Studies on Nitroenamines. Part III [1]. Synthesis and Spectral Properties of 4-Acyl-1-arylimidazoles

A. Gómez-Sánchez*, F. J. Hidalgo and J. L. Chiara

Instituto de la Grasa y sus Derivados, and Departamento de Química Orgánica, Facultad de Química, Universidad de Sevilla, Apartado de Correos No. 553, 41071 Seville, Spain

Received June 17, 1987

The catalytic (C/Pd) hydrogenation of 3-arylamino-2-nitro-2-enones (**1**) in the presence of carboxylic ortho esters (**2**) affords 4-acyl-1-arylimidazoles (**3**) in yields (20-70%) which depend on the degree of substitution of the imidazole ring. The spectral properties of compounds **3**, and particularly the ^{13}C-nmr spectra, reflect both the electronic and steric effects of the substituents on the π-electron delocalization and planarity of the bicyclic system.

J. Heterocyclic Chem., **24**, 1757 (1987).

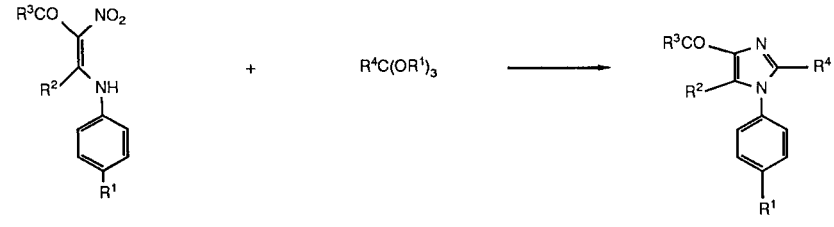
In spite of the biological interest of 4(5)-acylimidazoles [2], very few representatives of these compounds are known and no satisfactory procedure for their preparation has been described [2,3]. As a continutation of our studies on nitroenamines [1], we report here a simple synthesis of 4-acyl-1-arylimidazoles. The principle of the synthesis is the hydrogenation of a nitroenamine in the presence of an acylating reagent (Scheme). Nitroenamines have been used to prepare a variety of heterocyclic compounds [1,4] but to our knowledge no data exist on their reductive acylation, though this reaction would obviously provide a simple route to the imidazole ring and their nucleosides. Nitroenamines with different patterns of substitution, including their *N*-glycosyl derivatives, can be easily obtained [4,5].

1-Arylimidazoles, as other *N*-phenyl-substituted azoles, exhibit electron delocalization over the two rings which will tend to be coplanar. The extension of this delocalization and the degree of planarity depend on both the electronic and steric effects of the substituents in the phenyl and imidazole rings, as showed in the spectroscopic study of the newly prepared compounds.

Results and Discussion.

The starting methyl 3-arylamino-2-nitroacrylates **1a-c** were prepared (40-76%) in a one pot procedure from methyl nitroacetate, trimethyl orthoformate and the appropriate aniline as described [5]; similarly, 4-anilino-3-nitro-3-buten-2-one **1g** was prepared (60%) from nitroacetone, triethyl orthoformate and aniline. Methyl 3-arylami-

Scheme



1 **2** **3**

	R^1	R^2	R^3
a	H	H	MeO
b	Me	H	MeO
c	MeO	H	MeO
d	Cl	Me	MeO
e	Me	Me	MeO
f	MeO	Me	MeO
g	H	H	Me
h	H	CH_2 - $C(Me_2)$ - CH_2	

	R^4
a	H
b	Me

	R^1	R^2	R^3	R^4
a	H	H	MeO	H
b	Me	H	MeO	H
c	MeO	H	MeO	H
d	H	H	MeO	Me
e	Me	H	MeO	Me
f	MeO	H	MeO	Me
g	H	Me	MeO	H
h	Me	Me	MeO	H
i	MeO	Me	MeO	H
j	H	Me	MeO	Me
k	Me	Me	MeO	Me
l	MeO	Me	MeO	Me
m	H	H	Me	Me
n	H	CH_2 - $C(Me_2)$ - CH_2		Me

no-2-nitrocrotonates **1d-f** were obtained (90-98%) by reaction of methyl 3-ethoxy-2-nitrocrotonate with the appropriate aniline. 3-Anilino-5,5-dimethyl-2-nitro-2-cyclohexen-1-one **1h** was prepared (45%) from aniline and 3-hydroxy-5,5-dimethyl-2-nitro-2-cyclohexen-1-one.

