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Synthesis of novel N-aryl-3-dialkylamino-4-substituted maleimides

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The syntheses of several novel 3-dialkylamino-*N*-aryl-maleimides **3a-i** and **6** are described *via* a conjugate elimination-addition-elimination pathway. Syntheses of their various 4-substituted derivatives **4a-i, 5a-c** and **7-12** are also described. Introduction of a secondary amino group at C-3 position in *N*-arylmaleimides leads to the formation of enaminones **3a-i** and **6**, which undergo facile electrophilic substitutions at C-4 position in good to excellent yields to provide the highly functionalized maleimides **4a-i, 5a-c** and **7-12**.

Keywords: Maleimide, bromination, acylation, Vilsmeier-Haack reaction, enaminone

A number of natural products such as polycitrine[1], himanimide[2], antrodia camphoratimide[3], rebeccamycine and staurosporine[4] which contain maleimide as a part in their framework have been recently reported. All these molecules exhibit interesting biological properties (among others, angiogenesis inhibition[4], protein kinase inhibition[5], antiproliferative[6], antimicrobial[7] and antifungal activity[8]). Several other synthesized[9-11] compounds which are 3-and/or 4-substituted maleimides also exibit useful biological properties[12-18]. Maleimides also find applications in material science[19,20]. Therefore, development of versatile methods to functionalize the 3,4-positions in maleimide attract increasing attention in current synthesis. To date, functionalization of maleimides at the 3,4-positions has been reported mainly by arylation or heteroarylation by the Heck reaction and Suzuki reaction[21,22], cross-coupling reaction using indium organometallics[23] and alkynation by Sonogashira coupling reaction[24].

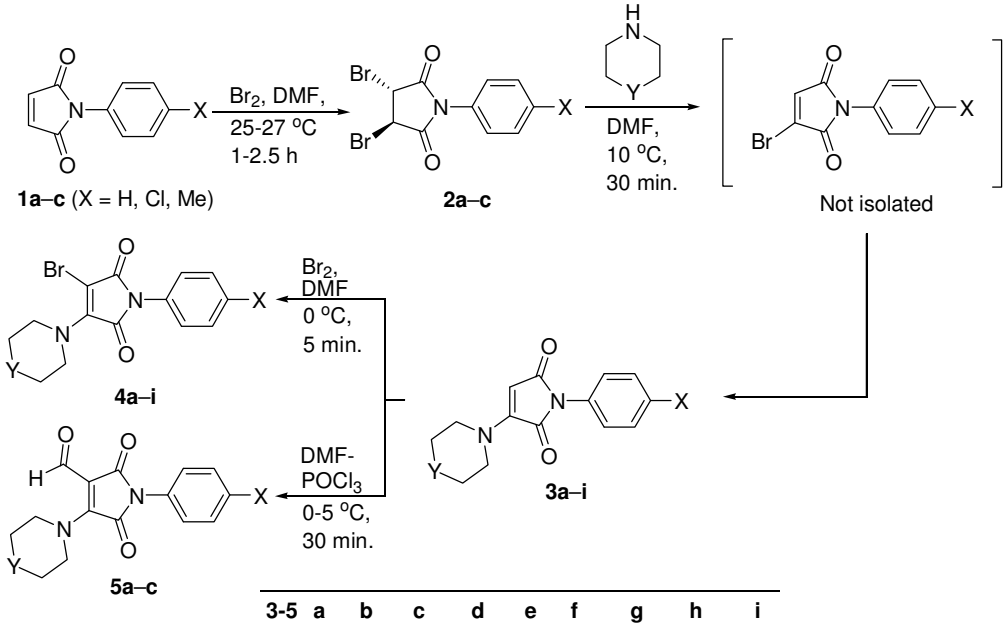
Herein is reported a versatile, simple and efficient method developed to introduce a variety of functional groups on 3-and/or 4-positions of maleimides through common enaminone intermediates.

Results and Discussion

The general approach for the synthesis of the 3-dialkylamino-*N*-arylmaleimides **3a-i** and **6** and their further functionalization leading to 3-dialkylamino-4-substituted-*N*-arylmaleimides **4a-i, 5a-c** and **7-12** is outlined in **Scheme I** and **Scheme II**. The *N*-arylmaleimides **1a-c** were obtained by reacting maleic anhydride and the corresponding aromatic amine in acetic acid in the presence of sulphuric acid, using our recently reported procedure[25]. **1a-c** were reacted with bromine in DMF at RT (25-27°C) to give the dibromo-succinimides **2a-c** in quantitative yield. ^{1}H NMR spectra and physical constants (**Tables I** and **II**) were found to be in agreement with the literature reports[26-28].

