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Studies on the Synthesis of Conjugated Five-Membered bis-Heterocyclic Dimethine Cyanine Dyes

A. I. M. Koraiem, R. M. Abu El-Hamd* & R. M. Abd El-All

Chemistry Department, Aswan-Faculty of Science, Aswan, Egypt

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ABSTRACT

The synthesis of some asymmetric and symmetric cationic dimethine cyanine dyes incorporating 1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo-[4,3-d]-isoxazole moieties is described. The dimethine cyanines were characterised by elemental analysis, IR and H^1 NMR spectra and their electronic spectra.

1 INTRODUCTION

Dimethine cyanine dyes have found various applications as photographic sensitisers for colour and non-colour films[1] and as textile dyes.[2] They have biological effects as growth inhibitors to bacteria,[3] and on the mitosis of fertilised sea urchin eggs.[4] They also effect the hormones controlling plant growth.[5]

As a continuation of our previous work,[6] new cationic asymmetric and symmetric dimethine cyanine dyes were prepared to study their spectral behaviour in respect of photosensitisation effects.

2 RESULTS AND DISCUSSION

Our approach to the synthesis of asymmetric and symmetric dimethine cyanine dyes started with 3,4-dimethyl-1,6-dihydropyrazolo[3,4-c]pyrazole

* To whom correspondence should be addressed.

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and 6H-pyrazolo[4,3-d]isoxazole derivatives (**1a** and **1b**).[7] Thus, selective oxidation of 3,4-dimethyl-1,6-dihydropyrazolo[3,4-c] pyrazole and 6H-pyrazolo[4,3-d]isoxazole derivatives (**1a, 1b**) with equi- or bimolecular ratios of SeO_2[8] in dioxane afforded the corresponding pyrazolo[3,4-c]-pyrazole and pyrazolo[4,3-d]isoxazole-3-carboxaldehyde (**2a, 2b**) or their 3,4-dicarboxaldehyde derivatives (**3a, 3b**).

For oxidation processes using an equimolar amount of SeO_2, it was noted that, in compound **1b**, the oxidation occurred at the methyl group attached to the isoxazole ring, rather than that in the pyrazole ring, because of the relative acceptor nature of the pyrazole ring.

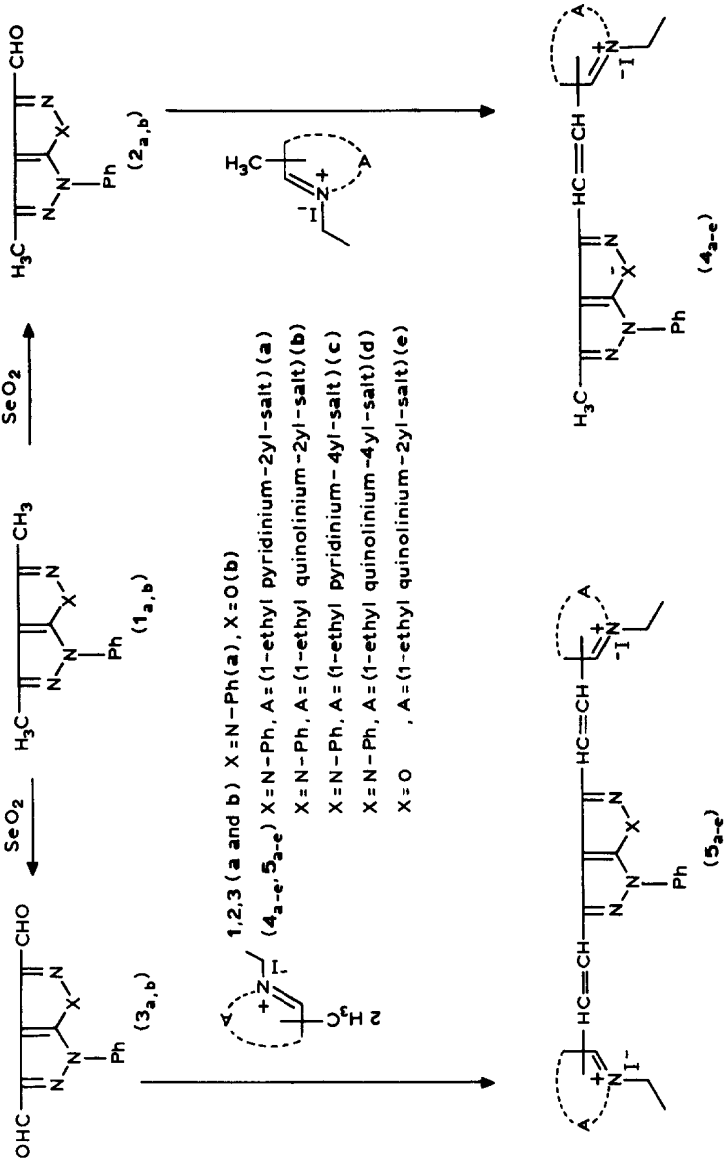
Reaction of compounds **2a** and **2b** with an equimolar amount of 2-(or 4-)-methyl quaternary salts yielded the corresponding asymmetrical 1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo[4,3-d]isoxazole-4[2(4)]-dimethine cyanines (**4a–4e**). Reaction of compounds **3a** and **3b** with dimolar amounts of 2-(or 4-)-methyl quaternary salts gave the symmetrical 1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo[4,3-d]isoxazole-bis-3,4[2(4)]dimethine cyanines (**5a–5e**), (Scheme 1).

