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Reaction of oxalyl chloride with 1-(1-arylimidazolin-2-yl)-3-arylureas. Identification of products and possible course of reaction.

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With biographical summary

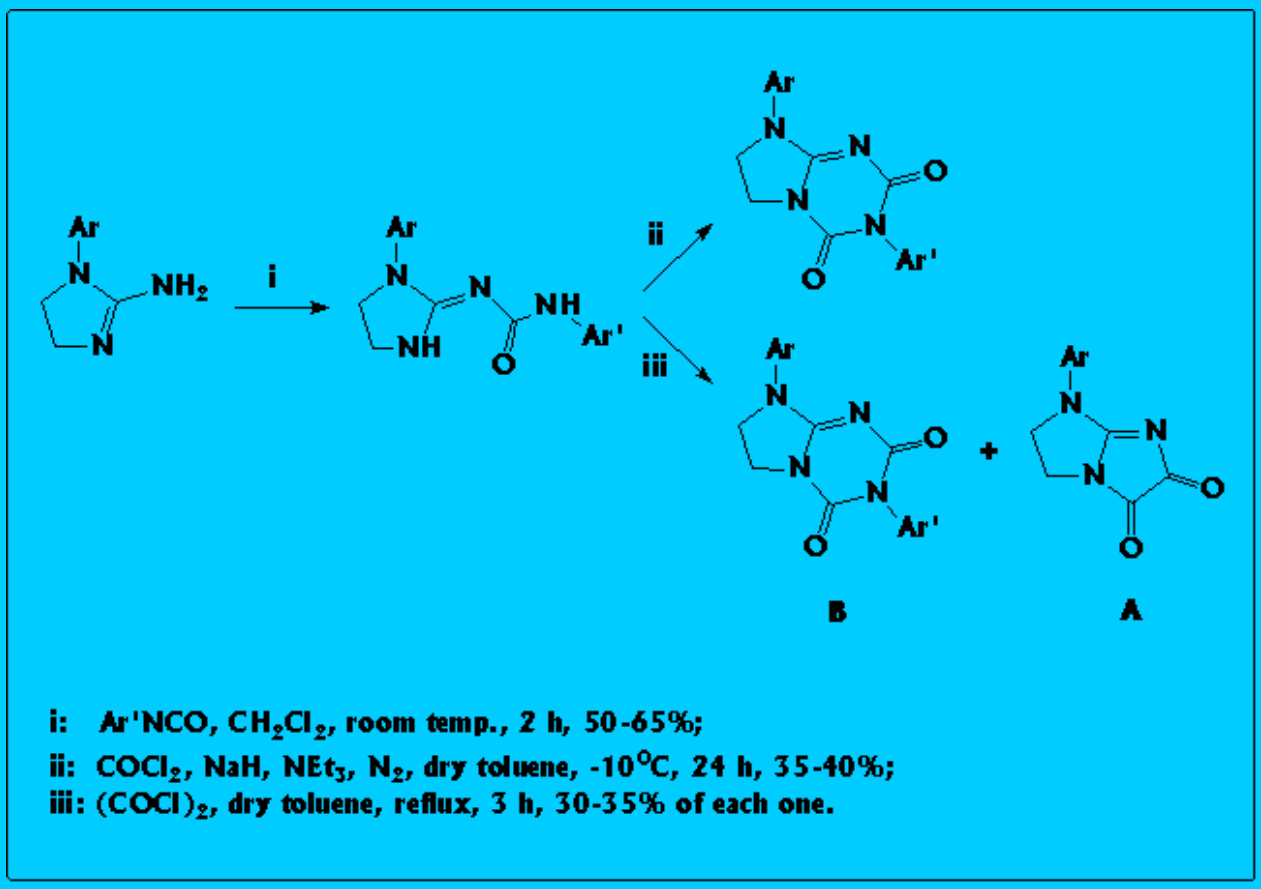
Abstract: It has been found that the condensation of 1-(1-arylimidazolin-2-yl)-3-arylurea derivatives with oxalyl chloride lead to formation of 1-aryl-5,6(1H)dioxo--2,3-dihydroimidazo[1,2-a]imidazole and 1,6-dihydro-5,7(1H)dioxo-2,3-dihydroimidazo[1,2-a][1,3,5]triazine systems. Probable course of reaction is discussed.