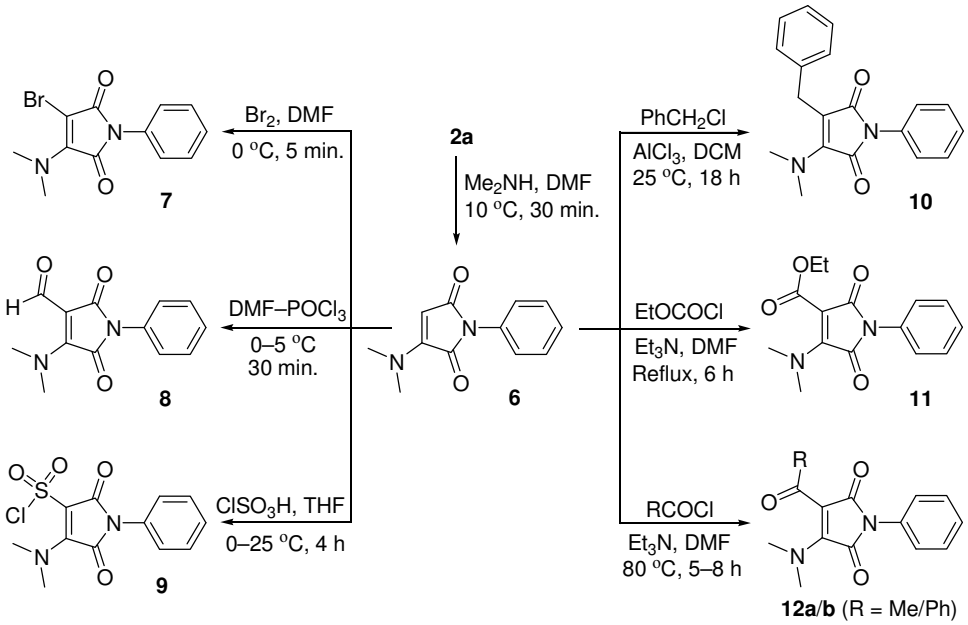
The synthesis of N-aryl-3-bromomaleimide was attempted by reacting **2a-c** with one to two moles of piperidine as the base to bring about dehydro-halogenation to obtain the monobromo compound; instead, complex mixtures with unreacted dibromo-succinimide were obtained (TLC). However, a clean reaction was observed when three moles of piperidine were used and the sole product was characterized by all spectroscopic means to be 3-piperidylmaleimide **3a (Scheme I)**. The reaction followed a base-induced elimination-conjugate addition-elimination path to provide the corresponding enaminone. This observation was generalized by reacting **2a-c** with three equivalents of morpholine, pyrrolidine or *N*,*N*-dimethylamine to give the corresponding 3-aminated *N*-arylmaleimides **3b-i** and **6 (Scheme I** and **Scheme II)** in high yields. ^{1}H NMR of **3a-i** and **6** showed a singlet at δ 4.84-5.09 attributed to the olefinic proton in addition to signals due to the secondary amino residue **(Table III)**.

Installation of an amino functionality at C–3 position in **3a-i** should increase nucleophilicity at the C–4 position. As expected, bromine reacted instantaneously with **3a-i** in DMF at 0°C to provide **4a-i** in almost quantitative yields. In the literature,



3-5	a	b	c	d	e	f	g	h	i
X	H	H	H	Cl	Cl	Cl	CH_3	CH_3	CH_3
Y	CH_2	O	None	CH_2	O	None	CH_2	O	None

Scheme I



Scheme II

there are only two reports[29,30] of 4-chloro analogues of **4a-c** made from the expensive dichloromaleic anhydride. The structures of products **4a-i** were confirmed by the absence of ^{1}H NMR signal at δ 4.84 to 5.09. Vilsmeier formylation of **3a-i** at low temperature (0 to 5°C) afforded **5a-c** in high yields. The IR of **5a-c** showed the characteristic conjugated aldehyde carbonyl stretching frequency at 1701-1706 cm^{-1} and (O=C-*H*) at 2777-2786 cm^{-1}. The reactions of the enaminone **6** with chlorosulphonic acid, benzyl chloride, ethyl chloroformate, acetyl chloride and benzoyl chloride were also examined and the functionally rich products **9, 10, 11, 12a** and **12b** were respectively obtained in good to excellent yields, opening up a broad vista for further elaboration. All the products obtained were fully characterized by ^{1}H NMR, ^{13}C NMR, elemental

analysis and mass spectrometry. The dimethylamino group in such enaminones (*e.g.* **6**) is known to be displaced[31,32] by other nucleophiles offering further promising pathways in synthesis.

