C_6H_5	$C_6H_4OCH_3$-*p*

Ar = C_6H_5	R′
4a:	C_6H_5
b:	$C_6H_4CH_3$-*o*
c:	$C_6H_4OCH_3$-*o*
d:	$C_6H_4OCH_3$-*p*

Ar = $C_6H_4OCH_3$-*o*	R′
4e:	$C_6H_4CH_3$-*o*
f:	$C_6H_4CH_3$-*p*
g:	$C_6H_4OCH_3$-*p*
h:	C_6H_4OH-*p*

Ar = $C_6H_4OCH_3$-*o*	R′	R″
5h:	C_6H_5	C_6H_5
i:	C_6H_4OH-*p*	C_6H_5
j:	$C_6H_4OCH_3$-*p*	C_6H_5
k:	$C_6H_4NO_2$-*o*	C_6H_5
l:	C_6H_5	$C_6H_4OCH_3$-*p*
m:	C_6H_5	C_6H_4OH-*p*
n:	C_6H_5	$C_6H_4OCH_3$-*o*

Scheme 1.



	Ar
7a:	C_6H_5
b:	$C_6H_4OCH_3$-*p*
c:	$C_6H_4OCH_3$-*o*

Ar = C_6H_5	R′
9a:	CH_3
b:	$CH_2C_6H_4NO_2$-*p*
c:	COC_6H_5
d:	$SO_2C_6H_4CH_3$-*p*

	Ar
8a:	C_6H_5
b:	$C_6H_4OCH_3$-*p*
c:	$C_6H_4OCH_3$-*o*

Ar = $C_6H_4OCH_3$-*p*	R′
9e:	CH_3
f:	C_2H_5
g:	$COCH_2C_6H_5$
h:	$SO_2C_6H_5$
i:	$SO_2C_6H_4CH_3$-*p*
j:	$COCH_3$

Ar = $C_6H_4OCH_3$-*o*	R′
9k:	CH_3
l:	C_2H_5
m:	$CH_2C_6H_5$
n:	$COCH_3$
o:	$SO_2C_6H_4CH_3$-*p*

Scheme 2.

amine hydrochloride in a methanol solution in the presence of sodium acetate to give 4-arylmethylene-2-phenyl-1-hydroxy-2-imidazolin-5-ones (**8a—c**) respectively.

The IR absorption spectra of the newly synthesized compounds showed absorption bands at 1710—1700 cm^{-1} and 3340—3330 cm^{-1}, which were assigned to the C=O and -OH stretching frequencies respectively, in addition to the -C=N- stretch appeared at 1640—1630 cm^{-1}. The ^1H NMR spectrum of **8c** in trifluoroacetic acid showed signals at 7.8 (S, 1H, -CH=C-), 7.4 (m, 5H, C=N-C_6H_5); 6.82 (m, 4H, C=C-C_6H_4) and 3.8 (S, 3H, -OCH_3) which are in good agreement with its structure.

Reaction of **8a—c** with alkyl halides, acid chlorides and sulfonyl chlorides in dry acetone in the presence of anhydrous potassium carbonate gave the corresponding ethers (**9a**, **9b**, **9e**, **9f**, **9m**, **9k**, and **9l**), esters (**9c**, **9g**, **9j**, and **9n**), and sulfonic esters (**9d**, **9h**, **9l**, and **9o**) respectively.

The IR spectra of compounds **9a—9o** showed an absorption band at 1715—1700 cm^{-1} attributed to the C-O group and another carbonyl, the ester group in compounds **9c**, **9g**, **9j**, and **9n** appeared at 1780—1770 cm^{-1}. The UV spectra of **8** and **9** were similar to those of 4-arylmethylene-2-phenyl-2-imidazolin-5-ones[4] and exhibited a principal absorption band at 385—406 nm.

The ^1H NMR spectrum of **9k** in trifluoroacetic acid showed signals at 7.8 (S, 1H, CH=C-), 7.44 (m, 5H, C=N-C_6H_5), 6.82 (m, 4H, C=C-C_6H_4) and 3.8 (S, 6H, C_6H_4-OCH_3 and N-OCH_3), which is in agreement with its structure.

