

0040-4020(94)01065-X

Novel Mesoionic Compounds Derived from 3,7-Diaryl-2*H*-Imidazo[2,1-*b*]/[1,3,4]oxadiazines

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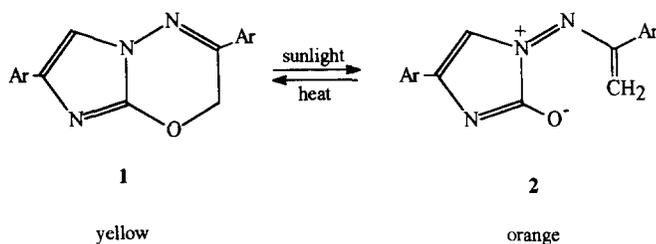
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Abstract: Reversible reaction in which imidazo-oxadiazines are converted into mesoionic compounds, takes place under conditions of the sunlight and heating.

We recently reported cathodic reduction of semicarbazones of phenacyl bromides as a facile and effective method of electrosynthesis of 3,7-diaryl-2*H*-imidazo[2,1-*b*]/[1,3,4]oxadiazines (**1**).¹ We now extend our work to study the chemistry of these compounds. The aim of the present work is the transformation of the oxadiazine derivatives (**1**) into heterocyclic compounds of other types. For example, simple Diels-Alder reaction with DMAD gives possibility to convert **1** into 3-aryl-7,8-dimethoxycarbonyl-2*H*-pyrrolo[2,1-*b*]/[1,3,4]oxadiazines.²

We have also communicated in a previous paper the sunlight-heating reversible transformation of compounds **1** into mesoionic compounds (**2**).³

Now, we present a study of this photochromic process (Scheme 1) by cyclic voltametry, HPLC and spectroscopic technics as well as an extended synthetic procedure of obtaining compound **2** and a description of a series of new mesoionic compounds.



Scheme 1

RESULTS AND DISCUSSION

We have observed³ that the irradiation of 3,7-diphenyl-2*H*-imidazo[2,1-*b*]/[1,3,4]oxadiazine (**1**) in solid state by sunlight, for a few seconds produces a change colour from the initial pale yellow to an orange. The irradiation was carried out also in benzene, chloroform or methanol solutions and in polyethylene. In Figure 1 are presented the UV and Visible spectra for **1a** in chloroform and benzene respectively in which it is possible to observe the transformations in these UV and Vis regions. In Table 1 are summarized the λ_{\max} values measured by UV and Visible for **1** and **2**.

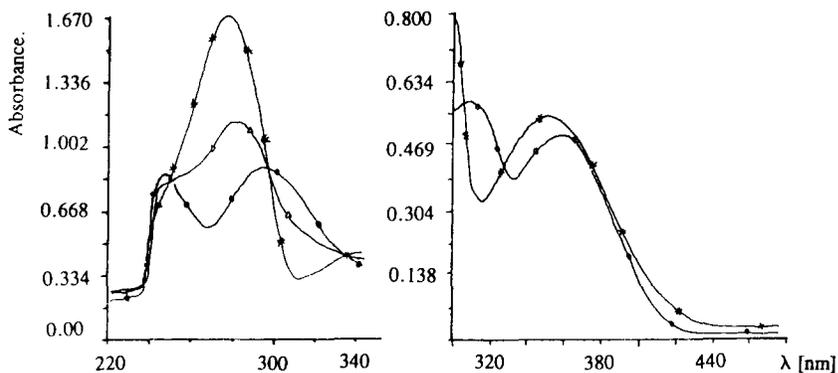


Fig. 1 Evolution of the UV(CHCl_3)(left) and Vis(C_6H_6)(right) spectrum of **1a** at different exposure times(seconds) of sunlight.