The structures of the compounds synthesised were confirmed by elemental analysis (Table 1), IR and H^1 NMR spectral data (Table 2). The dimethine cyanines were coloured compounds ranging from orange to intense violet, and were fairly (partially) soluble in polar (non-polar) organic solvents, exhibiting a green fluorescence. They gave a reversible colour change (violet $\leftrightarrow$ colourless) in basic–acidic medium respectively.

The electronic spectra of the asymmetric and symmetric di- and bis-dimethine cyanines (**4a–4e, 5a–5e**) in 95% ethanol showed single broad bands, the position and molar extinction coefficient of which were influenced by the nature of the heterocyclic quaternary residue, A, the band becoming more intense and showing a strong red shift with increasing conjugation. Dyes derived from quinolinium-4-yl-salts were more bathochromic than those from quinolinium-2yl-salts (Table 1). The absorption bands were also influenced by the nature of the heterocyclic residue fused with the 1-phenyl pyrazole residue; dyes based on 1,6-dihydropyrazolo[3,4-c]pyrazole (**4b, 5b**) having red shifts compared to those based on 6H-pyrazolo[5,3-d]isoxazole (**4e, 5e**) (Table 1).

Comparison of the absorption spectra of the asymmetric 4[2(4)]-dimethine-1,6-dihydropyrazolo[3,4-c]pyrazoles and/or 6H-pyrazolo[4,3-d]-isoxazole cyanines (**4a–4e**) with the symmetric bis 3,4[2-(or 4-]dimethine cyanines (**5a–5e**) shows that the latter are more bathochromic; that is, symmetrical probably due to the extra conjugation in these dyes (Table 1).

Quaternisation of **2a, 2b, 3a, 3b** using excess ethyl iodide gave the corresponding 2,5-bis-ethyl iodide quaternary salts incorporating the bi-heterocyclic system (compounds **6a, 6b, 7a, 7b**). Reaction of these


2M
SeO2
1M
SeO2
1,2,3 (a and b) X = N–Ph (a), X = O (b)
(4a–e, 5a–e) X = N–Ph, A = (1-ethyl pyridinium-2yl-salt) (a)
X = N–Ph, A = (1-ethyl quinolinium-2yl-salt) (b)
X = N–Ph, A = (1-ethyl pyridinium-4yl-salt) (c)
X = N–Ph, A = (1-ethyl quinolinium-4yl-salt) (d)
X = O , A = (1-ethyl quinolinium-2yl-salt) (e)

Scheme 1

TABLE 1

Characterisation Data for 1,6-Dihydropyrazole[3,4-c]pyrazole and/or 6H-Pyrazolo[4,3-d]isoxazole-3- or bis-3,4-Carboxaldehydes (**2a**, **2b**, **3a**, **3b**) and the Asymmetric and Symmetric di-/bis-Dimethine Cyanine Dyes (**4a–4e**, **5a–5e**)

