

REACTIONS OF α,β -UNSATURATED KETONES WITH ARYLACETONITRILES

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1,3-Diaryl-2-propene-1-ones *I* react with arylacetoneitriles *II* in the presence of sodium ethoxide at room temperature to give a single diastereomer of the corresponding 2,3-diaryl-4-arylbutyronitriles *III*. The structures of the reaction products were established by infrared, nuclear magnetic resonance, and mass spectral data as well as elemental analysis. The diastereomeric purity was determined by NMR measurements using lanthanide shift reagents. The observed resonances did not show any resolved diastereomeric proton signals.

The reactions of 1,3-diaryl-2-propene-1-ones *I* with ethyl phenylacetate in the presence of sodium ethoxide have been reported using different stoichiometric amounts of the starting materials. For example, when the reactions were carried out with equal stoichiometric amounts¹, the products were found to be 4-aryl-3,6-diphenyl-3,4-dihydro-2*H*-pyran-2-ones. However, when the same reactions were carried out using two moles of sodium ethoxide, two moles of 1,3-diaryl-2-propene-1-ones, and one mole of ethyl phenylacetate², the reaction products were found to be 5-benzoyl-4,6-diaryl-3,7-diphenyl-1,4,5,6,7-pentahydro-1*H*-cyclohexanones, respectively.

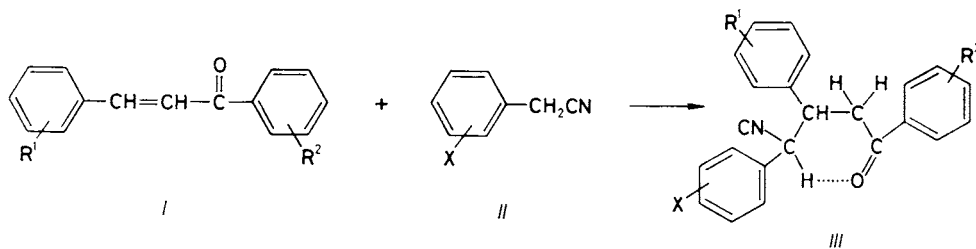
Al-Hajjar and his coworkers³⁻⁵, also described the condensation of these α,β -unsaturated ketones with thiourea, guanidine hydrochloride, and cyanoacetamide. The corresponding products were found to be 4,6-diaryl-3,4-dihydropyrimidine-2(1*H*)-thione, 2-amino-4,6-diarylpyrimidines and 4-aryl-3-cyano-6-phenyl-3(1*H*)pyridones, respectively.

In the present work, the reactions of 1,3-diaryl-2-propene-1-ones *I* with arylacetoneitriles *II* were carried out in the presence of a suspension of sodium ethoxide in dry ether. 2,3-Diaryl-4-arylbutyronitrile *III* was obtained as a result of Michael condensation of the carbanion ArCHCN^- with the double bond of the α,β -unsaturated ketone *I*, as shown in Scheme 1.

The structures of butyronitriles *IIIa-e* were determined by nuclear magnetic resonance, infrared and mass spectral data as well as by elemental analysis. The incremental addition of the achiral lanthanide shift reagent, europium(III)-tris-

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(1,1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate); $\{\text{Eu}(\text{Fod})_3\}$, to the butyronitriles resulted in a large induced shift in NMR spectra (Table I) without resolving any proton signals due to different diastereomers. This observation is indicative⁶ of the formation of only one diastereomer of the newly formed product. In addition, this conclusion is supported by the sharp melting point and chromatographic purity of the compounds isolated. The induced chemical shift data shown in Table I imply that the keto group probably does not coordinate preferentially the lanthanide shift reagent over the nitrile group, in disagreement with Grandjean⁷ and Mayo⁸ order of donation

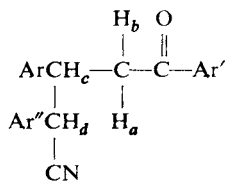


In formulae I - III: *a*, $\text{R}^1 = \text{R}^2 = \text{H}$; $\text{X} = p\text{-Cl}$; *b*, $\text{R}^1 = \text{R}^2 = p\text{-CH}_3\text{O}$; $\text{X} = o,o\text{-Cl}_2$; *c*, $\text{R}^1 = \text{H}$; $\text{R}^2 = p\text{-CH}_3\text{O}$; $\text{X} = p\text{-Cl}$; *d*, $\text{R}^1 = \text{H}$; $\text{R}^2 = p\text{-CH}_3\text{O}$; $\text{X} = o,o\text{-Cl}_2$; *e*, $\text{R}^1 = \text{R}^2 = p\text{-CH}_3\text{O}$; $\text{X} = p\text{-Cl}$

SCHEME 1

TABLE I

Induced chemical shift ($\Delta\delta$) for each proton type at (1 : 1) molar ratios of lanthanide shift reagent, europium(III)-tris(1,1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate), and the 2,3-diaryl-4-aryloxybutyronitriles, IIIa-e