Keywords: 1-(imidazoli-2-yl)urea, oxalyl chloride, 5,6(1H)dioxo-2,3-dihydroimidazo[1,2-a]imidazole, 5,7(1H)dioxo-2,3-dihydroimidazo[1,2-a][1,3,5]triazine.

Introduction

Looking for new and more convenient method of synthesis of 1,6-diaryl-5,7(1H)dioxo-2,3-dihydroimidazo[1,2-a][1,3,5]triazine derivatives [1] I investigated the reaction of 1-(1-arylimidazolin-2-yl)-3-arylurea derivatives with oxalyl chloride. So far known methods of synthesis of this heterocyclic system contain methods starting from either imidazoline or triazine derivatives. The one utilized by me is new, although some derivatives of 2-alkyltioimidazoline [2], 2-aminoimidazoline [3] and 1-(imidazolin-2-yl)imidazole [4] were previously converted into the respective derivatives of imidazo[1,2-a][1,3,5]triazine by condensation with isothio- or iso-cyanates. The title compounds were synthesized in two step reaction (Scheme 1). The upper branch of the Scheme 1 presents alternative way of obtaining the imidazo[1,2-a][1,3,5]triazine system by condensation with phosgene in presence of alkaline moderators (e.g. sodium hydride) [1].

Scheme 1



i: Ar'NCO, CH_2Cl_2, room temp., 2 h, 50-65%;
ii: $COCl_2$, NaH, NEt_3, N_2, dry toluene, -10°C, 24 h, 35-40%;
iii: $(COCl)_2$, dry toluene, reflux, 3 h, 30-35% of each one.

Results and Discussion

- **Products Identification.**

Formation of two co-products of reaction was established from their ^{1}H NMR spectra and confirmed by ^{13}C NMR and MS spectra (Table 1.).

NMR spectra were made on 200 MHz or 500 MHz (Bruker) spectrometers in D_6-DMSO in presence of TMS as an internal standard.

In spectra of imidazo[1,2-a]imidazole derivatives only C-2,C-3 and one aromatic substituent (N-1) signals were present. In case of C-2 hydrogen

atoms deshielding effect of two oxo groups which shifted up positions of C-2 and C-3 hydrogen atoms by ca. 0.6-0.8 ppm in comparison to respective

1-aryl-2-aminoimidazolines [5] is decreased by aromatic ring. Signal of C-2 and C-3 were spread apart by ca. 0.5 ppm.

Spectra of imidazo[1,2-a][1,3,5]triazine derivatives contained additional signals of second aromatic substituent (N-6). Rigid structure of triazine

moiety (the aromatic ring lacked between two carbonyl groups) cause torsion of imidazoline ring switching N-1 aromatic substituent outside of the

molecule plane. Planar (imidazo[1,2-a]imidazoles) and out-of-plane (imidazo[1,2-a][1,3,5]triazines) location of N-1 substituent affect the chemical

shift of C-2 hydrogen atoms in different way. For imidazo[1,2-a][1,3,5]triazine derivatives spectra distance between C-2 and C-3 signals was only

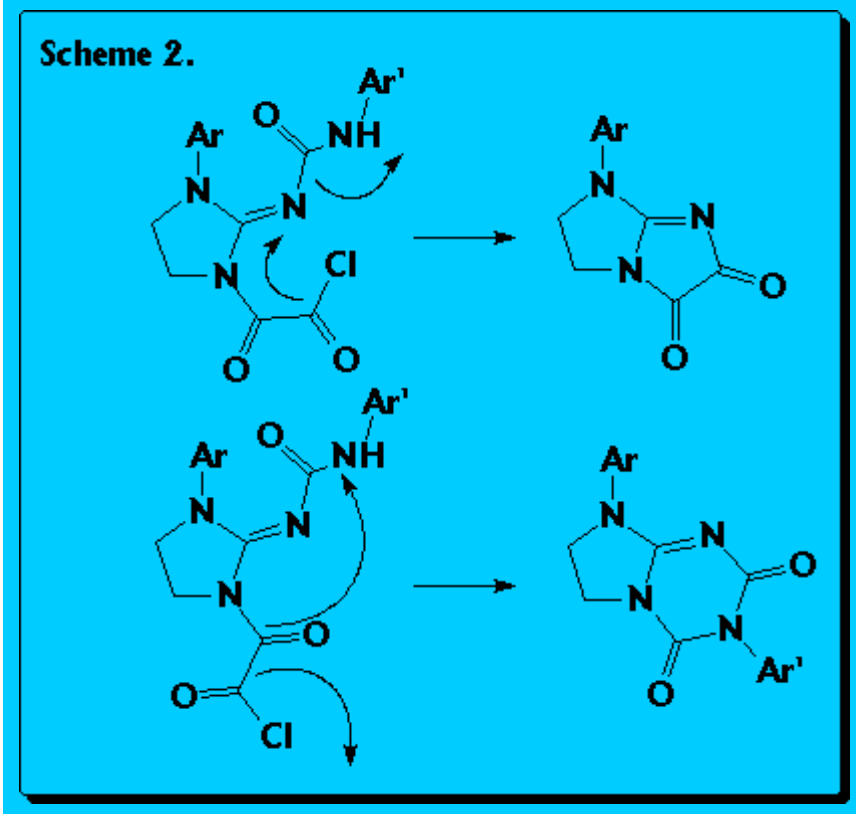
0.2 ppm and deshielding effect of carbonyl groups on them was lower (shifted up only by ca. 0.2 ppm).