Compound number	*MP* (°C)	*Yield* (%)	*Molecular formula*	*Nature of product*	*Analysis* (%) *Calculated* (*Found*)			λ_{max} (*nm*)	ε_{max} ($M^{-1} cm^{-1}$)
					C	*H*	*N*	*in 95% ethanol*	
2a	145	45	$C_{18}H_{14}N_4O$	Brown crystals	71·5 (71·9)	4·6 (4·1)	18·5 (17·3)	—	—
2b	135	52	$C_{12}H_9N_3O_2$	Brown crystals	63·4 (63·1)	4·0 (4·2)	18·5 (18·4)	—	—
3a	132	56	$C_{18}H_{12}N_4O_2$	Intense brown crystals	68·4 (68·7)	3·8 (4·0)	17·7 (18·1)	—	—
3b	125	62	$C_{12}H_7N_3O_3$	Red crystals	59·8 (59·2)	2·9 (3·2)	17·4 (17·2)	—	—
4a	157	40	$C_{26}H_{24}N_5I$	Brownish-violet crystals	58·5 (58·1)	4·5 (5·0)	13·1 (12·8)	480	600

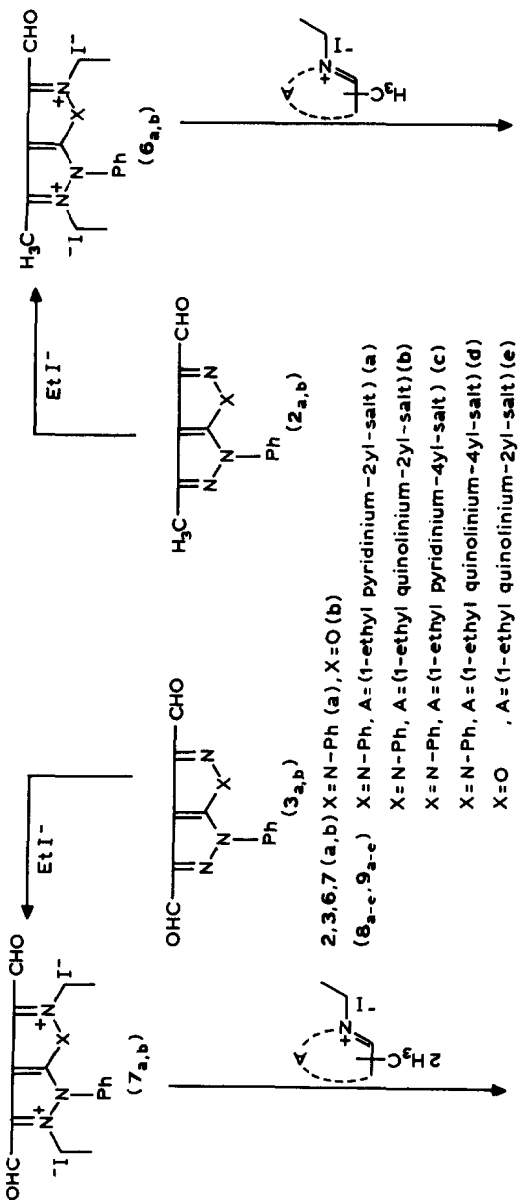
4b	138	65	$C_{30}H_{26}N_5I$	Shiny violet crystals	61·8 (61·1)	4·5 (5·1)	12·0 (12·3)	587, 685	15 196, 3 160
4c	195	42	$C_{26}H_{24}N_5I$	Brownish-violet crystals	58·5 (58·2)	4·5 (4·7)	13·1 (12·9)	485	5 780
4d	135	69	$C_{30}H_{26}N_5I$	Shiny blue crystals	61·8 (61·5)	4·5 (4·7)	12·0 (12·1)	595, 670, 707·5	2 900, 4 200, 4 000
4e	185	56	$C_{24}H_{21}N_4OI$	Violet crystals	56·7 (56·9)	4·1 (4·5)	11·0 (11·4)	505	9 800
5a	150	28	$C_{34}H_{32}N_6I_2$	Reddish-violet crystals	52·4 (52·1)	4·1 (4·7)	10·8 (10·3)	495	1 840
5b	114	75	$C_{42}H_{36}N_6I_2$	Shiny violet crystals	57·4 (57·6)	4·1 (3·5)	9·6 (9·5)	510, 500, 695	6 540, 4 710, 1 330
5c	120	39	$C_{34}H_{32}N_6I_2$	Brownish-violet crystals	52·4 (52·8)	4·1 (4·4)	10·8 (10·5)	500	928
5d	144	56	$C_{42}H_{36}N_6I_2$	Greenish-blue crystals	57·4 (57·7)	4·1 (4·1)	9·6 (9·9)	595, 678, 718	9 980, 15 280, 17 280
5e	188	60	$C_{36}H_{31}N_5OI_2$	Deep violet crystals	53·8 (54·1)	3·9 (4·4)	8·7 (9·2)	510, 540, 584	9 160, 8 756, 8 920