Biological Screening Results. Compounds of the type **8a—c** and **9h**, **9k**, **9o** were tested *in vitro* for their biological activities on some microbes *viz. Bacillus megaterium* and *Staphylococcus albus* and fungi as *Aspergillus fumigatus* and *Penicillium nigricans*. The more active compounds against *Bacillus megaterium* was **9o**, against *Staphylococcus albus* were **8b** and **9o**; against *Aspergillus fumigatus* were **8a**, **9h**, **9k** and against *Penicillium nigricans* was **9k**.

4-Arylmethylene-2-styryl-2-oxazolin-5-ones (**2**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N
2a	135[a]	$C_{18}H_{13}NO_2$	78.54 (78.08)	4.72 (4.39)	5.09 (5.00)
2b	210	$C_{20}H_{18}N_2O_2$	75.47 (75.38)	5.66 (5.42)	8.80 (8.68)
2c	130	$C_{18}H_{12}NO_2Br$	61.01 (60.80)	3.38 (3.19)	3.95 (3.72)
2d	230	$C_{18}H_{12}N_2O_4$	67.50 (67.27)	3.75 (3.40)	8.75 (8.38)
2e	140	$C_{19}H_{15}NO_3$	74.75 (74.63)	4.91 (4.68)	4.59 (4.26)

a) Lit, mp 135 °C[3]

N-Phenyl-2-acetamido-β-arylacrylamide (**3**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N
3a	197	$C_{17}H_{16}N_2O_2$	72.85 (72.47)	5.71 (5.35)	10.00 (9.66)
3b	220	$C_{18}H_{18}N_2O_3$	69.67 (69.66)	5.80 (5.46)	9.03 (9.33)

4-Arylmethylene-2-methyl-2-imidazolin-5-ones (**4**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N	R_f	λ_{max}/nm (ε_{max})
4a	143[a]	$C_{17}H_{14}N_2O$	77.86 (77.89)	5.34 (5.13)	10.68 (10.39)	0.25	358 (7800)
4b	135	$C_{18}H_{16}N_2O$	78.26 (78.18)	5.79 (5.48)	10.14 (10.02)	0.85	—
4c	160	$C_{18}H_{16}N_2O_2$	73.97 (73.62)	5.47 (5.23)	9.58 (9.36)	0.29	—
4d	150	$C_{18}H_{16}N_2O_2$	73.97 (73.72)	5.47 (5.28)	9.58 (9.32)	0.64	358 (8600)
4e	160	$C_{19}H_{18}N_2O_2$	74.50 (74.30)	5.88 (5.66)	9.15 (9.01)	0.80	—
4f	145	$C_{19}H_{18}N_2O_2$	74.50 (74.13)	5.88 (5.52)	9.50 (9.08)	0.81	378 (9200)
4g	182	$C_{19}H_{18}N_2O_3$	70.80 (70.61)	5.59 (5.30)	8.69 (8.31)	0.63	—
4h	220	$C_{18}H_{15}N_2O_3$	70.35 (70.06)	4.88 (4.76)	9.12 (9.10)	0.68	378 (8800)

a) Lit, mp 144 °C.[1]

Experimental

Melting points are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer infracord spectrophotometer. UV spectra were taken in ethanol on a Pye-Unicam SP 8000 spectrophotometer and ^1H NMR spectra were recorded on a Varian 60 MHz NMR instrument using TMS at the internal standard.

4-Arylmethylene-2-styryl-2-oxazolin-5-ones (2). A mixture of **1** (0.01 mol), appropriate aldehyde (0.012 mol) and anhydrous zinc chloride (0.001 mol) was fused together for 5 min. The cooled reaction mixture gave a yellow precipitate on adding ethanol, which recrystallized from the same solvent. The yield was about 80—85%.

N-Phenyl-2-acetamido-β-arylacrylamide (3). A mixture of **1** (0.01 mol), aniline (0.012 mol) and anhydrous sodium acetate (0.005 mol) in acetic acid (20 ml) was refluxed was refluxed for 3 h. The cooled reaction mixture was filtered off, then recrystallized from ethanol. The yield was about 85%.

4-Arylmethylene-2-methyl-2-imidazolin-5-ones (4). A mixture of **1** (0.01 mol), primary aromatic amine (0.012 mol) and anhydrous zinc chloride (0.001 mol) was fused together for 5 min. The yellow product was collected and crystallized from methanol. The yield was about 55—65%.