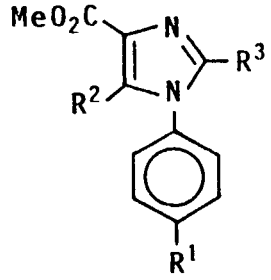
When compounds **1** were catalytically hydrogenated (C/Pd) in the presence of an excess of a carboxylic *ortho* ester **2**, the 3-acyl-1-arylimidazoles **3** were produced (Scheme). The reactions using the aminonitroenones **1g,h** were better performed using acetic acid as solvent; under these reaction conditions yields were higher and less by-products were observed (tlc). Physical constants, yields and analytical data of the products **3** appear in Table 1. The highest yields (60-70%) were obtained in the reactions of the crotonic esters **1d-f** and the ketone **1h** with triethyl orthoacetate **2b**; the products **3j-l, 3n** crystallized readily from the reaction mixture. The 2,5-unsubstituted derivatives **3a-c** were obtained in lower yields only after column chromatography, but the isolation procedure was considerably improved by treating the reaction mixture with picric acid; the picrates of the products crystallized readily and were obtained in 40-60% yield after recrystallization. Filtration of the picrates through a silica gel column afforded the free imidazoles.

Other reducing agents were also used in order to improve the yields and to extend the scope of the reaction, with negative results. For example, the reduction of methyl 3-anilino-2-nitroacrylate (**1a**) with aluminium amalgam [7] in methanol containing trimethyl orthoformate produced a higher proportion of **3a** than when using C/Pd and less by-products (as deduced from chromatographic control of the reactions). However, the formation of insoluble, strongly adsorbent aluminium hydroxyde made the isolation of the imidazole considerably more difficult and the yield was finally lower.

Attempts were made to extend this reaction to 3-alkylamino-2-nitroacrylic and crotonic esters, and to the related *N*-glycosyl derivatives, but complex mixtures of products resulted. Using methyl 3-(methylamino)-2-nitrocrotonate and methyl orthoformate, a crystalline product, mp 132-133°, was isolated (18% yield), which on the basis of its elemental analysis and spectral properties is assigned structure dimethyl 2,5-dimethylpyrazine-3,6-dicarboxylate (**4**).

Table 1

1-Aryl-4-methoxycarbonylimidazoles **3**



	R¹	R²	R³	Mp °C	Yield (%)	Formula	Recrystallization Solvent	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
3a	H	H	H	115-116	28	$C_{11}H_{10}N_2O_2$	EtOAc	65.3	5.0	13.9	65.2	5.2	13.8
	Picrate			141-142	61 [a]	$C_{17}H_{13}N_5O_4$	EtOH	47.3	3.0	16.2	47.6	3.1	16.6
3b	Me	H	H	133-134	17	$C_{12}H_{12}N_2O_2$	EtOAc	66.7	5.6	13.0	66.7	5.7	12.9
	Picrate			151-152	42 [a]	$C_{18}H_{15}N_5O_9$	MeOH	48.5	3.4	15.7	48.6	3.4	15.9
3c	MeO	H	H	104-105	16	$C_{12}H_{12}N_2O_3$	EtOAc	62.1	5.2	12.1	61.9	5.1	11.9
	Picrate			150-151	57 [a]	$C_{18}H_{15}N_5O_{10}$	EtOH	46.9	3.3	15.2	47.0	3.2	15.4
3d	H	H	Me	107-108	26	$C_{12}H_{12}N_2O_2$	EtOAc	66.7	5.6	13.0	66.5	5.6	12.9
3e	Me	H	Me	92-93	17	$C_{13}H_{14}N_2O_2$	EtOAc	67.8	6.1	12.2	67.6	6.3	12.4
3f	MeO	H	Me	133-134	25	$C_{13}H_{14}N_2O_3$	EtOAc	63.4	5.7	11.4	63.1	5.8	11.6
3g	H	Me	H	183-184	62	$C_{12}H_{12}N_2O_2$	EtOAc	66.7	5.6	13.0	67.0	5.6	12.7
3h	Me	Me	H	114-115	50	$C_{13}H_{14}N_2O_2$	EtOAc	67.8	6.1	12.2	67.6	6.2	12.0
3i	MeO	Me	H	124-125	42	$C_{13}H_{14}N_2O_3$	EtOAc	63.4	5.7	11.4	63.7	6.0	11.5
3j	H	Me	Me	174-175	57	$C_{13}H_{14}N_2O_3$	EtOAc	67.8	6.1	12.2	67.5	5.9	12.0
3k	Me	Me	Me	167-168	65	$C_{14}H_{16}N_2O_2$	EtOAc	68.8	6.6	11.5	68.8	6.7	11.7
3l	MeO	Me	Me	157-158	68	$C_{14}H_{16}N_2O_3$	EtOAc	64.6	6.2	10.8	64.3	6.1	10.9

[a] Calculated on the starting methyl 3-arylamino-2-nitroacrylate **1a-c**.