TABLE 2
IR and H^1 NMR Data of 3- and 3,4-Carboxaldehyde Molecules and Their Dimethine Cyanine Dyes

Compound number	*IR* (ν_{max}^{KBr} cm^{-1})	*H^1 NMR (DMSO) PPM*
2a	710–690 (*v*–mono–sub. benzene)	9·8 (s, 1H, CHO)
	2965 (*v*–CH_3 group)	8·0–7·3 (m, 10H, arom.)
	1660 (*v*–C=N)	2·1 (s, 3H, CH_3 group)
	1705 (*v*–CHO)	
3a	710–690 (*v*–mono–sub. benzene)	9·7 (s, 2H, 2-CHO group)
	1662 (*v*–C=N)	7·9–7·3 (m, 10H, arom.)
	1705 (*v*–CHO)	
4b	760–710 (*v*–mono + di–sub. benzene)	8·5–6·5 (m, 18H, arom. + hetero. + CH=CH system)
	1660 (*v*–C=N)	3·8 (t, 2H, CH_2I)
	2960–2920 (*v*–CH_3 + CH_2–) groups)	2·9 (q, 3H, CH_3I)
	2980 (*v*–ethiodide)	1·9 (s, 3H, CH_3– group)
	1310–1300 ·*v*–CH=CH)	
5b	760–710 (*v*–mono + di–sub. benzene)	8·1–6·5 (m, 26H, arom. + hetero. + 2 CH=CH systems)
	1660 (*v*–C=N)	4·1 (t, 4H, 2 CH_2I)
	2960–2920 (*v*–CH_2 + CH_2 groups)	3·2 (q, 6H, 2 CH_3I)
	2980 (*v*–ethiodide)	
	1310–1295 (*v*–CH=CH)	
9b	770–710 (*v*–mono + di–sub. benzene)	8·6–6·9 (m, 26H, arom. + hetero. + 2 CH=CH systems)
	2950–2920 (*v*–CH_3 + CH_2– groups)	4·1 (t, 4H, $2CH_2I$ joined to pyrazole nucleus)
	2990 (*v*–ethiodide)	3·9 (q, 6H, $2CH_3I$ joined to pyrazole nucleus)
	1310–1295 (*v*–CH=CH)	3·6 (t, 4H, $2CH_2I$ of quinoline nucleus)
	1660 (*v*–C=N)	2·8 (q, 6H, $2CH_3I$ of quinoline nucleus)

compounds with equi- or bi-molar ratios of 2-(or 4-)-methyl quaternary salts in presence of piperidine afforded the corresponding asymmetric and symmetric 1,6-dihydropyrazolo[3,4-c]pyrazolium and/or 6H-pyrazolo-[4,3-d]isoxazolium-4[2-(or 4-)]-di or bis-3,4[2-(or 4-)]-dimethine cyanines (**8a–8e, 9a–9e**) (Scheme 2).