4-Arylmethylene-2-styryl-2-imidazolin-5-ones (5). A mixture of **1** (0.01 mol), appropriate aromatic amine (0.012 mol) and aromatic aldehyde (0.012 mol) in acetic acid (20 ml) containing freshly fused sodium acetate (0.005 mol) was refluxed for 3 h, the reaction mixture was cooled, then poured into water. The crude product was collected and crystallized from ethanol. The yield was about 70—75%.

The same products were obtained from **2** and the corresponding aromatic amine when the reaction was carried out either in the presence of anhydrous zinc chloride or in acetic acid solution containing freshly fused sodium acetate as describe above.

4-Arylmethylene-2-styryl-2-imidazoline-5-thiones (6). A mixture of **5a**, **5b**, **5h**, **5i**, and **5j** (0.003 mol) and phosphorus pentasulfide (0.0035 mol) was refluxed in anhydrous pyridine (25 ml) for 7 h. The solvent was evaporated under reduced pressure and the residue was treated with dilute acetic acid.

The product was filtered and crystallized from ethanol as reddish-brown crystals, yield about 55%.

4-Arylmethylene-2-styryl-2-imidazolin-5-ones (**5**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N	R_f	λ_{max}/nm (ε_{max})
9a	105	$C_{17}H_{14}O_2N_2$	73.38 (73.16)	5.03 (4.86)	10.07 (10.02)	0.24	382 (14000)
9b	160	$C_{23}H_{17}O_4N_3$	69.17 (69.03)	4.26 (4.20)	10.52 (10.31)	0.82	—
9c	150	$C_{23}H_{16}O_3N_2$	75.00 (74.53)	4.34 (4.18)	7.60 (7.42)	0.93	—
9d	135	$C_{23}H_{18}O_4N_2S$	66.02 (65.79)	4.30 (4.02)	6.67 (6.42)	0.27	—
9e	130	$C_{18}H_{16}O_3N_2$	70.12 (69.93)	5.19 (5.03)	9.09 (9.06)	0.79	—
9f	136	$C_{19}H_{18}O_3N_2$	70.80 (70.63)	5.59 (5.32)	8.69 (8.43)	0.40	—
9g	145	$C_{25}H_{20}O_4N_2$	72.81 (72.60)	4.85 (4.65)	6.79 (6.69)	0.87	402 (15000)
9h	205	$C_{23}H_{18}O_5N_2S$	63.59 (63.38)	4.14 (4.02)	6.45 (6.13)	0.30	—
9i	150	$C_{24}H_{20}O_5N_2S$	64.28 (64.13)	4.46 (4.24)	6.25 (6.03)	0.25	—
9j	155	$C_{19}H_{16}O_4N_2$	67.85 (67.53)	4.76 (4.38)	8.33 (8.31)	0.96[a]	
9k	175	$C_{18}H_{16}O_3N_2$	70.12 (70.00)	5.19 (5.03)	9.09 (9.11)	0.83	—
9l	135	$C_{19}H_{18}O_3N_2$	70.80 (70.48)	5.59 (5.23)	8.69 (8.36)	0.50	406 (18000)
9m	145	$C_{24}H_{20}O_3N_2$	75.00 (74.81)	5.20 (5.04)	7.29 (7.08)	0.91	
9n	195	$C_{19}H_{16}O_4N_2$	67.85 (67.63)	4.76 (4.43)	8.33 (8.13)	0.63	—
9o	130	$C_{24}H_{20}O_5N_2S$	64.28 (64.20)	4.46 (4.12)	6.25 (6.13)	0.17	—

a) Using a benzene ethyl acetate mixture in the ratio 9 : 1 respectively.