The spectral data for compounds **3** (Tables 2-4) are fully consistent with the assigned structures and reflect the influence of the substituents on the interanular π-electron delocalization and the planitry of the system. The 2,5-unsubstituted compounds **3a-c** are most likely devoid of significant steric interaction and full interanular delocalization prevails. The increasing bathochromic shifts observed in the uv band at *ca.* 240 nm on passing from **3a** to **3c**, and the parallel decrease of the ν (C=O) frequency of the ester group, indicate the increasing electron donating power of the *p*-substituent of the phenyl ring. A similar effect is observed in the chemical shifts of the imidazole ring protons. Compounds **3a-c** present two one-proton doublets at δ 7.78-7.89 and 7.90-7.99 assigned to the imidazole ring protons. Comparison with compounds **3d-f** and **3g-i** clearly indicated that the high field doublet is due to H-5, and the other to H-2. The δ-values for both protons diminish with the increasing donating power of R'. In the 2- and/or 5-methyl substituted imidazoles **3c-l** these effects are less apparent or non-existing, probably as a consequence of

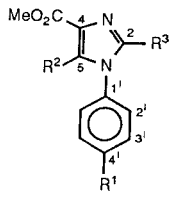
Table 2

UV and IR Data of Compounds **3a-l**

	UV (Methanol)	IR, cm^{-1} (Potassium Bromide)				
	λ max (nm) (log ϵ)	CO_2Me ν (C=O)	ν (CH) arom	Imidazole ring	ν (C=C)	Phenyl δ (C-H)
3a	241 (4.22)	1718 vs	3130 m 3115 m 3040 m	1534 s 1505 m 1428 m	1597 m 1592 s 1498 s	698 s 762 s
3b	243 (4.25)	1704 s	3130 m 3085 s 3015 w	1548 s 1538 s 1522 s 1435 s	1605 w 1584 w 1502 sh	814 s
3c	247 (4.22)	1689 s	3105 s 3070 w 3020 w	1537 s 1514 s 1428 s	1605 w 1590 w 1584 w 1500 sh	828 s
3d	240 (4.17)	1716 s	3130 w 3065 w 3025 w	1540 s 1520 w 1492 m 1435 m	1602 vw 1589 w	702 s 762 s
3e	241 (4.14)	1702 s	3135 m 3085 w 3030 w	1553 s 1515 s 1440 m	1585 vw 1502 sh	817 s
3f	241 (4.27)	1698 s	3130 m 3065 w 3045 m	1547 s 1507 s 1443 s	1598 m 1578 m 1500 sh	848 s
3g	237 (4.07)	1706 s	3110 s 3095 m 3045 m 3025 m	1558 m 1493 s 1427 s	1616 m 1592 m	699 m 774 s
3h	238 (4.27)	1700 s	3105 w 3040 w	1556 s 1512 s 1495 s 1448 s	1600 vw 1582 w 1500 sh	818 s
3i	238 (4.28)	1680 s	3110 w 3045 w 3005 w	1552 s 1510 s 1437 s	1603 m 1592 m 1500 sh	836 s
3j	244 (4.09)	1709 vs	3050 w 3040 m	1538 m 1492 m 1432 m	1594 w 1581 vw	710 m 776 m
3k	244 (4.23)	1690 vs	3045 w 3035 w	1532 s 1515 m 1427 s	1573 s	842 s
3l	242 (4.21)	1692 s	3035 w	1535 m 1516 s 1436 m	1608 m 1575 s 1505 sh	848 s

Table 3

^{1}H-NMR Data of Compounds **3a-l** [a]