These structures were established by elemental analysis (Table 3) and by


Et I⁻
Et I⁻
2,3,6,7 (a,b) X = N–Ph (a), X = O (b)
(8a–e, 9a–e) X = N–Ph, A = (1-ethyl pyridinium-2yl-salt) (a)
X = N–Ph, A = (1-ethyl quinolinium-2yl-salt) (b)
X = N–Ph, A = (1-ethyl pyridinium-4yl-salt) (c)
X = N–Ph, A = (1-ethyl quinolinium-4yl-salt) (d)
X = O , A = (1-ethyl quinolinium-2yl-salt) (e)

Scheme 2

TABLE 3

Characterisation Data for 1,6-Dihydropyrazolo[3,4-c]pyrazolium and/or 6H-Pyrazolo[4,3-d]isoxazolium 2,5-bis-yl Salt-3- or 3,4-bis-Carboxaldehydes (**6a**, **6b**, **7a**, **7b**) and Asymmetric and Symmetric di-/bis-Dicationic Methine Cyanine Dyes (**8a–8e**, **9a–9e**)

Compound number	*MP* (°C)	*Yield* (%)	*Molecular formula*	*Nature of product*	*Analysis* (%) *Calculated* (*Found*)			λ_{max} (*nm*)	ε_{max} ($M^{-1} cm^{-1}$)
					C	*H*	*N*	*in 95% ethanol*	
6a	145	42	$C_{22}H_{24}N_4O_2I_2$	Intense brown crystals	43·0 (43·3)	3·9 (3·4)	9·1 (9·0)	—	—
6b	119	51	$C_{16}H_{19}N_3O_2I_2$	Red crystals	35·6 (35·4)	3·5 (3·7)	7·8 (8·0)	—	—
7a	135	56	$C_{22}H_{22}N_4O_2I_2$	Brown crystals	42·0 (42·2)	3·5 (3·7)	8·9 (8·8)	—	—
7b	141	63	$C_{16}H_{17}N_3O_3I_2$	Red crystals	34·7 (34·9)	3·1 (3·1)	7·6 (7·8)	—	—
8a	130	22	$C_{30}H_{34}N_5I_3$	Brownish-red crystals	42·6 (42·9)	4·0 (4·3)	8·2 (8·6)	540sh	712

8b	118	51	$C_{34}H_{36}N_5I_3$	Violet crystals	45·6 (46·1)	4·0 (4·3)	7·8 (8·1)	547, 585, 690	6 980, 10 120,
8c	127	23	$C_{30}H_{34}N_5I_3$	Brownish-violet	42·6 (42·8)	4·0 (4·2)	8·3 (8·4)	390, 480, 510sh, 605	11 480, 8 880, 8 000, 4 396
8d	110	48	$C_{34}H_{36}N_5I_3$	Green crystals	45·6 (46·1)	4·0 (4·2)	7·8 (8·0)	460, 615, 710	2 400, 3 500, 8 770
8e	173	38	$C_{28}H_{31}N_4OI_3$	Violet crystals	41·0 (41·1)	3·8 (4·2)	6·8 (7·2)	509	12 880
9a	150	25	$C_{38}H_{42}N_6I_4$	Red crystals	41·8 (42·3)	3·9 (4·3)	7·7 (8·2)	550sh, 590	6 400, 9 120
9b	208	68	$C_{46}H_{46}N_6I_4$	Intense violet crystals	46·4 (47·0)	3·9 (3·4)	7·3 (7·5)	580, 700	38 600, 600
9c	160	35	$C_{38}H_{42}N_6I_4$	Brownish-violet crystals	41·8 (42·3)	3·9 (4·1)	7·7 (8·0)	410, 484·8	10 940, 10 000
9d	198	49	$C_{46}N_{46}N_6I_4$	Greenish-blue crystals	46·4 (46·9)	3·9 (4·2)	7·1 (7·5)	580, 600, 720	1 800, 2 740, 2 020
9e	180	53	$C_{40}H_{41}N_5OI_4$	Violet crystals	43·1 (43·2)	3·7 (4·9)	6·3 (6·2)	535, 584	9 720, 10 396

IR and H^1 NMR spectra (Table 2). The dyes were deeply coloured compounds (reddish-violet to intense violet), fairly (partially) soluble in polar (non-polar) organic solvents and exhibited a blue/green fluorescence. They gave a reversible colour change (violet ↔ yellow) in basic–acidic medium respectively.