Compound	H_a	H_b	H_c	H_d	Aromatics	OCH_3
IIIa	1.17	1.67	1.92	1.52	0.49	—
IIIb	0.38	0.57	0.92	1.36	0.15	0.08
IIIc	1.92	2.24	2.42	2.20	1.00	0.15
III d	2.64	2.91	1.95	1.90	0.75	0.11
III e	2.17	3.50	2.18	2.21	1.08	0.04
						0.06

power (ketone > nitrile). This could be explained by the presence in the butyronitriles of one or more methoxy groups that also may donate electrons to the central atom of the shift reagent and thus compete with the carbonyl group. As a result of this effect, there was no trend in the induced shift values which made the interpretation of these values more complicated. In spite of this, the use of the lanthanide shift reagent NMR as a method for determining the diastereometric purity of these non-rigid polyfunctional butyronitriles seems reasonable, since the formation of a single diastereomer was also confirmed by the fact that only a small difference in chemical yields of compounds *IIIa–e* was observed before and after crystallization. This excludes the possibility of selective crystallization of one diastereomer from a mixture containing both of them.

EXPERIMENTAL

IR spectra were recorded in KBr pellets using a Pye-Unicam SP 300 instrument. ^1H NMR spectra were determined on a Bruker WP 80-SY instrument in C^2HCl_3 solutions containing tetramethylsilane as internal standard. Mass spectra were measured on a 7070-E VG Analytical organic mass spectrometer. Compounds were analyzed by M-H-W Laboratories Phoenix, Arizona, U.S.A.. Melting points were determined on an electrothermal melting point apparatus and were uncorrected.

2-(*p*-Chlorophenyl)-3-phenyl-4-benzoylbutyronitrile (*IIIa*)

p-Chlorobenzyl cyanide (4.55 g) was dissolved in ether (150 ml) containing sodium ethoxide (2.0 g) followed by addition of 1,3-diphenyl-2-propene-1-one (6.24 g). The mixture turned deep red after one hour and was evaporated to give a gummy material which solidified upon treatment, with light petroleum and standing in air current. The resulting solid was crystallized from aqueous ethanol as yellow granules, 6.65 g (62%), m.p. 121–122°C. IR spectrum (KBr) ν , cm^{-1} : 1 600 (aromatic), 1 690 (C=O), 2 240 (C \equiv N). NMR spectrum δ (C^2HCl_3): 6.98–8.05 (14 H, m, aromatics), 4.53 (1 H, d, $J = 4.3$ Hz, Ar $^{\alpha}$ CHCN), 3.68 (1 H, m, ArCH—), 3.81 (1 H, dd, $J = 10.3$ Hz, $J = 7.1$ Hz, —CH—C—), 3.46 (1 H, dd, $J = 10.3$, $J = 7.2$ Hz, —CH—C—). For $\text{C}_{23}\text{H}_{18}\text{ClNO}$ (359.5) calculated: 76.77% C, 5.01% H, 9.87% Cl, 3.89% N; found: 76.59% C, 5.08% H, 9.78% Cl, 3.78% N. Mass spectrum (m/z): 359, 361 (M^+).

2-(*o,o*-Dichlorophenyl)-3-(*p*-methoxyphenyl)-4-(*p*-methoxybenzoyl)butyronitrile (*IIIb*)

o,o-Dichlorobenzyl cyanide (5.60 g) was dissolved in ether (200 ml) containing sodium ethoxide (2.0 g). To this mixture, 1,3-bis(*p*-methoxyphenyl)-2-propene-1-one (8.0 g) was added. Precipitate formed after 30 min was filtered off and crystallized from glacial acetic acid to supply 6.5 g (48%) of *IIIb*, m.p. 157–159°C. IR spectrum (KBr) ν , cm^{-1} : 1 595 (aromatic), 1 690 (C=O), 2 240 (C \equiv N). NMR spectrum δ (C^2HCl_3): 6.77–7.74 (11 H, m, aromatics), 4.99 (1 H, d, $J = 11.2$ Hz, Ar $^{\alpha}$ CHCN), 4.40 (1 H, m, ArCH—), 3.82 (3 H, s, OCH_3), 3.76 (3 H, s, OCH_3), 3.24 (1 H, dd, $J = 10.1$ Hz, $J = 6.8$ Hz, —CH—C—), 2.85 (1 H, dd, $J = 10.1$ Hz, $J = 6.9$ Hz, —CH—C—).

For $C_{25}H_{21}Cl_2NO_3$ (454) calculated: 66.08% C, 4.63% H, 15.64% Cl, 3.08% N; found: 66.32% C, 4.51% H, 15.69% Cl, 3.01% N. Mass spectrum (m/z): 453, 455, 457 (M^+).