	H-2	H-5	CO_2CH_3	Ph	R^1	R^3	R^2
3a	7.89 d J = 1.5	7.99 d J = 1.5	3.93 s	7.48 m	—	—	—
3b	7.84 d J = 1.3	7.95 d J = 1.3	3.93 s	7.31 s	2.42 s	—	—
3c	7.78 d J = 1.4	7.90 d J = 1.4	3.94 s	7.34 d (2H) 7.02 d (2H) J = 8.9	3.87 s	—	—
3d	—	7.72 s	3.92 s	7.42 m	—	2.39 s	—
3e	—	7.69 s	3.91 s	7.32 d (2H) 7.18 d (2H) J = 8.3	2.44 s	2.37 s	—
3f	—	7.67 s	3.91 s	7.23 d (2H) 7.02 d (2H) J = 8.9	3.88 s	2.35 s	—
3g	7.65 s	—	3.94 s	7.43 m	—	—	2.47 s
3h	7.54 s	—	3.93 s	7.34 d (2H) 7.17 d (2H) J = 8.4	2.45 s	—	2.46 s
3i	7.52	—	3.93 s	7.21 d (2H) 7.03 d (2H) J = 9.0	3.88 s	—	2.44 s
3j	—	—	3.92 s	7.38 m	—	2.22 s	2.32 s
3k	—	—	3.91 s	7.35 d (2H) 7.08 d (2H) J = 8.2	2.46 s	2.22 s	2.31 s
3l	—	—	3.91 s	7.13 d (2H) 7.04 d (2H) J = 9.1	3.89 s	2.21 s	2.31 s

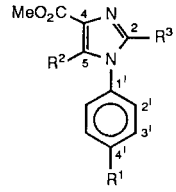
[a] δ (ppm); J (Hz). In deuteriochloroform.

the larger steric requirement of the substituents which increases the energy barrier, and inhibits planarity and delocalization. In the ^{13}C-nmr spectra, the signals due to the carbon atoms of the imidazole ring were assigned through the proton-coupled spectra and, again, by comparing the spectra of the 2,5-unsubstituted compounds **3a-c** with those of the 2-methyl **3d-f** and 5-methyl-derivatives **3g-i**. The chemical shifts of the phenyl carbon atoms reflected both the steric effects of the methyl substituents in the imidazole ring and the electronic effect of the *p*-substituent in the phenyl ring. According to Begtrup [8], the chemical shifts of C-2′ and C-4′ in *N*-phenylazoles are most affected by the steric hindrance to full interanular delocalization, in such a way that the values of $\delta_{C\text{-}2'}$ and $\delta_{C\text{-}3'}$-$\delta_{C\text{-}2'}$ can be diagnostic of the amount of the hindrance: the delocalization is extensive if $\delta_{C\text{-}2'}$ is ~118-121 and $\delta_{C\text{-}3'}$-$\delta_{C\text{-}2'}$ ~9.0-10.6, and it is hindered if $\delta_{C\text{-}2'}$ ~124.5-125.5 and $\delta_{C\text{-}3'}$-$\delta_{C\text{-}2'}$ ~3.3-4.6. The values of these parameters for compounds **3** appear in Table 4. The values of $\delta_{C\text{-}2'}$ 121.7 and $\delta_{C\text{-}3'}$-$\delta_{C\text{-}2'}$ 8.4 for the 2,5-unsubstituted compound **3a** indicated extensive interanaular delocalization. The introduction of a methyl group at C-2 or C-3, or in both carbons (compounds **3d**, **3g**, and **3j**), progressively increases $\delta_{C\text{-}2'}$ and decreases $\delta_{C\text{-}3'}$-$\delta_{C\text{-}2'}$, as the hindrance to delocalization

progressively increases. In the remaining compounds, the electronic effect of the *p*-substituent in the phenyl ring must also be considered. The 4′-Me substituent and, particularly, the 4′-OMe substituent will shift the C-2′ and C-3′ resonances, and the amount and sign of these shifts can be taken as equal to those produced by these groups in the *meta*- and *ortho*-carbons of the corresponding mono-substituted benzene (that is, $\Delta\delta_C$ −0.1 and +0.7 for C-2′ and C-3′, respectively, for the 4′-Me compounds; $\Delta\delta_C$ +1.0 and −14.4, respectively, for the 4′-OMe compounds [9]). If these increments are added to the experimental $\delta_{C\text{-}2'}$ and $\delta_{C\text{-}3'}$, a set of "corrected" chemical shifts, δ^*_C, is obtained

Table 4

^{13}C-NMR Spectral Data of Compounds **3a-l** [a]