As was observed with dyes **4a–4e** and **5a–5e**, the absorption maxima of **8a–e** and **9a–9e** in 95% ethanol showed bathochromic or hypsochromic shifts depending on the type of substituent attached to the 3- or the 3,4-positions of the 1,6-dihydropyrazolo[3,4-c]pyrazolium and/or 6H-pyrazolo-[4,3-d]isoxazolium nucleus, the nature of the cyanine molecule and the nature of the bi-heterocyclic residue (Table 3). Quaternisation results in a bathochromic shift of 2–60 nm in dyes **8a–e** and **9a–9e** and also increased absorbance relative to dyes **4a–4f** and **5a–5f** respectively.

3 EXPERIMENTAL

3.1 General

Melting points are uncorrected. The IR spectra were determined on a Unicam SP 1200 spectrophotometer (KBr). Absorption spectra were recorded on a Shimadzu UV–VIS 240 spectrophotometer and H^1 NMR spectra on an EM-390 90 NMR spectrometer.

3.2 Synthesis of 3,4-dimethyl-1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo[4,3-d]isoxazole derivatives (1a, 1b)[7]

To a solution of 4-acetyl-3-methyl-1-phenyl-2-pyrazolin-5-one (0·01 mol) in glacial acetic acid–hydrochloric acid mixture (25 ml) was added phenylhydrazine (0·01 mol) and the reaction mixture refluxed for 20 h. The oily product formed was triturated with light petrol (BP 80°C) and the solid product obtained was recrystallised from acetic acid to give 3,4-dimethyl-1,6-diphenyl-1H,6H-pyrazolo[3,4-c]pyrazole-(1) as yellow crystals, MP 234°C, yield 70%. (Found: C, 74·6; H, 5·4; N, 19·1. $C_{18}H_{16}N_4$ requires C, 75·0; H, 5·5; N, 19·4%).

3.3 Synthesis of 1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo-[4,3-d]isoxazole-3- or 3,4-carboxaldehyde (2a, 2b, 3a, 3b)

A mixture of **1a** or **1b** (0·01 mol) was refluxed with SeO_2 (0·01 M or 0·02 M) for 8–10 h in dioxane. The reaction mixture was filtered hot from selenium metal, the filtrate concentrated and the product, thus isolated, was washed with water and recrystallised from ethanol. The results are listed in Table 1.

3.4 Synthesis of asymmetric and symmetric 3- or bis-3,4-dimethine cyanine incorporating 1,6-dihydropyrazolo[3,4-c]pyrazole and/or 6H-pyrazolo[4,3-d]-isoxazole moieties (4a–4e, 5a–5e)

A mixture of **2a** and **2b** or **3a** and **3b** (0·01 mol) and the approximate 2-(or 4-)-methyl quaternary salt (α,γ-picoline, quinaldine or lepidine ethiodide) (0·1 or 0·02 mol) was dissolved in ethanol (40 ml) and piperidine (3–5 drops) were added. The reaction mixture was refluxed for 10–12 h, filtered hot, concentrated and cooled. The precipitated products, after dilution with water, were collected and recrystallised from ethanol to give the compounds **4a–4e** and **5a–5e**, data for which is given in Table 1.

3.5 Synthesis of 1,6-dihydropyrazolo[3,4-c]pyrazolium and/or 6H-pyrazolo-[4,3-d]isoxazolium-bis-2,5-yl salt-3- or 3,4-carboxaldehyde (6a, 6b, 7a, 7b) 7a, 7b)

Compounds **2a** and **2b** or **3a** and **3b** were suspended in excess ethyl iodide and heated in a sealed tube at 140°C for 3 h. The tube was cooled, opened and the products collected, washed with ether and recrystallised from ethyl alcohol. Results are given in Table 3.

3.6 Synthesis of asymmetric and symmetric 1,6-dihydropyrazolo[3,4-c]-pyrazolium and/or 6H-pyrazolo[4,3-d]isoxazolium-4[2-(or 4-)] and 3,4[2-(or 4-)]-dimethine cyanine moieties (8a–8e, 9a–9e)

To a mixture of **6a** and **6b** or **7a** and **7b** (0·01 mol) and the appropriate 2-(or 4-)-methyl quaternary salt (α or γ-picoline, quinaldine or lipidine ethodide) (0·01 or 0·02 mol) in ethanol, piperidine (3–6 drops) was added. The reaction mixture was refluxed for 15–17 h. Separation of the products was carried out in a similar manner to that described above. The results are listed in Table 3.

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