TRANSFORMATIONS OF 2-FORMYL-N-NITROARYLIMIDAZOLES

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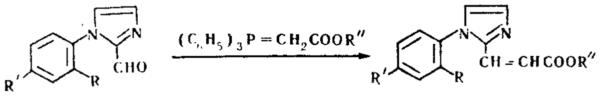
Esters of 1-aryl-β-2-imidazolylacrylic acid were synthesized by the Wittig reaction from 2-formyl-1-arylimidazoles. The reaction of these aldehydes with arylamines and 1,2-dianilinoethane was examined.

Continuing our study of the transformations of 1-aryl-2-formylimidazoles [1-3], we subjected 1-phenyl- and 1-nitroaryl-2-formylimidazoles (I-V) to the Wittig reaction. Esters of acrylic acids are formed in good yield by the action of carbalkoxymethylenetriphenylphosphorane on I-IV on prolonged refluxing in benzene solution; the yield of ester from the 1-phenyl-substituted compound is considerably higher than the yields from the other aldehydes (II-V). The reaction of V with the phosphorane was carried out in DMF at 100°C. The resulting esters were hydrolyzed with 15% alcoholic potassium hydroxide in the cold to give imidazolylacrylic acids* in almost quantitative yields.



I – V

VI – X

I, VIa $R=R'=H$; II, VIIa,b $R=NO_2$; $R'=H$; III, VIIIa,b $R=NO_2$; $R'=CH_3$; IV, IX a,b $R=NO_2$; $R'=OCH_3$; V, Xa,b $R=H$; $R'=NO_2$; VI—Xa $R''=CH_3$; b $R''=C_2H_5$.

As in the case of 3-formylindoles [4], aldehydes II-V react with benzylidenetriphenylphosphorane more readily than with carbethoxytriphenylphosphoranes. It can be established by means of thin-layer chromatography (TLC) that the reaction is complete after 48-72 h. However, the yield of styryl derivatives of N-nitroarylimidazoles is low, since these compounds are extremely unstable and undergo resinification during isolation. They were therefore converted to the picrates and subjected to analysis in this form.

A nitro group in the ortho or para position relative to the nitrogen somewhat hinders the reaction of II-V with carbalkoxytriphenylphosphorane. Ester VIa was obtained in 92% yield, while the yield of VII-X did not exceed 79%. The effect of a nitro group in the reaction of formylimidazoles with 1,2-dianilinoethane and aromatic amines is particularly appreciable. While 2-formyl-1-methyl-5-nitrobenzimidazole or 3-formyl-1-acetylindole [5] rapidly form diphenylimidazolidine derivatives in quantitative yield and I reacts in 6 h to give a product in 50% yield, the yield on very prolonged heating in the reaction of aldehydes II-V is less than 10%. Compound I is converted to a Schiff base on reaction with o-aminophenol and 2-amino-4-nitrophenol, while II-V do not form azomethines with these amines.

EXPERIMENTAL

1-(o-Nitro-p-tolyl)imidazole (XI). This compound was obtained in 80% yield by the method in [7, 8]; the reaction mixture was refluxed for 15 h to give light-yellow needles with mp 82-83° (from heptane). Found: C 58.9; H 4.6; N 20.3%. $C_{10}H_9N_3O_3$. Calculated: C 59.1; H 4.4; N 20.7%.

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* Considering the method used to prepare the esters, the trans structure can be assigned to them [9].

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TABLE 1. Esters of 1-Aryl-β-2-imidazolylacrylic Acid

Compound	Reaction solvent	Reaction time, h	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
VIa	DMF + benzene	36—40	115	$C_{13}H_{12}N_2O_2$	68,9	5,3	12,4	68,4	5,3	12,3	92,5
VIIa	Benzene	36	145	$C_{13}H_{11}N_3O_4$	56,8	3,8	15,7	57,1	4,0	15,4	62
VIIb	The same	36	189*	$C_{14}H_{13}N_3O_4 \cdot C_6H_3N_3O_7$	46,7	3,3	16,5	46,5	3,1	16,3	60
VIIIa	The same	36	172,5	$C_{14}H_{13}N_3O_4 \cdot C_6H_3N_3O_7$	46,6	2,8	16,5	46,5	3,1	16,3	73
VIIIb	The same	60	180*	$C_{15}H_{15}N_3O_4 \cdot C_6H_3N_3O_7$	47,7	3,3	16,0	47,5	3,4	15,9	70
IXa	The same	60	156	$C_{14}H_{13}N_3O_5$	55,2	4,0	14,0	55,4	4,3	13,9	79
IXb	The same	60	129*	$C_{15}H_{15}N_3O_5 \cdot C_6H_3N_3O_7$	45,9	3,5	15,4	46,1	3,3	15,4	77
Xa	DMF	15	178	$C_{13}H_{11}N_3O_4$	56,8	4,3	15,6	57,1	4,0	15,4	65
X	The same	12	218	$C_{14}H_{13}N_3O_4$	58,8	4,3	14,4	58,5	4,5	14,6	68