	C-2	C-4	C-5	C-1′	C-2′	C-3′	C-4′	CO_2CH_3		R¹	CH_3-C2	CH_3-C5
3a	136.4 d	134.8 s	124.1 d	136.3 s	121.7 d	130.1 d	128.4 d	163.1 s	51.8 q	—	—	—
3b	136.4 d	134.5 s	124.2 d	134.0 s	121.5 d	130.6 d	138.5 s	163.2 s	51.8 q	21.0 q	—	—
3c	136.6 d	134.5 s	124.6 d	129.6 s	123.4 d	115.1 d	159.6 s	163.2 s	51.8 q	55.6 q	—	—
3d	146.1 s	132.2 s	126.7 d	137.0 s	125.5 d	129.7 d	129.1 d	163.4 s	51.8 q	—	13.8 q	—
3e	146.2 s	131.9 s	126.8 d	134.4 s	125.3 d	130.3 d	139.7 s	163.5 s	51.7 q	21.1 q	13.7 q	—
3f	146.3 s	131.9 s	127.0 d	129.7 s	126.8 d	114.8 d	159.9 s	163.4 s	51.5 q	55.6 q	13.6 q	—
3g	136.6 d	129.1 s	136.3 s	135.1 s	126.0 d	129.8 d	129.4 d	163.9 s	51.6 q	—	—	10.4 q
3h	136.7 d	129.4 s	136.4 s	132.7 s	125.8 d	130.3 d	139.4 s	164.2 s	51.5 q	21.2 q	—	10.4 q
3i	136.9 d	129.3 s	136.6 s	128.0 s	127.3 d	114.8 d	160.1 s	164.3 s	51.5 q	55.6 q	—	10.4 q
3j	144.7 s	130.1 s	137.1 s	135.5 s	127.4 d	129.9 d	129.5 d	164.3 s	51.4 q	—	13.8 q	10.8 q
3k	144.9 s	130.3 s	137.2 s	132.9 s	127.2 d	130.5 d	139.7 s	164.4 s	51.3 q	21.2 q	13.8 q	10.8 q
3l	145.1 s	128.1 s	137.4 s	127.1 s	128.5 d	115.0 d	160.1 s	164.4 s	51.3 q	55.6 q	13.8 q	10.8 q

	$\delta^*_{C\text{-}1'}$	$\delta^*_{C\text{-}2'}$	$\delta^*_{C\text{-}3'}$	$\delta^*_{C\text{-}4'}$	$\delta^*_{C\text{-}3'}$-$\delta^*_{C\text{-}2'}$
3a	136.3	121.7	130.1	128.4	8.4
3b	136.9	121.6	129.9	129.6	8.3
3c	137.3	122.4	129.5	128.2	7.1
3d	137.0	125.5	129.7	129.1	4.2
3e	137.3	125.4	129.6	130.8	4.2
3f	137.4	125.8	129.2	128.5	3.4
3g	135.1	126.0	129.8	129.4	3.8
3h	135.6	125.9	129.6	130.5	3.7
3i	135.7	126.3	129.2	128.7	2.9
3j	135.5	127.4	129.9	129.5	2.5
3k	135.8	127.3	129.8	130.8	2.5
3l	134.8	127.5	129.4	128.7	1.9

[a] δ (ppm) in deuteriochloroform.

for the 4'-substituted compounds, which also appear in Table 4. Inspection of the Table shows that while the $\delta^*_{C\text{-}2'}$ and $\delta^*_{C\text{-}3'}$-$\delta^*_{C\text{-}2'}$ for compounds **3b** and **3c** have the values corresponding to an unhindered full interanular delocalized system, $\delta^*_{C\text{-}2'}$ progressively increases, and $\delta^*_{C\text{-}3'}$-$\delta^*_{C\text{-}2'}$ progressively decreases, with the 2-Me, 5-Me and 2,5-dimethyl substitution in the imidazole ring, as could be anticipated. Therefore, the Begtrup's rule can also be applied to *N*-phenyl azoles having a substituent in the phenyl ring, provided that the electronic effect of the substituent is taken into account.

EXPERIMENTAL

Tlc was performed on Silica Gel 60 F_{254} (Merck) with detection with uv (254 nm) and/or by charring with sulfuric acid. Column chromatography was performed with Silica Gel 60 (230-400 mesh; Merck). Elemental analyses were conducted at the Instituto de Química Orgánica General, C.S.I.C., Madrid. Melting points were determined in open glass capillaries in a Büchi apparatus and are uncorrected. The uv spectra were recorded with a Perkin-Elmer 554 spectrophotometer, and ir spectra with a Perkin-Elmer 299 spectrophotometer. ^{1}H- and ^{13}C-nmr spectra were determined at 200 and 50 MHz, respectively, with a Varian XL-200 spectrometer; chemical shifts refer to internal Me_4Si.

Methyl 3-Arylamino-2-nitroacrylates **1a-c**.

These compounds were prepared as described [5].

Methyl 3-Arylamino-2-nitrocrotonates **1d-f**.