- **Mechanism Discussion.**

In the chemical literature oxalyl chloride is known as selective reagent for carbonyl group introduction. Products obtained in this research suggest

that the second step of the reaction can be either electrophylic COCl group attack on N(1) or CO group attack on N(3) nitrogen atoms of the urea

moiety (Scheme 2).



It seems that both reaction courses are almost equally possible since the yield of imidazo[1,2-a]imidazole and imidazo[1,2-a][1,3,5]triazine

derivatives obtained in this reaction ranged from 30 - 35 % for each product.

Tables

Table 1: Physicochemical properties of obtained compounds.

No.	Ar	Ar'	m.p. [^{0}C]	Formula (m.w.)
A1	Ph	-	280-1	$C_{11}H_9N_3O_2$ (215.217)
A2	4-CH_3Ph	-	237-8	$C_{12}H_{11}N_3O_2$ (229.244)
A3	4-ClPh	-	262-4	$C_{11}H_8ClN_3O_2$ (249.662)
A4	4-CH_3OPh	-	235-7	$C_{12}H_{11}N_3O_3$ (245.244)
B1	Ph	4-ClPh	260-2	$C_{17}H_{13}ClN_4O_2$ (304.776)
B2	Ph	3-ClPh	293-4	$C_{17}H_{13}ClN_4O_2$ (304.776)
B3	Ph	1-naphthyl	297-8	$C_{21}H_{16}N_4O_2$ (356.391)
B4	4-CH_3Ph	4-ClPh	309-10	$C_{18}H_{15}ClN_4O_2$ (318.803)
B5	4-CH_3Ph	3-ClPh	260-2	$C_{18}H_{15}ClN_4O_2$ (318.803)
B6	4-ClPh	4-ClPh	299-301	$C_{17}H_{12}Cl_2N_4O_2$ (375.221)
B7	4-ClPh	3-ClPh	285-7	$C_{17}H_{12}Cl_2N_4O_2$ (375.221)
B8	4-CH_3OPh	4-ClPh	268-70	$C_{18}H_{15}ClN_4O_3$ (334.803)
B9	4-CH_3OPh	3-ClPh	257-9	$C_{18}H_{15}ClN_4O_3$

				(334.803)

Table 2: Spectral data of obtained compounds.