Experimental Section

Melting points were determined on a gallenkamp melting point apparatus. The ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian XL-300 spectrometer. Chemical shifts were reported in ppm relative to tetramethylsilane (TMS) and multiplicities are given as *s* (singlet), *bs* (broad singlet), *d* (doublet), *t* (triplet), *q* (quartet), or *m* (multiplet). Infrared spectra were recorded as KBr pellets on a Shimadzu FTIR-408 spectrophotometer. Mass spectra were recorded on a Shimadzu GC-MS QP 2010A mass spectrometer with an ionization potential of 70 eV. Elemental analyses were performed on a Thermo Quest Flash 1112 Series EA analyzer. Reactions were monitored by thin layer chromatography carried out on 0.2 mm silica gel 60 F_{254} (Merck) plates using UV light of 254 and 366 nm for detection. Compounds were purified by column chromatography using silica gel (Merck, 60-120 mesh) where column dimension is 39×2 cm^2 and elution volume used was about 200-400 mL for each product.

Table I — Physical constants for 3,4-dibromosuccinamides **2a-c**

Entry	X	Observed m.p. (°C)	Literature m.p. (°C)
2a	H	158-60	157-59 (Ref 26, 27)
2b	Cl	160-62	159-60 (Ref 28)
2c	CH_3	162-64	160-64 (Ref 28)

Table II — Physical constant and combustion analysis of synthesized new compounds

Compd	Molecular formula	m.p. (°C)	Elemental Analysis					
			Calcd %			Found %		
			C	H	N	C	H	N
3a	$C_{15}H_{16}N_2O_2$	122-24	70.29	6.29	10.93	70.45	6.21	10.72
3b	$C_{14}H_{14}N_2O_3$	118-20	65.11	5.46	10.85	65.25	5.23	10.74
3c	$C_{14}H_{14}N_2O_2$	128-30	69.41	5.82	11.56	69.59	5.71	11.52
3d	$C_{15}H_{15}ClN_2O_2$	102-04	61.97	5.20	9.64	61.72	5.29	9.53
3e	$C_{14}H_{13}ClN_2O_3$	136-38	57.44	4.48	9.57	57.33	4.40	9.36
3f	$C_{14}H_{13}ClN_2O_2$	160-62	60.77	4.74	10.12	60.62	4.84	10.25
3g	$C_{16}H_{18}N_2O_2$	112-14	71.09	6.71	10.36	71.22	6.86	10.21
3h	$C_{15}H_{16}N_2O_3$	200-02	66.16	5.92	10.29	66.29	5.76	10.15
3i	$C_{15}H_{16}N_2O_2$	150-52	70.29	6.29	10.93	70.12	6.41	10.75
6	$C_{12}H_{12}N_2O_2$	142-44	66.65	5.59	12.96	66.42	5.67	12.85
4a	$C_{15}H_{15}BrN_2O_2$	96-98	53.75	4.51	8.36	53.61	4.73	8.55
4b	$C_{14}H_{13}BrN_2O_3$	94-96	49.87	3.89	8.31	49.65	3.97	8.51
4c	$C_{14}H_{13}BrN_2O_2$	108-10	52.36	4.08	8.72	52.53	4.17	8.85
4d	$C_{15}H_{14}BrClN_2O_2$	114-16	48.74	3.82	7.58	48.46	3.88	7.67
4e	$C_{14}H_{12}BrClN_2O_3$	118-20	45.25	3.25	7.54	45.54	3.36	7.49
4f	$C_{14}H_{12}BrClN_2O_2$	122-24	47.28	3.40	7.88	47.57	3.38	7.66
4g	$C_{16}H_{17}BrN_2O_2$	118-20	55.03	4.91	8.02	55.27	4.88	8.22
4h	$C_{15}H_{15}BrN_2O_3$	136-38	51.30	4.31	7.98	51.21	4.47	7.82
4i	$C_{15}H_{15}BrN_2O_2$	112-14	53.75	4.51	8.36	53.55	4.36	8.22
7	$C_{12}H_{11}BrN_2O_2$	108-10	48.84	3.76	9.49	48.71	3.62	9.59
5a	$C_{16}H_{16}N_2O_3$	162-64	67.59	5.67	9.85	67.44	5.89	9.66
5b	$C_{15}H_{14}N_2O_4$	166-68	62.93	4.93	9.79	62.60	4.64	9.52
5c	$C_{15}H_{14}N_2O_3$	148-50	66.66	5.22	10.36	66.46	5.44	10.62
8	$C_{13}H_{12}N_2O_3$	166-68	63.93	4.95	11.47	63.77	4.85	11.52
9	$C_{12}H_{11}ClN_2O_4S$	98-100	45.79	3.52	8.90	45.64	3.85	8.77
10	$C_{19}H_{18}N_2O_2$	122-24	74.49	5.92	9.14	74.34	5.78	9.01
11	$C_{15}H_{16}N_2O_4$	96-98	62.49	5.59	9.72	62.55	5.41	9.58
12a	$C_{14}H_{14}N_2O_3$	106-08	65.11	5.46	10.85	65.33	5.41	10.48
12b	$C_{19}H_{16}N_2O_3$	112-14	71.24	5.03	8.74	71.01	5.25	8.83