* Picrate; crystallized from butanol and ethanol.

TABLE 2. 1-Aryl-2-styrylimidazoles

Compound	Aryl	Reaction time, h	Picrate mp, °C	Empirical formulas of the picrates	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
XVIa*	2-Nitrophenyl	72	168	$C_{17}H_{13}N_3O_2 \cdot C_6H_3N_3O_7$	52,8	2,9	16,6	53,1	3,1	16,2	25
XVIb			172,5								
XVIIa†	4-Nitrophenyl	48	204	$C_{17}H_{13}N_3O_2 \cdot C_6H_3N_3O_7$	52,8	3,2	16,3	53,1	3,1	16,2	30
XVIIb			208								
XVIIIa	2-Nitro-4-(methoxyphenyl)	72	226	$C_{18}H_{15}N_3O_3 \cdot C_6H_3N_3O_7$	52,7	3,6	15,5	52,4	3,3	15,2	50
XVIIIb†			236								

* Crystallized from butanol.

† Crystallized from ethanol; XVIII was crystallized from methanol.

TABLE 3

Compound	R	Reaction time,* h	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
XXI	1-Phenyl-2-imidazolyl	6	161	$C_{24}H_{22}N_4$	78,5	6,2		78,7	6,0		50
XXII	1-(o-Nitrophenyl)-2-imidazolyl	16	62	$C_{24}H_{21}N_5O_2$	70,4	5,4		70,1	5,1		2—4
XXIII	1-(p-Nitrophenyl)-2-imidazolyl	20	173	$C_{24}H_{21}N_5O_2$	69,8	5,1	16,7	70,1	5,1	17,0	4—6
XXIV	5-Nitro-1-methyl-benzimidazolyl	1	230	$C_{23}H_{21}N_5O_2$	68,9	5,2	16,9	69,2	5,3	17,5	~ 100

* The reaction was carried out in methanol or ethyl acetate.

1-(o-Nitro-p-methoxyphenyl)imidazole (XII). This compound was similarly synthesized, but the mixture was refluxed for 10 h to give light-yellow needles with mp 97-98° (from aqueous alcohol) in 92% yield. Found: C 54.5; H 4.5; N 19.1%. $C_{10}H_9N_3O_3$. Calculated: C 54.8; H 4.1; N 19.2%.

1-(p-Nitrophenyl)-2-hydroxymethylimidazole (XIII). This compound was obtained in 78% yield from 1-(p-nitrophenyl)imidazole and 32% solution of formaldehyde by the method in [6]. The yellow prisms had mp 203° (from ethanol). Found: C 54.9; H 4.5; N 19.4%. $C_{10}H_9N_3O_3$. Calculated: C 54.8; H 4.1; N 19.2%.

Aldehydes I-V were synthesized by oxidation of 1-aryl-2-hydroxymethylimidazoles [3] with active manganese dioxide at 20°. In the isolation of V, a product of condensation with the aldehyde (XIV) forms during removal of the acetone by distillation. Prolonged refluxing of the solution of V in acetone made it possible to obtain XIV in quantitative yield.

1-(p-Nitrophenyl)-2-formylimidazole (V). This compound was obtained in 80% yield as light-yellow prisms with mp 193° (from benzene). Found: C 55.4; H 3.3; N 19.5%. $C_{10}H_7N_3O_3$. Calculated: C 55.3; H 3.2; N 19.4%.

1-(p-Nitrophenyl)-2-(α-hydroxy-γ-oxobutyl)imidazole (XIV). This compound was obtained as pale-yellow needles with mp 218° (from methanol). Found: C 56.9; H 4.8; N 15.6%. $C_{13}H_{13}N_3O_4$. Calculated: C 56.7; H 4.7; N 15.3%.