* 0
 Δ 20
 \circ 120

Table 1. Variation of t_r (min) (HPLC) and λ_{\max} (nm) UV (CHCl_3)/VISIBLE (C_6H_6) from **1** to **2**.
 3,7-Diaryl-2*H*-imidazo[2,1-*b*]/[1,3,4]oxadiazines (**1**) Mesoionic compounds (**2**)

Ar :	t_r	UV	VISIBLE	Colour	t_r	UV	VISIBLE	Colour
a: C_6H_5	17.38	278	350	pale yellow	10.08	248, 298	358	orange
b: 4-MeO- C_6H_4	18.25	292	352	pale yellow	10.46	258, 346	364	orange
c: 4-Me- C_6H_4	31.0	280	348	pale yellow	13.88	248, 316	358	orange
d: 4-Cl- C_6H_4	31.6	284	356	yellow	13.88	246, 312	364	orange-red
e: 4-Br- C_6H_4	37.8	280	356	yellow	18.02	248, 312	368	orange-red

All the 3,7-diaryl-2*H*-imidazo[2,1-*b*]/[1,3,4]oxadiazines (**1**) are yellow products in the same range of yellow colour, however the irradiated products show different types of orange colours with different intensity.

The differences in colour from one compound to another appear to be mainly due to variation in the relative intensities of the individual vibrational components of the visible band rather than to shifts of the band as a whole.

The colour changes were also registered by HPLC using a reverse phase column and MeOH/H₂O (8:2) as eluant with a constant flow of 0.3 mL/min. Before irradiation, only one peak for each imidazo-oxadiazine derivatives is observed. When the exposure time is lower than 1 min, a new peak corresponding to the mesoionic compound appears. On the other hand, the peak corresponding to **1** disappeared completely when the exposition time was higher than 1 min. These results are summarized in Table 1.

Cyclic voltammetric data on mercury cathode of the phenyl-imidazo-oxadiazine **1a** in EtOH/LiClO₄ showed two irreversible peaks in the cathodic region at -1.65V and -1.85V (vs Ag/Ag⁺) (Fig. 2†). However the irradiated product showed a reversible peak at E_{pc} = -0.87V and E_{pa} = -0.81V (Fig. 2††) as could be expected for the proposed mesoionic structure. In Table 2 are summarized the potential values for **1** and **2**.

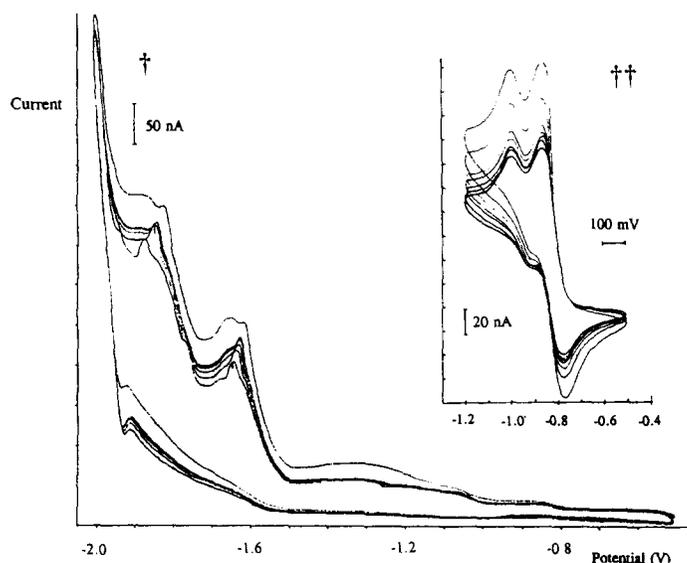


Fig. 2 Cyclic voltammograms of **1a** (a) and **2a** (b) in EtOH/LiClO₄. c = 5. 10⁻⁴ M.

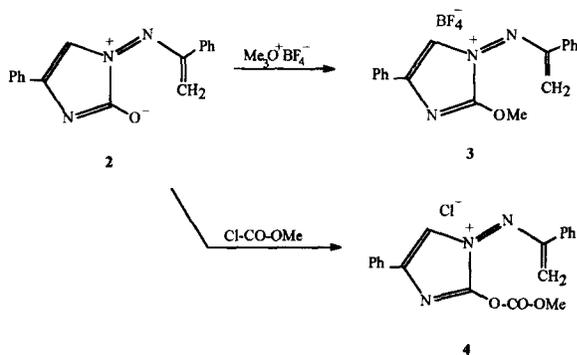
Table 2. Peak Potentials (vs Ag/Ag⁺) for **1** and **2** in EtOH/LiClO₄.

