Conjugated Schiff Bases; XI[1]. A New Preparation of Some 5,5-Disubstituted Hydantoins

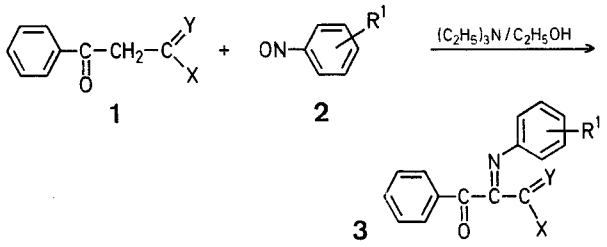
Janusz MOSKAL

Zakład Chemii Organicznej, Instytut Chemii, Uniwersytet Jagielloński, 30060 Kraków

Aleksandra MOSKAL

Zakład Chemii Organicznej, Instytut Farmakologii, Polska Akademia Nauk, 31920 Kraków, Polska (Poland)

It has recently been reported[1] that conjugated Schiff bases are useful starting materials for the synthesis of five-membered heterocycles. In the present communication we describe a new, simple synthesis of 5,5-disubstituted 2,4-dioxoimidazolidines from aryl isocyanates and conjugated Schiff bases containing the 1-oxa-4-azabutadiene system[2,3,4]. These Schiff bases are easily obtained by the condensation reaction of appropriate β-dicarbonyl compounds with nitrosobenzenes in the presence of basic catalysts[5,6].

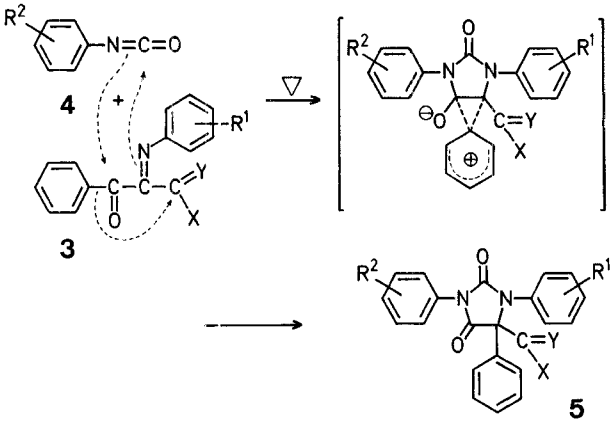


1 2 3

3	R^1	X	Y
a	H	-NH-C$_6$H$_5$	O
b	H	-NH-(2-pyridyl)	O
c	H	-NH-C$_6$H$_4$-OCH$_3$	O
d	H	-NH-C$_6$H$_4$-Cl	O
e	H	-OC$_2$H$_5$	O
f	4-N(CH$_3$)$_2$	-NH-C$_6$H$_5$	O
g	4-Br	-NH-C$_6$H$_5$	O
h	4-Cl	-NH-C$_6$H$_5$	S
i	H	-NH-C$_6$H$_4$-Cl	S
j	H	-C$_6$H$_5$	O

The 1-oxa-4-azabutadienes **3** undergo 1,3-cycloaddition[7,8] with aryl isocyanates **4** to give 2,4-dioxoimidazolidine derivatives **5**. The cycloaddition proceeds as a thermally induced reaction which is practically independent of the polarity of the solvent; thus, a synchronous mechanism should be operative in the addition in which the conjugated Schiff bases **3** are the 1,3-dipolar components and the aryl isocyanates **4** are the dipolarophiles. The cycloaddition process is accompanied by a 1,2-migration of the aryl group, thereby suggesting a σ-complex-type transition state.