Table III — IR, ^{1}H NMR, ^{13}C NMR and mass spectral data of synthesized new compounds

Compd	IR (cm^{-1})	^{1}H NMR / ^{13}C NMR ($CDCl_3$, δ, ppm)	MS (*m/z*)
3a	1749, 1701, 1612	^{1}H NMR: 1.63 (s, 6H, 2×CH_3), 3.72 (bs, 4H, 2×CH_2), 5.10 (s, 1H), 7.25-7.50 (m, 5H, Ar-H). ^{13}C NMR: 23.6 (2C's), 25.4, 48.2 (2C's), 87.9, 127.2 (2C's), 128.6 (2C's), 130.4, 132.3, 149.6, 165.4, 169.0.	256 [M^+]
3b	1751, 1703, 1620	^{1}H NMR: 3.70 (bs, 8H, 4×CH_2), 5.03 (s, 1H), 7.19-7.39 (m, 5H, Ar-H) ^{13}C NMR: 47.1 (2C's), 66.0 (2C's), 89.8, 127.2 (2C's), 128.8 (2C's), 130.1, 132.8, 149.5, 165.4, 168.8.	258 [M^+]
3c	1741, 1703, 1616 cm^{-1}.	^{1}H NMR: 2.05 (s, 4H, 2×CH_2), 3.38 (s, 2H, CH_2), 3.98 (s, 2H, CH_2), 4.92 (s, 1H), 7.31-7.49 (m, 5H, Ar-H). ^{13}C NMR: 23.6, 25.9, 48.7, 50.1, 85.6, 126.8 (2C's), 128.4 (2C's), 130.6, 132.0, 147.8, 164.8, 169.4.	242 [M^+]
3d	1740, 1693, 1620	^{1}H NMR: 1.64 (s, 6H, 3×CH_2), 3.55 (bs, 4H, 2×CH_2), 4.99 (s, 1H), 7.25-7.50 (m, 4H, Ar-H).	290 [M^+] 292 [M+2]
3e	1757, 1701, 1612	^{1}H NMR: 3.80 (s, 8H, 4×CH_2), 5.09 (s, 1H), 7.27-7.50 (m, 4H, Ar-H).	292 [M^+] 294 [M+2]
3f	1751, 1706, 1625	^{1}H NMR: 1.97 (s, 4H, 2×CH_2), 3.29 (s, 2H, CH_2), 3.89 (s, 2H, CH_2), 4.84 (s, 1H), 7.31-7.35 (m, 4H, Ar-H).	276 [M^+] 278 [M+2]
3g	1741, 1693, 1608	^{1}H NMR : 1.65 (s, 6H, 3×CH_2), 2.39 (s, 3H, CH_3), 3.72 (bs, 4H, 2×CH_2), 5.00 (s, 1H), 7.10-7.30 (m, 4H, Ar-H).	270 [M^+]
3h	1749, 1699, 1612	^{1}H NMR: 2.29 (s, 3H, CH_3), 3.79 (bs, 8H, 4×CH_2), 5.09 (s, 1H), 7.10–7.30 (m, 4H, Ar-H).	272 [M^+]
3i	1741, 1703, 1616	^{1}H NMR: 2.00 (s, 4H, 2×CH_2), 2.39 (s, 3H, CH_3), 3.35 (s, 2H, CH_2), 3.95 (s, 2H, CH_2), 4.85 (s, 1H), 7.18-7.30 (m, 4H, Ar-H).	256 [M^+]