Ar:	E _{c1} (V) (1)	E _{c2} (V) (1)	E _{pc} (V) (2)	E _{pa} (V) (2)
a: C ₆ H ₅	-1.65	-1.85	-0.87	-0.81
b: 4-MeO-C ₆ H ₄	-1.7	-1.85	-1.02	-0.95
c: 4-Me-C ₆ H ₄	-1.7	-1.86	-0.97	-0.90
d: 4-Cl-C ₆ H ₄	-1.54	-1.78	-0.88	-0.82
e: 4-Br-C ₆ H ₄	-1.52	-1.77	-0.89	-0.82

The changes observed in this photochromic process correspond to a drastic change in the structure of the products as can be observed in their IR and NMR spectra. In IR appears a strong band between 1680-1690 cm⁻¹ which did not appear in the starting material. The ¹HNMR showed the disappearance of a singlet at around 5.35 ppm (compound **1**) and appearance of two doublets at lower field (compound **2**). By the same way, the singlet at 7.32 ppm for =CH in **1a** is moved near to 8.44 ppm in **2a**.

All the compounds **2** are solids and have the same molecular weight, determined by MS, as the starting materials.

The mesoionic structure was also confirmed by chemical methods. The photochromic product **2a**, being treated with $\text{Me}_3\text{O}^+ \text{BF}_4^-$, led to the corresponding salt (**3**) which was isolated and identified by spectroscopic technics. Likewise when **2a** was allowed to react with methyl chloroformate the corresponding carbonate **4** was formed. Scheme 2.



Scheme 2

When **2** in solid state was allowed to stay in the dark at room temperature, it lost its orange colour to give the initial yellow corresponding to the imidazo-oxadiazine **1**. This reversible process can be accelerated by heating the mesoionic compound (**2**) under reflux in the dark. Obtention of compound **1** in this process was proved by spectroscopic technics.

Photochemical sensibility of **1a** had been observed by *Beyer*^{4,5} but the structure of the photochromic product had not been determined.

The proposed mechanism involves the cleavage of a C-O bond in the imidazo part of the molecule **1**. This would imply similar behaviour for other molecules with parallel structural features. Several pyran derivatives exhibit similar reversible photochromic process as described by *Becker et al.*^{6,7}. It is also a general property of molecules with the 2H-pyran skeleton.

The importance of this photochemical effect is the implication of such behaviour in the nature. So, on leaves this kind of process take place through chromenes and pyrans.⁸ Grown of the fruits are controled by them, and allow the possibility of complex structures synthesis through the more colored and reactive form.

By other hand, photochromic compounds synthesized in the laboratory, have found applications on optical uses.⁹ By the same way, the chemistry of mesoionic compounds have been improved considerably in the last years and many new mesoionic structures have been synthesized. Some of them have been useful on medicine (muscle-relaxant, local anesthetic, cardiotropic...)¹⁰ or electronic research (electrophotographic, photoreceptors...)¹¹

EXPERIMENTAL SECTION

Nuclear magnetic resonance ¹H and ¹³C were recorded in the indicated solvents on Varian Unity 300 apparatus. The chemical shifts (δ , in ppm) are referred to internal solvent relative to TMS (¹H) or

deuteriochloroform (^{13}C). The chemical shifts are given in ppm. Perkin Elmer Model 583 infrared spectrophotometer was used to determine IR spectra as dispersions in KBr. Mass spectra (EI 70eV) were determined using a Hewlett-Packard Model 5988A mass-selective detector equipped with a Hewlett-Packard MS Chem-Station. Analytical HPLC was performed on a Hewlett-Packard 1050 instrument with a UV detector selected $\lambda=254$ nm using a reverse-phase column. UV/Vis spectra were performed on a Diode-array spectrophotometer Hewlett-Packard Model 8452A. Cyclic voltametric potentials were determined on an Metrohm apparatus Model 663 VA STAND and the potential values are given in volts.

3,7-Diaryl-2H-imidazo[2,1-b][1,3,4]oxadiazines **1(a-e)** were synthesized according to the literature.¹

General Procedure.

Conversion of **1** into mesoionic-compounds **2**:

For photoconversion of Imidazo-oxadiazines, 0.727 mmole of **1** in C_6H_6 , CHCl_3 or MeOH (25 mL) were irradiated by sunlight for 1 minute and were quantitatively transformed into **2**. The intense orange colour of the photoproduct obtained by irradiation in solid state, disappeared by standing the sample in the dark at room temperature. This reaction can be faster reversed by refluxing in the dark.