A suspension of methyl 3-ethoxy-2-nitrocrotonate (2 mmoles) [10] in ethanol (3 ml) was treated with a solution of the appropriate aniline (2 mmoles) in ethanol (2 ml). The mixture was stirred at room temperature for 5 minutes and refrigerated, whereupon the product crystallized.

Methyl 3-(*p*-Chloroanilino)-2-nitrocrotonate (**1d**).

This compound was obtained in 98% yield, mp 90-91° (from ethanol); ir (potassium bromide): 3260 [ν (NH)], 1715 [ν (C=O)], 1596 [ν (C=C) + δ (N-H)], and 1475 cm^{-1} [ν (NO_2)], *Z*-form; ^{1}H-nmr (deuteriochloroform): *Z*-form (58%), δ 2.10 (s, 3H, CH_3-C=), 3.89 (s, 3H, CO_2Me), 7.12 and 7.41 (2 m, 4H, Ph), 11.86 (br, 1H, NH); *E*-form (42%), δ 2.14 (s, 3H, CH_3-C=), 3.84 (s, 3H, CO_2Me), 7.12 and 7.41 (2m, 4H, Ph), 10.98 (br, 1H, NH).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_4$: C, 48.8; H, 4.1; N, 10.4; Cl, 13.1. Found: C, 48.8; H, 4.2; N, 10.6; Cl, 13.3.

Methyl 2-Nitro-3-(*p*-toluidino)crotonate (**1e**).

This compound was obtained in 98% yield, mp 87-88° (from ethanol); ir (potassium bromide): 3218 [ν (NH)], 1715 [ν (C=O), *Z*-form], 1663 [ν (C=O), *E*-form], 1578 [ν (C=C) + δ (NH)], 1505 [ν (NO_2), *E*-form], 1470 cm^{-1} [ν (NO_2), *Z*-form]; ^{1}H-nmr (deuteriochloroform): *Z*-form (65%), δ 2.10 (br, 3H, CH_3-C=), 3.88 (br, 3H, CO_2Me), 7.0 and 7.2 (2m, 4H, Ph), 11.95 (br, 1H, NH); *E*-form (35%), δ 2.10 (br, 3H, CH_3-C=), 3.88 (br, 3H, CO_2Me), 7.0 and 7.2 (2m, 4H, Ph), 11.04 (br, 1H, NH).

Anal. Calcd. for $C_{12}H_{14}N_2O_4$: C, 57.6; H, 5.6; N, 11.2. Found: C, 57.7; H, 5.9; N, 11.2.

Methyl 3-(*p*-Anisidino)-2-nitrocrotonate (**1f**).

This compound was obtained in 95% yield, mp 83-84° (from ethanol); ir (potassium bromide): 3150 [ν (NH)], 1715 [ν (C=O), *Z*-form], 1670 [ν (C=O), *E*-form], 1602 [ν C=C) + δ (NH), *Z*-form], 1576 [ν (C=C) + δ (NH), *E*-form], 1504 [ν (NO_2), *E*-form] and 1470 cm^{-1} [ν (NO_2), *Z*-form]; ^{1}H-nmr (deuteriochloroform): *Z*-form (58%), δ 2.09 (br, 3H, CH_3-C=), 3.85 (s, 3H, MeO), 3.88 (br, 3H, CO_2Me), 6.97 and 7.13 (2d, 4H, J = 9.6 Hz, Ph), 11.88 (br, 1H, NH); *E*-form (32%), δ 2.09 (br, 3H, CH_3-C=), 3.85 (s, 3H, MeO), 3.88 (br, 3H, CO_2Me), 6.97 and 7.13 (2d, 4H, J = 9.6 Hz, Ph), 10.98 (br, 1H, NH).

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: C, 54.1; H, 5.3; N, 10.5. Found: C, 53.9; H, 5.4; N, 10.6.

4-Anilino-3-nitro-3-buten-2-one (**1g**).