6	1753, 1691, 1624	^{1}H NMR: 3.22 (bs, 6H, 2 × CH_3, NMe_2), 4.95 (s, 1H, CH), 7.33-7.43 (m, 5H, Ar-H). ^{13}C NMR: 41.0 (2C's), 87.4, 126.2 (2C's), 127.1, 128.2 (2C's), 131.8, 150.3, 165.5, 169.4.	216 [M^+]
4a	1760, 1701, 1608	^{1}H NMR: 1.89 (s, 6H, 3×CH_2), 4.00 (s, 4H, 2×CH_2), 7.34-7.49 (m, 5H, Ar-H). ^{13}C NMR: 23.7, 26.5 (2C's), 49.7 (2C's), 80.8, 127.0 (2C's), 128.7 (2C's), 130.0, 132.7, 144.1, 164.3, 165.0.	334 [M^+] 336 [M+2]
4b	1763, 1708, 1622	^{1}H NMR: 3.83 (t, 4H, *J* = 6 Hz, 2×CH_2), 4.05 (t, 4H, *J* = 6 Hz, 2×CH_2), 7.26-7.39 (m, 5H, Ar-H). ^{13}C NMR: 48.6 (2C's), 66.9 (2C's), 83.3, 127.2 (2C's), 129.1 (2C's), 129.8, 133.4, 143.6, 164.6, 164.9.	336 [M^+] 338 [M+2]
4c	1759, 1707, 1612	^{1}H NMR: 1.96 (s, 4H, 2×CH_2), 4.02 (s, 4H, 2×CH_2), 7.26-7.45 (m, 5H, Ar-H). ^{13}C NMR: 25.1 (2C's), 50.9(2C's), 84.2, 127.1 (2C's), 128.9 (2C's), 130.3, 133.0, 142.8, 164.0, 165.8.	320 [M^+] 322 [M+2]
4d	1757, 1703, 1606	^{1}H NMR: 1.66 (s, 6H, 3×CH_2), 3.87 (s, 4H, 2×CH_2), 7.20-7.40 (m, 4H, Ar-H).	368 [M^+] 370 [M+2] 372 [M+4]
4e	1762, 1710, 1622	^{1}H NMR: 3.87 (s, 4H, 2×CH_2), 4.04 (s, 4H, 2×CH_2), 7.20–7.50 (m, 4H, Ar-H).	370 [M^+] 372 [M+2] 374 [M+4]
4f	1753, 1712, 1620	^{1}H NMR:1.95 (s, 4H, 2×CH_2), 4.00 (s, 4H, 2×CH_2), 7.19-7.55 (m, 4H, Ar-H).	354 [M^+] 356 [M+2] 358 [M+4]
4g	1759, 1704, 1608	^{1}H NMR: 1.74 (s, 6H, 3×CH_2), 2.37 (s, 3H, CH_3), 3.95 (s, 4H, 2×CH_2), 7.20-7.27 (m, 4H, Ar-H).	348 [M^+] 350 [M+2]
4h	1764, 1707, 1622	^{1}H NMR: 2.37 (s, 3H, CH_3), 3.82 (t, 4H, *J* = 6 Hz, 2×CH_2), 4.03 (t, 4H, *J* = 6 Hz, 2×CH_2), 7.16-7.27 (m, 4H, Ar-H).	350 [M^+] 352 [M+2]

Contd —

Table III — IR, ^{1}H NMR, ^{13}C NMR and mass spectral data of synthesized new compounds — *Contd*