The spectral data and physical properties of **2** are summarized as follows. The m.p.'s are the same as for the isomers **1**, because of reversal on heating.

Mesoionic-compound (2a) derived from 3,7-diphenyl-2H-imidazo[2,1-b][1,3,4]oxadiazine (**1a**).

IR $\nu[\text{cm}^{-1}]$: 3057, 1685, 1591, 1573, 1306, 1284, 773, 691. ^1H NMR (300MHz, CDCl_3): $\delta[\text{ppm}]$: 8.44 (s, 1H, =CH), 8.22-7.53 (m, 10 H_{arom}), 5.94 (d, 1H, $J=1.5\text{Hz}$), 5.66 (d, 1H, $J=1.5\text{Hz}$). ^{13}C NMR (75.4MHz, CDCl_3): $\delta[\text{ppm}]$: 164.14, 152.3, 146.7, 134.3, 133.3, 132.4, 130, 128.98, 128.86, 128.4, 128.23, 125.31, 113.93. MS (EI): m/z : 275 (M^+).

Mesoionic-compound (2b) derived from 3,7-Bis(4-methoxyphenyl)-2H-imidazo[2,1-b][1,3,4]oxadiazine (**1b**).

IR $\nu[\text{cm}^{-1}]$: 3071, 2934, 2839, 1678, 1605, 1583, 1562, 1512, 1318, 1290, 1258, 1178, 1025, 836, 663. ^1H NMR (300MHz, CDCl_3): $\delta[\text{ppm}]$: 8.38 (s, 1H, =CH), 8.2 (d, 2 H_{arom} , $J=8\text{Hz}$), 7.29 (d, 2 H_{arom} , $J=8\text{Hz}$), 7.0 (d, 2 H_{arom} , $J=8\text{Hz}$), 6.87 (d, 2 H_{arom} , $J=8\text{Hz}$), 5.82 (d, 1H, $J=1.1\text{Hz}$, = CH_2), 5.52 (d, 1H, $J=1.1\text{Hz}$, = CH_2), 3.91 (s, 3H, OMe), 3.80 (s, 3H, OMe). ^{13}C NMR (75.4MHz, CDCl_3): $\delta[\text{ppm}]$: 164.34, 163.42, 160.37, 152.80, 146.86, 130.71, 129.93, 127.49, 127.12, 125.21, 114.84, 114.17, 112.21, 55.62, 55.34. MS (EI) m/z : 335 (M^+).

Mesoionic-compound (2c) derived from 3,7-Bis(4-methylphenyl)-2H-imidazo[2,1-b][1,3,4]oxadiazine (**1c**).

IR $\nu[\text{cm}^{-1}]$: 3028, 2920, 2857, 1683, 1588, 1563, 1504, 1456, 1306, 1284, 1171, 1119, 822. ^1H NMR (300 MHz, CDCl_3): $\delta[\text{ppm}]$: 8.41 (s, 1H, =CH), 8.10 (d, 2 H_{arom} , $J=8.1\text{Hz}$), 7.35 (d, 2 H_{arom} , $J=8.1\text{Hz}$), 7.25 (d, 2 H_{arom} , $J=8.1\text{Hz}$), 7.153 (d, 2 H_{arom} , $J=8.1\text{Hz}$), 5.89 (d, 1H, $J=1.2\text{Hz}$, = CH_2), 5.59 (d, 1H, $J=1.2\text{Hz}$, = CH_2), 2.45 (s, 3H, Me), 2.34 (s, 3H, Me). ^{13}C NMR (75.4MHz, CDCl_3): $\delta[\text{ppm}]$: 164.15, 152.78, 147.05, 144.77, 139.16, 131.87, 130.22, 130.05, 129.57, 129.37, 128.57, 125.51, 113.23, 21.73, 21.22. MS (EI) m/z : 303 (M^+).

Mesoionic-compound (2d) derived from 3,7-Bis(4-chlorophenyl)-2H-imidazo[2,1-b][1,3,4]oxadiazine (**1d**).