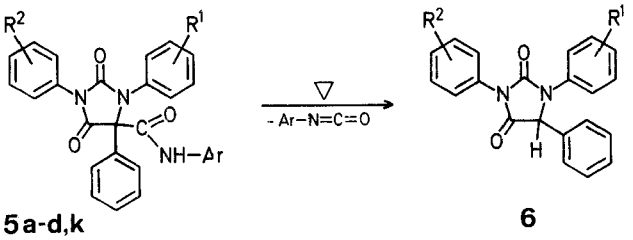
The 2,4-dioxoimidazolidine structure of products **5** was confirmed by analytical and spectrometric data. Thus, the ^{13}C-N.M.R. spectrum of the representative compound **5a** showed signals which are characteristic of the quaternary C-atom (δ = 74.7 ppm), of the 2- and 4-carbonyl C-atoms (δ = 151.9 and 160.7 ppm, respectively), and of the anilide carbonyl C-atom (δ = 168.3 ppm). Signals in the range of δ = 122.8–132.5 ppm were found for the aromatic C-atoms. The I.R. spectra showed characteristic absorption bands at ν = 1780 and 1725 cm^{-1} originating from stretching vibrations of the 2- and 4-carbonyl groups[10]. The ^{1}H-N.M.R.-, U.V.-, and mass spectra were also consistent with the proposed structure.



4 3 5

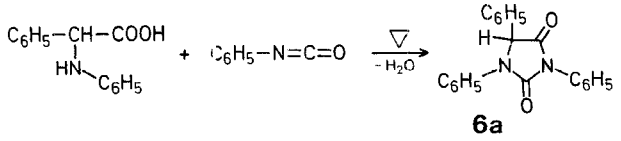
3	R^1	R^2	X	Y
a	H	H	-NH-C$_6$H$_5$	O
b	H	H	-NH-(2-pyridyl)	O
c	H	H	-NH-C$_6$H$_4$-OCH$_3$	O
d	H	H	-NH-C$_6$H$_4$-Cl	O
e	H	H	-OC$_2$H$_5$	O
f	4-N(CH$_3$)$_2$	H	-NH-C$_6$H$_5$	O
g	4-Br	H	-NH-C$_6$H$_5$	O
h	4-Cl	H	-NH-C$_6$H$_5$	S
i	H	H	-NH-C$_6$H$_4$-Cl	S
j	H	H	-C$_6$H$_5$	O
k	H	4-Cl	-NH-C$_6$H$_5$	O
l	H	4-Cl	-OC$_2$H$_5$	O

Electron-induced fragmentation of the cycloaddition products **5** containing anilide groups suggested that these compounds could easily lose one molecule of aryl isocyanate by thermal elimination. In fact, heating of the compounds **2a, b, c, d, k** above their melting points (~210°) leads to elimination of an aryl isocyanate molecule with formation of the corresponding 2,4-dioxo-1,3,5-triarylimidazolidine **(6)**.



5a-d,k 6

The structure of compounds **6** was confirmed by their ^{1}H-N.M.R. spectra. The signal of the anilide proton in compounds **5** at δ ≈ 8.50 ppm had disappeared and a new signal was observed at δ ≈ 5.50 ppm. The I.R. spectra of compounds **5** did not change upon conversion of **5** into **6**. Finally, the structure of compounds **6** was proven by an independent synthesis of **6a** from *N*-phenylphenylglycine and phenyl isocyanate in boiling xylene[9].



6a

0039-7881/79/1032-0794 $ 03.00

Table 1. 3-Substituted 2,4-Diaryl-1-oxa-4-azabutadienes **3**

3	Yield [%]	m.p. found	m.p. reported	Molecular formula[a]	Mass Spectrum[b] *m/e*
a	80	146–147°	146°[11]	$C_{21}H_{16}N_2O_2$ (328.4)	
b	65	145–146°		$C_{20}H_{15}N_3O_2$ (329.4)	329 (M^+); 224 ($M^+ - C_6H_5CO$); 209 ($M^+ - PyrNCO$); 120 ($PyrNCO^+$); 105 ($C_6H_5CO^+$, 100%)
c	80	98–100°		$C_{22}H_{18}N_2O_3$ (358.4)	358 (M^+); 209 ($M^+ - OCNC_6H_4OCH_3$); 149 ($H_3COC_6H_4NCO^+$); 105 ($C_6H_5CO^+$); 104 (100%)
d	75	140–141°	140°[3]	$C_{21}H_{15}ClN_2O_2$ (362.8)	
e	72	84–85°		$C_{17}H_{15}NO_3$ (281.3)	281 (M^+), 208 ($M^+ - COOC_2H_5$); 176 ($M^+ - C_6H_5CO$); 105 ($C_6H_5CO^+$, 100%); 29 ($C_2H_5^+$)
f	80	194°	194°[12]	$C_{23}H_{21}N_3O_2$ (371.4)	
g	60	143–144°		$C_{21}H_{15}BrN_2O_2$ (407.3)	406 (M^+); 408 ($M^+ + 2$); 301, 303 ($M^+ - C_6H_5CO$); 287, 289 ($M^+ - C_6H_5NCO$); 105 ($C_6H_5CO^+$, 100%)
h	70	134°	134°[13]	$C_{21}H_{15}ClN_2OS$ (378.9)	
i	65	112°	112°[13]	$C_{21}H_{15}ClN_2OS$ (378.9)	
j	70	82–84°	82–84°[2]	$C_{21}H_{15}NO_2$ (313.4)	