Compd	IR (cm^{-1})	^{1}H NMR / ^{13}C NMR ($CDCl_3$, δ, ppm)	MS (*m/z*)
4i	1755, 1710, 1622	^{1}H NMR: 1.95 (s, 4H, 2×CH_2), 2.39 (s, 3H, CH_3), 4.25 (s, 4H, 2×CH_2), 7.17-7.30 (m, 4H, Ar-H).	334 [M^+] 336 [M+2]
7	1753, 1699, 1614	^{1}H NMR: 3.45 (s, 6H, 2×CH_3), 7.26-7.45 (m, 5H, Ar-H).	294 [M^+] 296 [M+2]
5a	2858, 2777, 1758, 1701, 1668	^{1}H NMR: 1.81 (s, 6H, 3×CH_2), 4.12 (s, 2H, CH_2), 4.40 (s, 2H, CH_2), 7.26-7.46 (m, 5H, Ar-H), 9.78 (s, 1H, CHO). ^{13}C NMR: 23.7, 27.3, 27.6, 51.0, 57.7, 97.8, 127.6 (2C's), 129.2 (2C's), 129.6, 133.8, 148.0, 163.5, 169.4, 182.1.	284 [M^+]
5b	2871, 2786, 1760, 1706, 1676	^{1}H NMR: 3.87 (s, 4H, 2×CH_2), 4.21 (s, 2H, CH_2), 4.47 (s, 2H, CH_2), 7.27-7.50 (m, 5H, Ar-H), 9.77 (s, 1H, CHO). ^{13}C NMR: 49.9, 55.8, 67.1, 67.4, 98.0, 126.3 (2C's), 128.1, 128.8 (2C's), 130.7, 147.5, 163.6, 169.2, 182.1	286 [M^+]
5c	2860, 2780, 1764, 1704, 1660	^{1}H NMR: 2.06 (m, 4H, 2×CH_2), 4.18 (m, 4H, 2×CH_2), 7.30-7.54 (m, 5H, Ar-H), 9.83 (s, 1H, CHO). ^{13}C NMR: 21.0, 25.1, 50.8 (2C's), 99.9, 126.0 (2C's), 129.1, 129.4 (2C's), 137.4, 142.8, 164.4, 166.3, 183.0.	270 [M^+]
8	2866, 2767, 1757, 1708, 1656	^{1}H NMR: 3.62 (s, 6H, 2 × CH_3), 7.32-7.45 (m, 5H, Ar-H), 9.78 (s, 1H, CHO). ^{13}C NMR: 42.5, 48.3, 98.0, 126.3 (2C's), 127.9, 128.8 (2C's), 130.9, 149.4, 163.3, 169.4, 182.1.	244 [M^+]
9	1760, 1701, 1629, 1373, 1174	^{1}H NMR : 3.68 (s, 6H, 2×CH_3), 7.58-7.68 (m, 5H, Ar-H)	314 [M^+]
10	1753, 1691, 1623	^{1}H NMR :δ 3.26 (s, 6H, 2×CH_3), 3.94 (s, 2H, CH_2), 7.20-7.47 (m, 10H, Ar-H). ^{13}C NMR: 28.5, 42.9 (2C's), 100.7, 126.0 (2C's), 127.1 (2C's), 127.8 (2C's), 128.4, 128.6, 128.8 (2C's), 132.1, 140.8, 145.3, 166.7, 171.5.	306 [M^+]
11	1751, 1730, 1693	^{1}H NMR: 1.45 (t, 3H, *J* = 9 Hz, CH_3), 3.65 (s, 6H, 2 × CH_3), 4.43 (t, 2H, *J* = 9 Hz, O-CH_2), 7.22-7.43 (m, 5H, Ar-H). ^{13}C NMR: 16.1, 42.2, 48.4, 60.8, 98.1, 122.0, 128.1 (2C's), 130.2, 133.1 (2C's), 149.8, 162.2, 163.4, 169.3.	288 [M^+]
12a	1755, 1708, 1693	^{1}H NMR:2.59 (s, 3H, CH_3), 3.21 (bs, 3H, CH_3), 3.65 (bs, 3H, CH_3), 7.29-7.50 (m, 5H, Ar-H). ^{13}C NMR: 30.8, 42.3, 47.3, 100.8, 126.6 (2C's), 127.9, 128.9 (2C's), 131.2, 151.7, 163.9, 168.1, 192.6.	258 [M^+]
12b	1753, 1712, 1685	^{1}H NMR: 3.10 (s, 6H, 2×CH_3), 7.22-7.38 (m, 5H, Ar-H); 7.42-7.63 (m, 5H, Ar-H).	320 [M^+]

General procedure for the synthesis of 2a-c: To a solution of *N*-arylmaleimide **1a-c** (1 mmol) in DMF (3 mL) was added dropwise a solution of bromine (1 mmol) in DMF (2 mL) at 25°C and stirred further for 1 to 2.5 hr (TLC, hexane:ethyl acetate, 2:1). The reaction mixture was poured onto crushed ice. The precipitated white solid was filtered, washed with cold water, dried and purified by recrystallization using ethanol. Yield 95-96%.