A solution of aniline (30 mmoles), triethyl orthoformate (30 mmoles), and 0.5 ml of acetic acid in 15 ml of ethanol was briefly brought to a boil and allowed to cool to room temperature. To this was added nitroacetone (30 mmoles), and the resulting solution was refluxed for 4 hours. Refrigeration overnight yielded crystalline **1g**. The product (60%) had mp 118-119° (from ethanol); ir (potassium bromide): 3180 [ν (NH), *Z*-form], 3150 [ν (NH), *E*-form], 1673 [ν (C=O), *Z*-form], 1650 [ν (C=O), *E*-form], 1605 and 1585 [ν (C=C) + δ (NH)], 1510 [ν (NO_2)], 1303 cm^{-1} [ν (NO_2)]; ^{1}H-nmr (deuteriochloroform): *Z*-form (14%), δ 2.66 (s, 3H, CH_3-CO), 8.67 (d, 1H, J = 16 Hz, CH=C), 7.3-7.5 (m, 5H, Ph), 11.34 (br, s, 1H, NH); *E*-form (86%), δ 2.69 (s, 3H, CH_3-CO), 9.04 (d, 1H, J = 13.8 Hz, CH=C), 7.3-7.5 (m, 5H, Ph), 12.49 (br s, 1H, NH).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.48; H, 4.71; N, 13.75.

3-Anilino-5,5-dimethyl-2-nitro-2-cyclohexenone (**1h**).

A solution of aniline (10 mmoles), 3-hydroxy-5,5-dimethyl-2-nitro-2-cyclohexen-1-one (2-nitrodimedon) [11] (5 mmoles) and 0.5 ml of acetic acid in 10 ml of ethanol was refluxed for 8 hours. The solvent was evaporated under reduced pressure and 10 ml of ether were added. Refrigeration overnight yielded crystalline **1h**. The product (45%) had mp 135-136° (from ethanol); ir (potassium bromide): 3150 [ν (NH)], 1668 [ν (C=O)], 1570 [ν (C=C) + δ (NH)], 1486 cm^{-1} [ν (NO_2)]; ^{1}H-nmr (deuteriochloroform): δ 1.04 (s, 6H, CH_3), 2.42 (s, 2H, CH_2), 2.58 (s, 2H, CH_2), 7.3-7.6 (m, 5H, Ph), 11.81 (br, s, 1H, NH).

Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.6; H, 6.2; N, 10.8. Found: C, 64.6; H, 6.1; N, 10.6.

Methyl 1-Arylimidazole-4-carboxylates **3a-c**.

A suspension of methyl 3-arylamino-2-nitroacrylate **1a-c** (2 mmoles) in triethyl orthoformate (5 ml) was hydrogenated in the presence of Pd-C (10%) (150 mg) at 2.5 bars and 70°. After 1.5 hours the starting nitroester was completely transformed (tlc). The mixture was filtered through a Celite bed, and the filtrate was evaporated to a syrupy residue which was coevaporated several times with methanol. The product was a mixture containing **3a-c** as the main component.

Treatment of the above mixture with a saturated solution of picric acid in methanol and refrigeration overnight afforded the imidazole picrates which were filtered off and washed with ethanol before analysis.

Column chromatography of the mixture, using ether as eluent, afforded the analytically pure bases **3a-c**. Alternatively, the picrates were filtered through a column of silica gel, using ether as eluent. Evaporation of the fractions containing pure **3a-c** afforded the pure compounds.

Physical constants and yields of **3a-c**, and their picrates, appear in Table 1. Tables 2, 3, and 4 summarize the spectral data of **3a-c**.

Methyl 1-Aryl-2-methyl-, 1-Aryl-5-methyl- and 1-Aryl-2,5-dimethyl-imidazole-4-carboxylates **3d-l**.

A suspension of the appropriate nitroester **1a-f** (2 mmoles) in trimethyl orthoformate or triethyl orthoacetate (2 ml) was hydrogenated in the presence of Pd-C (10%) (100 mg) at 2.5 bars and 70° until tlc indicated the complete transformation of the starting nitro compound (1-3 hours). The catalyst was removed by filtration through a bed of Celite, and the filtrate was evaporated to a syrupy mixture which contained **3d-l** as the main component. Crystallization of this syrup from ethanol afforded **3j-l** which was recrystallized from the same solvent. Compounds **3d-i** were obtained crystalline after column chromatography of the syrupy mixture, and were recrystallized from ethanol.

Physical constants of **3d-l** are given in Table 1. Their spectral data are summarized in Tables 2, 3, and 4.

4-Acetyl-2-methyl-1-phenylimidazole (**3m**).