4-Arylmethylene-2-styryl-2-imidazoline-5-thiones (**6**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N	S	λ_{max}/nm (ε_{max})
6a	280	$C_{24}H_{18}N_2S$	78.68 (78.40)	4.91 (4.52)	7.65 (7.43)	8.74 (8.81)	442 (24000)
6e	260	$C_{26}H_{23}N_3S$	76.28 (76.07)	5.62 (5.31)	10.26 (10.13)	7.82 (7.46)	—
6h	240	$C_{25}H_{20}N_2OS$	75.75 (75.26)	5.05 (5.06)	7.07 (7.00)	8.08 (8.31)	463 (1500)
6i	210	$C_{25}H_{20}N_2O_2S$	72.81 (72.60)	4.85 (4.62)	6.79 (6.63)	7.76 (7.34)	—
6j	260—62	$C_{26}H_{22}N_2OS$	76.09 (76.30)	5.36 (5.12)	6.82 (6.75)	7.80 (7.63)	—

4-Arylmethylene-2-phenyl-1-hydroxy-2-imidazolin-5-ones (**8**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N	R_f	λ_{max}/nm (ε_{max})
8a	235	$C_{16}H_{12}O_2N_2$	72.72 (72.38)	4.54 (4.32)	10.60 (10.38)	0.60	382 (12000)
8b	245	$C_{17}H_{14}O_3N_2$	69.38 (69.08)	4.76 (4.36)	9.52 (9.46)	0.70	406 (17800)
8c	220	$C_{17}H_{14}O_3N_2$	69.38 (69.32)	4.76 (4.39)	9.52 (9.32)	0.90	406 (18000)

*4-Arylmethylene-2-phenyl-1-hydroxy-2-imidazolin-5-ones (**8**).* A mixture of **7** (0.03 mol) and hydroxylamine hydrochloride (0.04 mol) in methanol (30 ml) containing sodium acetate (0.04 mol) was refluxed on a water bath for 6 h. The reaction mixture was cooled and the yellow precipitate was collected, washed with water and recrystallized from ethanol, yield 60%.

*Reaction of **8** with Alkyl Halides and Acid Chlorides.* A mixture of **8** (0.001 mol) and appropriate alkyl halide or acid chloride (0.0012 mol) in acetone (30 ml) in the presence of anhydrous potassium carbonate (0.01 mol) was refluxed for 2 h. The solvent was filtered and evaporated. The crude product obtained was crystallized from ethanol to give **9** yield about 70%.

Ethers and esters of 4-arylmethylene-2-phenyl-1-hydroxy-2-imidazolin-5-ones (**9**)

Compd No.	Mp θ_m/°C	Formula	Calcd (Found) (%) C	H	N	R_f	λ_{max}/nm (ε_{max})
5a	238	$C_{24}H_{18}N_2O$	82.28 (82.06)	5.14 (5.02)	8.00 (7.81)	0.93	410 (13000)
5b	205	$C_{25}H_{20}N_2O$	82.41 (82.92)	5.49 (5.32)	7.69 (7.52)	0.90	—
5c	190	$C_{25}H_{20}N_2O_2$	78.94 (78.61)	5.26 (5.00)	7.36 (7.12)	0.74	410 (13300)
5d	275	$C_{24}H_{18}N_2O_2$	78.68 (78.51)	4.91 (4.62)	7.65 (7.41)	0.27	—
5e	130	$C_{26}H_{23}N_3O$	79.38 (79.21)	5.85 (5.64)	10.68 (10.43)	0.92	—
5f	129	$C_{25}H_{20}N_2O_2$	78.94 (78.71)	5.26 (5.13)	7.36 (7.14)	0.80	—
5g	190	$C_{25}H_{20}N_2O_2$	78.94 (78.70)	5.26 (5.03)	7.36 (7.12)	0.87	—
5h	185	$C_{25}H_{20}N_2O_2$	78.94 (78.71)	5.26 (5.04)	7.36 (7.17)	0.86	432 (21000)
5i	240	$C_{25}H_{20}N_2O_3$	75.75 (75.41)	5.05 (5.00)	7.07 (7.01)	0.46	—
5j	136	$C_{26}H_{22}N_2O_3$	76.09 (76.01)	5.36 (5.24)	6.82 (6.61)	0.17	—
5k	215	$C_{25}H_{20}N_3O_4$	70.42 (70.31)	4.69 (4.31)	9.85 (9.51)	0.66	—
5l	180	$C_{26}H_{22}N_2O_3$	76.09 (76.01)	5.36 (5.07)	6.82 (6.59)	0.18	432 (14000)
5m	250	$C_{25}H_{20}N_2O_3$	75.75 (75.64)	5.05 (5.31)	7.07 (7.03)	0.67	—
5n	175	$C_{26}H_{22}N_2O_3$	76.09 (76.01)	5.36 (5.23)	6.82 (6.68)	0.79	432 (24000)

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