[a] The microanalyses of the new compounds were in satisfactory agreement with the calculated values: C, ±0.3; H, ±0.3; N, ±0.2; Br, −0.1.

[b] The mass spectra were recorded with an LKB 9000S Spectrometer in the Regional Laboratory of Physicochemical and Structural Analysis, Kraków.

Table 2. I.R.- and ^{1}H-N.M.R.-spectral Data of Compounds **3**

3	I.R. (Nujol or hexachlorobutadiene)[a] ν_{max} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS)[b] δ [ppm]
b	3348 (NH); 1685 (C=O); 1660 (C–$O_{anilide}$); 1640 (C=N)	6.86–8.17 (m, $14H_{arom}$); 9.88 (s, 1H, NH)
c	3365 (NH); 2840 (OCH_3); 1689 (C=O); 1658 (C–$O_{anilide}$); 1632 (C=N)	3.72 (s, 3H, OCH_3); 6.91–8.02 (m, $14H_{arom}$); 9.73 (s, 1H, NH)
e	2835 (OCH_2CH_3); 1746 (C–O_{ester}); 1670 (C=O); 1632 (C=N); 1240 (C–O)	0.98$_{anti}$, 1.31$_{syn}$ (t, t, 3H, OCH_2CH_3); 4.12$_{anti}$, 4.25$_{syn}$ (q, q, 2H, OCH_2CH_3); 6.94–7.76 (m, $8H_{arom}$); 8.02 (d, $2H_{arom}$)
g	3340 (NH); 1688 (C=O); 1665 (C–$O_{anilide}$); 1638 (C=N)	6.95–7.98 (m, $12H_{arom}$); 8.15 (d, $2H_{arom}$); 9.65 (s, 1H, NH)

[a] The I.R. spectra were recorded on an IR-71 Zeiss Jena spectrophotometer mulls.

[b] The ^{1}H-N.M.R. spectra were recorded on a Tesla BS-478 spectrometer.

3-Substituted 2,4-Diaryl-1-oxa-4-azabutadienes (3); General Procedure:

The acetophenone derivative **1** (0.015 mol) and the nitrosobenzene **2** (0.015 mol) are dissolved in ethanol. To this solution, anhydrous triethylamine (0.1 ml) is added and the mixture is stirred on a steam bath at ~70°. An exothermic reaction ensues after a few minutes and the color of the mixture changes from deep green to pale orange. The product crystallizes upon cooling. It is isolated by suction and repeatedly recrystallized from ethanol.

5-Substituted 2,4-Dioxo-1,3,5-triarylimidazolidines (5); General Procedure:

A solution of the appropriate 3-substituted 2,4-diaryl-1-oxa-4-azabutadiene (**3**; 0.020 mol) and an aryl isocyanate (**4**; 0.020 mol) in dry benzene (30 ml) is refluxed for 3 h. Then, petroleum ether (5–10 ml) is added. The colorless crystalline material which precipitates is isolated by suction and repeatedly recrystallized from benzene or ethanol.

2,4-Dioxo-1,3,5-triarylimidazolidines (6); General Procedure:

The appropriate imidazolidine derivative **5** (0.010 mol) is placed in a small flask or glass tube and heated above its melting point (usually 200–210°) in vacuum (10 torr) for 2 h. During this time the eliminated aryl isocyanate is removed completely. The residue solidifies on cooling. It is recrystallized from hexane/benzene (1:1); yields: 90–95%.