Methyl 1-(o-Nitrophenyl)-β-2-imidazolylacrylate (VIIa). A solution of 0.54 g (2.5 mmole) of II and 0.84 g (2.5 mmole) of carbomethoxytriphenylphosphorane [9] in 3 ml of benzene was heated on a water bath for 36 h, after which the benzene was evaporated, and the residue was dissolved in chloroform. The chloroform solution was chromatographed on aluminum oxide (with elution by ether) to give 0.4 g of product (Table 1).

1-(o-Nitrophenyl)-β-2-imidazolylacrylic Acid (XVa). A 0.3-g (1 mmole) sample of VIIa was introduced at 20° into 4 ml of 15% alcoholic potassium hydroxide. After 3-4 h, the precipitate was removed by filtration, washed with water and a small amount of alcohol, and dissolved in 4 ml of hot water. Compound XVa was isolated by acidification of the solution with concentrated hydrochloric acid. The precipitate was removed by filtration and washed with water to give a quantitative yield of pale-yellow needles with mp 231° (from aqueous alcohol). Found: C 55.3; H 3.5; N 16.5%. $C_{12}H_9N_3O_4$. Calculated: C 55.6; H 3.5; N 16.2%.

1-(p-Nitrophenyl)-β-2-imidazolylacrylic Acid (XVb). This compound was similarly obtained as colorless needles with mp 276° (from alcohol). Found: C 55.4; H 3.5%. $C_{12}H_9N_3O_4$. Calculated: C 55.6; H 3.5%.

1-(o-Nitrophenyl)-2-styrylimidazole (XVI). A 1.88-g (6 mmole) sample of triphenylbenzylphosphonium chloride was added to a solution of sodium ethoxide, obtained from 0.15 g (6.5 mmole) of sodium and 10 ml of absolute ethanol, and the mixture was stirred vigorously for 5 min. A solution of 1.08 g (5 mmole) of II in 5 ml of absolute alcohol was then added dropwise, after which the mixture was stirred at 20° for another 24 h and at 60° for 48 h. The alcohol was vacuum-evaporated, and the semicrystalline mass was extracted with ether. The residue contained unchanged phosphonium salt. The ether was evaporated, and the resulting oil was chromatographed on aluminum oxide with chloroform, with collection of the layer with R_f 0.7. The isomers were then separated on aluminum oxide with elution by ether, in which R_f of XVIa is 0.9 and R_f of XVIb is 0.8. The picrate of XVIa was obtained as lemon-yellow needles with mp 168° (from butanol), while the picrate of XVIb had mp 172.5° (from DMF—water) (Table 2).

1-Phenyl-2-(2'-imidazolal)hydroxyaniline (XIX). A saturated aqueous solution of 1.72 g (10 mmole) of I was added to a suspension of 1.10 g (10 mmole) of o-aminophenol in alcohol, and the mixture was heated on a water bath for 30 min. The resulting solution was allowed to stand in a refrigerator for 2 days, and the precipitate was removed by filtration, washed with ether, and dried in a vacuum desiccator to give 2.18 g (83%) of light-yellow needles with mp 131-132° (from alcohol). Found: N 15.9%. $C_{16}H_{13}N_3O$. Calculated: N 16.0%.

1-Phenyl-2-imidazolal-2'-hydroxy-5'-nitroaniline (XX). Alcohol solutions of 0.30 g (1.7 mmole) of I and 0.27 g (1.75 mmole) of p-nitro-o-aminophenol were mixed, and the resulting precipitate was removed by filtration and washed with alcohol and ether to give 0.48 g (89%) of a product with mp 173-174.5° (from alcohol). Found: N 18.2%. $C_{16}H_{12}N_4O_3$. Calculated: N 18.2%.

1-Phenyl-2-(N,N'-diphenylimidazolidinyl)imidazole (XXI). A solution of 0.43 g (2.5 mmole) of I and 0.55 g (2.5 mmole) of 1,2-dianilinoethane in 2 ml of methanol was refluxed for 6 h and allowed to stand overnight in a refrigerator; the next day, the precipitate was removed by filtration and washed with ether to give 0.40 g of colorless silky needles (from methanol) (Table 3).

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