IR $\nu[\text{cm}^{-1}]$: 3093, 2924, 1680, 1588, 1562, 1491, 1301, 1091, 833. ^1H NMR (300MHz, CDCl_3): $\delta[\text{ppm}]$: 8.40 (s, 1H, =CH), 8.14 (d, 2 H_{arom} , $J=8.4\text{Hz}$), 7.53 (d, 2 H_{arom} , $J=8\text{Hz}$), 7.29-7.35 (m, 4 H_{arom}), 5.903 (s, 1H, = CH_2), 5.672 (s, 1H, = CH_2). ^{13}C NMR (75.4MHz, CDCl_3): $\delta[\text{ppm}]$: 163.17, 151.98, 145.86, 140.20, 134.86, 132.8, 130.68, 129.81, 129.51, 129.44, 128.64, 126.67, 114.53. MS (EI) m/z : 343 (M^+).

Mesoionic-compound (2e) derived from 3,7-Bis(4-bromophenyl)-2H-imidazo[2,1-b][1,3,4]oxadiazine (**1e**).

IR ν [cm^{-1}]: 2925, 2855, 1686, 1585, 1486, 1398, 1298, 1275, 1073, 1007, 825, 736. ^1H NMR (300MHz, CDCl_3): δ [ppm]: 8.40 (s, 1H, =CH), 8.06 (d, 2 H_{arom} , $J=8.4\text{Hz}$), 7.71 (d, 2 H_{arom} , $J=8.8\text{Hz}$), 7.49 (d, 2 H_{arom} , $J=8.8\text{Hz}$), 7.22 (d, 2 H_{arom} , $J=8.4\text{Hz}$), 5.91 (d, 1H, $J=1.4\text{Hz}$, = CH_2), 5.68 (d, 1H, $J=1.4\text{Hz}$, = CH_2). ^{13}C NMR (75.4MHz, CDCl_3): δ [ppm]: 163.33, 151.97, 145.92, 133.22, 132.42, 131.60, 129.75, 129.58, 128.92, 128.31, 126.91, 123.09, 114.62. MS (EI) m/z : 433 (M^+).

Conversion of 2a into the salt 3:

0.1 g (0.363 mmole) of **2a** was dissolved in dry CH_2Cl_2 (25 mL) and was added to an equimolecular amount of $\text{Me}_3\text{O}^+ \text{F}_4\text{B}^-$ (47 mg, 0.363 mmole) under argon atmosphere. The reaction mixture was stirred for 24h. The solvent was then evaporated to give crude **3**, which was redissolved in $\text{CHCl}_3/\text{Et}_2\text{O}$ (1:1) and the solution was crystallized in this medium. Compound **3** showed the following physical and spectroscopical properties:

M.p.: 107-109 °C. IR ν [cm^{-1}]: 3062, 2935, 1682, 1592, 1570, 1308, 1286, 1082 (BF_4^-), 774, 696. ^1H NMR (300MHz, CDCl_3): δ [ppm]: 9.4 (s, 1H, =CH), 8.45-7.37 (m, 10 H_{arom}), 6.08 (d, 1H, $J=2.5\text{Hz}$), 6.04 (d, 1H, $J=2.5\text{Hz}$), 4.38 (s, 3H, OMe). MS (EI) m/z : 290 (M^+).

Conversion of 2a into the carbonate 4:

0.1 g (0.363 mmole) of **2a** was dissolved in dry CH_2Cl_2 (25 mL). Equimolecular amount of methylchloroformate was added and stirred during 12h. When the reaction was completed the corresponding carbonate was detected by HPLC. Mass spectrometry and infrared spectroscopy for **4** are given as follows. IR (Film) ν [cm^{-1}]: 3064, 2958, 1770 (C=O), 1680, 1592, 1572, 1310, 1286, 1174, 1070, 1036, 776, 696. MS (EI) m/z (relative intensity): 334 (M^+ , 5), 275 ($M^+ - \text{COOMe}$, 43), 273 (70), 232 (28), 202 (25), 142 (28), 116 (52), 114 (93), 104 (63), 102 (70), 77 (100).

We thank DGICYT, PB 91-0158 for financial support. *B. Batanero* wish to thank Alcalá de Henares Council about the economical help to carry out this work.

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