2,4-Dioxo-1,3,5-triphenylimidazolidine (**6a**); yield: 94%; m.p. 116–117°.

$C_{21}H_{16}N_2O_2$	calc.	C 76.81	H 4.91	N 8.53
(328.4)	found	76.6	4.7	8.2

M.S.: *m/e* = 328 (M^+); 181 (100%); 104 ($C_6H_5NCH^+$).

I.R. (Nujol): ν = 1780 (4-C=O); 1720 cm^{-1} (2-C=O).

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 5.53 (s, 1H, CH); 7.05–5.55 ppm (m, $15H_{arom}$).

3-(4-Chlorophenyl)-2,4-dioxo-1,5-diphenylimidazolidine (**6k**); yield: 90%; m.p. 144–145°.

$C_{21}H_{15}ClN_2O_2$	calc.	C 69.52	H 4.17	Cl 9.77	N 7.72
(362.8)	found	70.0	4.1	9.4	7.6

M.S.: *m/e* = 362, 364 (M^+); 215 (100%); 138, 140 ($ClC_6H_4NCH^+$).

I.R. (Nujol): ν = 1785 (4-C=O); 1728 (2-C=O); 680 cm^{-1} (C–Cl).

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 5.41 (s, 1H, CH); 7.08–7.62 ppm (m, $14H_{arom}$).

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Table 3. 5-Substituted 2,4-Dioxo-1,3,5-triarylimidazolidines (**5**)

5	Yield [%]	m.p.	Molecular formula[a]	Mass Spectrum *m/e*
a	70	196–197°	$C_{28}H_{21}N_3O_3$ (447.5)	328 ($M^+ - C_6H_5NCO$); 181 (100%); 119 ($C_6H_5NCO^+$)
b	65	189–190°	$C_{27}H_{20}N_4O_3$ (440.5)	328 ($M^+ - PyrNCO$); 181 (100%); 120 ($PyrNCO^+$)
c	75	192–194°	$C_{29}H_{23}N_3O_4$ (477.5)	328 ($M^+ - OCNC_6H_4OCH_3$); 181 (100%); 149 ($OCNC_6H_4OCH_3^+$)
d	72	184–186°	$C_{28}H_{20}ClN_3O_3$ (481.9)	328 ($M^+ - OCNC_6H_4Cl$); 181 (100%); 153, 155 ($OCNC_6H_4Cl^+$)
e	76	158–159°	$C_{24}H_{20}N_2O_4$ (400.4)	400 (M^+); 327 ($M^+ - COOC_2H_5$); 180 (100%)
f	52	194–195°	$C_{30}H_{26}N_4O_3$ (490.6)	371 ($M^+ - C_6H_5NCO$); 181 (100%); 119 ($C_6H_5NCO^+$)
g	64	181–182°	$C_{28}H_{20}BrN_3O_2$ (510.4)	406, 408 ($M^+ - C_6H_5NCO$); 181 (100%); 119 ($C_6H_5NCO^+$)
h	62	218°	$C_{28}H_{20}ClN_3O_3S$ (514.0)	362, 364 ($M^+ - C_6H_5NCS$); 181 (100%); 135 ($C_6H_5NCS^+$)
i	60	189–190°	$C_{28}H_{20}CLN_3O_3S$ (514.0)	328 ($M^+ - SCNC_6H_4Cl$); 181 (100%); 169, 171 ($SCNC_6H_4Cl^+$)
j	56	163–164°	$C_{28}H_{20}N_2O_3$ (432.5)	432 (M^+); 327 ($M^+ - C_6H_5CO$); 105 ($C_6H_5CO^+$, 100%)
k	77	170–171°	$C_{28}H_{20}ClN_3O_3$ (481.9)	362, 364 ($M^+ - C_6H_5NCO$); 215 (100%); 119 ($C_6H_5NCO^+$)
l	56	105–106°	$C_{24}H_{19}ClN_2O_4$ (435.9)	434, 436 (M^+); 361, 363 ($M^+ - COOC_2H_5$); 180 (100%)

[a] The microanalyses of all products (except **3h** and **3k**) were in satisfactory agreement with the calculated values: C, ±0.3; H, ±0.3; N, ±0.2; Cl, ±0.3; Br, −0.2; S, ±0.40; **3h**: H, +0.5; **3k**: C, −0.5.