A suspension of 4-anilino-3-nitro-3-buten-2-one (**1g**) (2 mmoles) in tri-

ethyl orthoacetate (5 ml) and acetic acid (15 ml) was hydrogenated in the presence of Pd-C (10%) (115 mg) at 4 bars and 25°. After 1 hour the starting **1g** was completely transformed (tlc). The resulting solution was filtered through a Celite bed, and the filtrate was evaporated under reduced pressure to a syrupy residue which was coevaporated with toluene. Column chromatography of the mixture, using hexane/ethyl acetate 2:1 as eluent afforded analytically pure **3m** (20%), which melted at room temperature; ir (deuteriochloroform): 1672 [ν (C=O)], 1598, 1542, 1500 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.39 (s, 3H, CH_3-C=N), 2.56 (s, 3H, CH_3-CO), 7.30-7.56 (m, 5H, Ph), 7.69 (s, 1H, H-C=C); ^{13}C-nmr (deuteriochloroform): δ 13.4 (q, CH_3-C=N), 26.3 (q, CH_3-CO), 124.8 (d, C-5), 125.1 (d, C-2'), 128.8 (d, C-4'), 129.5 (d, C-3'), 136.5 (s, C-1'), 140.3 (s, C-4), 145.4 (s, C-2), 193.4 (s, CO).

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.8; H, 6.3; N, 13.7.

2,6,6-Trimethyl-6,7-dihydro-1-phenyl-5-*H*-benzimidazol-4-one (**3n**).

A suspension of 3-anilino-5,5-dimethyl-2-nitro-2-cyclohexenone (**1h**) (2 mmoles) in triethyl orthoacetate (5 ml) and acetic acid (15 ml) was hydrogenated in the presence of Pd-C (10%) (115 mg) at 4 bars and 25°. After 1 hour the starting **1h** was completely transformed (tlc). The resulting solution was filtered through a Celite bed, and the filtrate was evaporated under reduced pressure to a syrupy residue which was coevaporated several times with toluene, yielding crystalline **3n** (68%). The product **3n** was recrystallized from methanol and had mp 190-191°; ir (potassium bromide): 1675 [ν (C=O)], 1532, 1498, and 1422 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.11 (s, 6H, $(CH_3)_2C$), 2.30 (s, 3H, CH_3-C=), 2.45 (s, 2H, CH_2), 2.46 (s, 2H, CH_2), 7.2-7.6 (m, 5H, Ph); ^{13}C-nmr (deuteriochloroform): δ 13.4 (q, CH_3-C=N), 28.2 (q, $(CH_3)_2C$), 35.2 (t, CH_2), 35.4 (s, CMe_2), 51.8 (t, CH_2), 126.4 (d, C-2'), 129.2 (d, C-4'), 129.7 (d, C-3'), 133.7 (s, C-5), 134.8 (s, C-1'), 143.6 (s, C-4), 147.2 (s, C-2), 190.7 (s, CO).

Anal. Calcd. for $C_{16}H_{18}N_2O$: C, 75.6; H, 7.1; N, 11.0. Found: C, 75.5; H, 7.2; N, 10.9.

Acknowledgements.

We thank the Consejo Superior de Investigaciones Científicas and the Comisión Asesora de Investigación Científica y Técnica for financial support, Professor J. Bellanato (Instituto de Optica, C.S.I.C., Madrid) for recording some of the ir spectra, and the Instituto de Química Orgánica General (C.S.I.C., Madrid) for the microanalyses.

REFERENCES AND NOTES

[1] Part **II**. A. Gómez-Sánchez, F. J. Hidalgo, and J. L. Chiara, *Carbohydr. Res.*, **167**, 000 (1987).

[2] E. P. Krebs and E. Bondi, *Helv. Chim. Acta*, **51**, 497 (1979).

[3] G. Kempler, J. Spindler, H. J. Fiebig and G. Sarodnick, *J. Prakt. Chem.*, **313**, 977 (1971).

[4] S. Rajappa, *Tetrahedron*, **37**, 1435 (1981).

[5] A. Gómez-Sánchez, F. J. Hidalgo, J. L. Chiara and J. Bellanato, *An. Quím.*, **C, 81**, 139 (1985).

[6] A. Gómez-Sánchez, *et al*, unpublished results.

[7] E. J. Corey, I. Vlattas, and K. Harding, *J. Am. Chem. Soc.*, **91**, 535 (1969).

[8] M. Begtrup, *Acta Chem. Scand.*, **27**, 3101 (1973), and references cited therein.

[9] G. C. Levy, R. L. Lichter, and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance Spectroscopy", 2nd Ed, John Wiley and Sons, Inc, New York, NY, 1980, p 111.

[10] K. K. Babievskii, V. M. Belikov, and M. A. Tikonova, *Dokl. Akad. Nauk. SSSR*, **193**, 1055 (1070).

[11] B. Eistert, H. Elias, E. Kosch, and R. Wollheim, *Chem. Ber.*, **92**, 130 (1959).