No.	MS (EI,15eV)	1H NMR (D_6-DMSO, TMS, d, ppm)	13C NMR (D_6-DMSO, TMS, d, ppm)
A1	215 (M^+)	4.01(dd,2H,C-3), 4.50 (dd,2H,C-2), 7.30-7.83 (3 x m, 5H, phenyl).	38.2 (C-3), 51.5 (C-2), 120.8 (C-10,C-14), 126.6 (C-12), 129.8 (C-11,C-13), 136.8 (C-9), 158.4 (C-5), 169.8 (C-8), 174.7 (C-6).
A2	229 (M^+)	2.32 (s,3H,CH_3), 3.94 (dd,2H,C-3), 4.46 (dd, 2H,C-2), 7.32, 7.66 (2 x d, 4H, aryl).	20.4 (CH_3) 37.8 (C-3), 51.0 (C-2), 120.0 (C-10,C-14), 129.7 (C-11,C-13), 134.1 (C-12), 135.4 (C-9), 157.9 (C-5), 169.0 (C-8), 174.0 (C-6).
A3	249 (M^+)	4.05 (dd, 2H, C-3), 4.40 (dd, 2H, C-2), 7.25, 7.55 (2 x d, 4H, aryl).	
A4	245 (M^+)	3.2 (s, 3H, O-CH_3), 4.0 (dd, 2H, C-3), 4.35 (dd, 2H, C-2), 7.3, 7.6 (2 x d, 4H, aryl).	
B1	304 (M^+)	3.8 (dd, 2H, C-3), 4.05 (dd, 2H, C-2), 7.21, 7.36 (2 x d, 4H, 4-chlorophenyl), 7.25-7.55 (3 x m, 5H, phenyl).	40.0 (C-3), 46.0 (C-2), 120.6 (C-12), 120.8 (C-10, -14), 123.7 (C-18), 129.4 (C-16, -20), 129.6 (C-11, -13), 129.8 (C-17, -19), 134.4 (C-9), 136.0 (C-15), 154.6 (C-7), 154.9 (C-5), 155.5 (C-8).
B2	304 (M^+)	3.85 (dd, 2H, C-3), 4.02 (dd, 2H, C-2), 7.2- 7.45 (3 x m, 4H, 3-chlorophenyl), 7.25-7.60 (3 x m, 5H, phenyl).	40.0 (C-3), 45.9 (C-2), 120.9 (C-10,-14), 126.2 (C-20), 126.9 (C-16), 129.0 (C-12), 129.1 (C-18), 129.4 (C-11,-13), 130.2 (C-19), 132.9(C-17), 134.7 (C-9), 140.0 (C-15), 154.6 (C-7), 154.9 (C-5), 155.5 (C-8).
B3	356 (M^+)	4.05 (dd, 2H, C-3), 4.2 (dd, 2H, C-2), 7.05-7.95 (m, 12H, phenyl + 1-naphthyl).	40.0 (C-3), 45.8 (C-2), 118.5 (C-16), 120.8 (C-10,-14), 121.8 (C-18), 122.3 (C-23), 125.2 (C-22), 126.0(C-21), 128.6 (C-12), 129.4 (C-11,-13), 129.6 (C-20), 133.2 (C-24), 134.5 (C-19), 134.7 (C-9), 149.8 (C-15), 154.6 (C-7), 154.8 (C-5), 155.5 (C-8).
B4	318 (M^+)	2.32 (s, 3H, CH_3), 4.08 (dd, 2H, C-3), 4.18 (dd, 2H, C-2), 7.30- 7.63 (3 x m, 8H, 4-chlo-rophenyl + 4-tolyl).	20.9 (CH_3), 40.0 (C-3), 46.0 (C-2), 120.8 (C-10,-14), 129.5 (C-16,-20), 129.8 (C-17,-19), 129.9 (C-11,-13), 133.2 (C-18), 134.4 (C-12), 134.5 (C-9), 136.0 (C-15), 149.0 (C-7), 154.6 (C-5), 155.5 (C-8).
B5	318 (M^+)	2.32 (s, 3H, CH_3), 4.0 (dd, 2H, C-3), 4.2 (dd, 2H, C-2), 7.18- 7.68 (m, 8H, 3-chlorophenyl + 4-tolyl).	20.1 (CH_3), 40.0 (C-3), 45.9 (C-2), 120.9 (C-10,-14), 126.2(C-20), 126.9 (C-16), 129.0 (C-18), 129.1 (C-12), 129.4 (C-11,-13), 130.2 (C-19), 134.7(C-17), 136.5 (C-9), 137.4 (C-15), 152.4 (C-7), 155.1 (C-5), 155.7 (C-8).
B6	375 (M^+)	4.05 (dd, 2H, C-3), 4.15 (dd, 2H, C-2), 7.30- 7.55 (3 x m, 8H, 2 x 4-chlorophenyl).	

B7	375 (M^+)	2.32 (s, 3H, CH_3), 4.02 (dd, 2H, C-3), 4.14 (dd, 2H, C-2), 7.15- 7.6 (m, 8H, 3-chloro-phenyl + 4-chlorophenyl).	
B8	334 (M^+)	3.2 (s, 3H, O-CH_3), 4.25 (dd, 2H, C-3), 4.3 (dd, 2H, C-2), 7.25-7.75 (m, 8H, 4-chlorophe-nyl + 4-methoxyphenyl).	
B9	334 (M^+)	3.2 (s, 3H, O-CH_3), 4.24 (dd, 2H, C-3), 4.28 (dd, 2H, C-2), 7.15-7.7 (m, 8H, 3-chlorophe-nyl + 4-methoxyphenyl).	

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