Table 4. I.R.-, U.V.-, and ^{1}H-N.M.R.-spectral Data of Compounds **5**

5	I.R. (Nujol or hexachlorobutadiene)[a] ν_{max} [cm^{-1}]	U.V. (methanol)[c] λ_{max} [nm] (ε)	^{1}H-N.M.R. ($CDCl_3$/TMS)[b] δ [ppm]
a	3370 (NH); 1780 (4-C=O); 1723 (2-C=O); 1702 (C=$O_{anilide}$)	229 (28500), 242 (23720)	7.08–7.64 (m, 20H_{arom}); 8.09 (s, 1H, NH)
b	3338 (NH); 1775 (4-C=O); 1728 (2-C=O); 1712 (C=$O_{anilide}$)	220 (33200), 241 (25600), 276 (7200)	7.12–7.58 (m, 15H_{arom}); 8.00–8.60 (m, 5H_{arom}); 8.65 (s, 1H, NH)
c	3342 (NH); 2865 (OCH_3); 1785 (4-C=O); 1725 (2-C=O); 1700 (C=$O_{anilide}$)	218 (36000), 264 (17590), 275 (12470)	3.72 (s, 3H, OCH_3); 6.75–6.85 (m, 2H_{arom}); 7.14–7.53 (m, 17H_{arom}); 8.22 (s, 1H, NH)
d	3365 (NH); 1785 (4-C=O); 1730 (2-C=O); 1698 (C=$O_{anilide}$); 665 (C–Cl)	218 (41000), 239 (34500)	7.12–7.53 (m, 19H_{arom}); 8.40 (s, 1H, NH)
e	1783 (4-C=O); 1749 (C=O_{ester}); 1725 (2-C=O)	230 (28000)	1.07 (t, 3H, OCH_2-CH_3); 4.22 (q, 2H, OCH_2-CH_3); 7.03–7.70 (m, 15H_{arom})
f	3380 (NH); 2852 (NCH_3); 1785 (4-C=O); 1725 (2-C=O); 1710 (C=$O_{anilide}$)	265 (30800); 304 (6000)	2.88 (s, 6H, NCH_3); 6.63–6.75 (m, 2H_{arom}); 7.00–7.48 (m, 17H_{arom}); 8.40 (s, 1H, NH)
g	3352 (NH); 1780 (4-C=O); 1720 (2-C=O); 1690 (C=$O_{anilide}$); 690 (C–Br)	232 (40000)	7.08–7.70 (m, 19H_{arom}); 8.62 (s, 1H, NH)
h	3300 (NH); 1780 (4-C=O); 1728 (2-C=O); 1180 (C=S); 670 (C–Cl)	215 (50500), 240 (29000), 263 (14800), 276 (12100)	7.20–7.53 (m, 19H_{arom}); 8.88 (s, 1H, NH)
i	3312 (NH); 1783 (4-C=O); 1722 (2-C=O); 1190 (C=S); 675 (C–Cl)	222 (39800), 270 (9800), 282 (8800), 310 (4530)	7.20–7.48 (m, 19H_{arom}); 8.94 (s, 1H, NH)
j	1792 (4-C=O); 1734 (2-C=O); 1698 (C=O)	230 (33650)	7.17–7.53 (m, 18H_{arom}); 7.75–8.05 (m, 2H_{arom})
k	3356 (NH); 1778 (4-C=O); 1722 (2-C=O); 1702 (C=$O_{anilide}$); 665 (C–Cl)	227 (31450), 240 (27080)	6.95–7.60 (m, 19H_{arom}); 8.43 (s, 1H, NH)
l	1785 (4-C=O); 1755 (C=O_{ester}); 1732 (2-C=O)	233 (39400)	1.14 (t, 3H, OCH_2-CH_3); 4.25 (q, 2H, OCH_2-CH_3); 7.12–7.65 (m, 14H_{arom})

[a, b] see Table 2.

[c] The U.V. spectra were recorded on a VSU-2P Zeiss Jena Spectrophotometer.

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