General procedure for the synthesis of 3a-i and 6: To a solution of *trans*-3,4-dibromo-N-arylsuccinimide **2a-c** (1 mmol) in DMF (5 mL), secondary amine (3 mmol) was added dropwise at 10°C and stirred for 10 min. The reaction mixture was poured over crushed ice. The precipitated golden yellow solid was filtered, washed with cold water, dried and was purified by silica gel column chromatography (hexane:ethyl acetate, 6:4). Yield 94-97%.

General procedure for the synthesis of 4a-i and 7: To a solution of 3-dialkylamino-N-arylmaleimide **3a-i** or **6** (1 mmol) in DMF (3 mL) was added dropwise a solution of bromine (1 mmol) in DMF (2 mL) at 0°C. After addition of bromine, the reaction mixture was poured over crushed ice. The precipitated yellow solid was filtered, washed with cold water, dried and purified by silica gel column chromatography (hexane:ethyl acetate, 6:4). Yield 93-96%.

General procedure for the synthesis of 5a-c and 8: To a Vilsmeier-Haack adduct prepared from DMF (3 mL) and $POCl_3$ (1.2 mmol) at 0°C was added **5a-c** or **6**

(1 mmol) and stirred at 0-5°C for 30 min. The reaction mixture was poured into cold water. The yellow solid was separated on neutralization with 10% aqueous $NaHCO_3$ solution, was filtered, washed with cold water, dried and purified by column chromatography (hexane:ethyl acetate, 6:4). Yield 81-86%.

3-Chlorosulfonyl-4-dimethylaminomaleimide, 9: To a solution of N-phenyl-3-dimethylaminomaleimide (**6**, 0.5 g, 2.3 mmol) in dry THF (5 mL) was added chlorosulphonic acid (0.80 g, 6.9 mmol) at 0°C and then reaction mixture was stirred to 25-27°C for 4 hr (TLC checked), triethylamine was then added slowly at 0°C to neutralize excess chlorosulphonic acid. The solvent was removed under reduced pressure and the solid residue was extracted in dichloromethane, solvent stripped off and the yellow solid purified by column chromatography (hexane:ethyl acetate, 8:2). Yield 72%.

N-Phenyl-3-benzyl-4-dimethylaminomaleimide, 10: To a solution of N-phenyl-3-dimethylaminomaleimide (**6**, 0.5 g, 2.3 mmol) in DCM (10 mL), anhydrous $AlCl_3$ (0.31 g, 2.3 mmol) followed by benzyl chloride (0.29 g, 2.3 mmol) was added and the reaction mixture was stirred for 18 hr. The solvent was removed under reduced pressure and the residue was extracted with ethyl acetate and washed with water, saturated $NaHCO_3$ solution and brine and dried over $MgSO_4$. The solid obtained on evaporation of solvent was purified by silica gel column chromatography by using hexane:ethyl acetate (6:4). Yield 69%.

General procedure for the synthesis of 11, 12a and 12b: To a solution of N-phenyl-3-dimethyl-aminomaleimide (**6**, 1.0 mmol) in DMF (5 mL), ethyl chloroformate/acetyl chloride or benzoyl chloride (1.0 mmol) was added and to this mixture triethylamine (3.0 mmol) was added slowly at 25-27°C. The resulting reaction mixture was then refluxed for 5-8 hr and poured over crushed ice. The yellow solid separated was filtered, dried and purified by silica gel column chromatography (hexane:ethyl acetate, 6:4). Yield 56-60%.

Conclusion

An elegant method to synthesize enaminones from N-aryl maleimides has been demonstrated. Enaminones such as **3a-i** and **6** have revealed their potential to introduce many more electrophiles to get a variety of functional groups placed on the 4-position. Further studies on these derivatives are under active progress in our laboratory.

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