2-(*p*-Chlorophenyl)-3-phenyl-4-(*p*-methoxybenzoyl)butyronitrile (*IIIc*)

p-Chlorobenzyl cyanide (4.55 g) was dissolved in ether (150 ml) containing sodium ethoxide (2.0 g). To this mixture, 1-(*p*-methoxyphenyl)-3-phenyl-3-propene-1-one (7.40 g) was added. The mixture turned deep red immediately. After 10 min, a precipitate was formed which was filtered off and crystallized from acetic acid as yellow plates, 5.87 g (50%), m.p. 167–169°C. IR spectrum (KBr) ν , cm^{-1} : 1 600 (aromatic), 1 700 (C=O), 2 230 (C≡N). NMR spectrum δ (C^2HCl_3): 6.66–8.04 (12 H, m, aromatics), 4.42 (1 H, d, $J = 4.2$ Hz, Ar^rCHCN), 3.75 (3 H, s,

OCH_3) 3.90 (1 H, m $ArCH-$), 3.76 (1 H, dd, $J = 10.3$ Hz, $J = 7.2$ Hz, $-CH-\overset{O}{\parallel}C-$), 3.35

(1 H, dd, $J = 10.3$ Hz, $J = 7.4$ Hz, $-CH-\overset{O}{\parallel}C-$). For $C_{24}H_{20}ClNO_2$ (389.5) calculated: 73.94% C, 5.13% H, 9.11% Cl, 3.59% N; found: 74.02% C, 5.50% H, 9.32% Cl, 3.63% N. Mass spectrum (m/z): 389, 391 (M^+).

2-(*o,o*-Dichlorophenyl)-3-phenyl-4-(*p*-methoxybenzoyl)butyronitrile (*IIIa*)

o,o-Dichlorobenzyl cyanide (5.64 g) was dissolved in ether (150 ml) containing sodium ethoxide (2.0 g). Then 1-(*p*-methoxyphenyl)-3-phenyl-2-propene-1-one (7.14 g) was added. The mixture was stirred for 12 h meanwhile a precipitate was formed which was filtered off and crystallized from acetic acid, 6.93 g (55%), m.p. 169–171°C. IR spectrum (KBr) ν , cm^{-1} : 1 605 (aromatic), 1 680 (C=O), 2 245 (C≡N). NMR spectrum δ (C^2HCl_3): 6.83–7.75 (12 H, m, aromatics), 5.02 (1 H, d, $J = 11.0$ Hz, Ar^rCHCN), 4.45 (1 H, m, $ArCH$), 3.78 (3 H, s, OCH_3), 3.44 (1 H,

dd, $J = 10.2$ Hz, $J = 7.0$ Hz, $-CH-\overset{O}{\parallel}C-$), 2.97 (1 H, dd, $J = 10.2$ Hz, $J = 6.9$ Hz, $-CH-\overset{O}{\parallel}C-$).

For $C_{24}H_{19}Cl_2NO_2$ (424) calculated: 69.92% C, 4.48% H, 16.75% Cl, 3.30% N; found: 66.63% C, 4.55% H, 16.62% Cl, 3.45% N. Mass spectrum (m/z): 423, 425, 427 (M^+).

2-(*p*-Chlorophenyl)-3-(*p*-methoxyphenyl)-4-(*p*-methoxybenzoyl)butyronitrile (*IIIe*)

p-Chlorobenzyl cyanide (4.55 g) was dissolved in ether (150 ml) containing sodium ethoxide (2.0 g). To this suspension 1,3-bis(*p*-methoxyphenyl)-2-propene-1-one (8.0 g) was added. The mixture which turned red immediately was stirred for 24 h and poured into water (100 ml). The ether layer was dried over magnesium sulfate and evaporated to furnish a gummy residue which was treated with light petroleum to give a brown solid which was crystallized from methanol as yellow crystals, 7.2 g (57%), m.p. 122–124°C. IR spectrum (KBr) ν , cm^{-1} : 1 600 (aromatic), 1 685 (C=O), 2 245 (C≡N). NMR spectrum δ (C^2HCl_3): 6.68–8.02 (12 H, m, aromatics), 4.48 (1 H, d, $J = 4.2$ Hz, Ar^rCHCN), 3.95 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 3.80 (1 H, m,

$ArCH-$), 3.89 (1 H, dd, $J = 10.4$ Hz, $J = 7.1$ Hz, $C-\overset{O}{\parallel}CH-$), 3.54 (1 H, dd, $J = 10.4$ Hz,

$J = 7.2$ Hz, $CH-\overset{O}{\parallel}C-$). For $C_{25}H_{22}ClNO_3$ (419.5) calculated: 71.51% C, 5.24% H, 8.46% Cl, 3.34% N; found: 71.73% C, 5.39% H, 8.56% Cl, 3.62% N. Mass spectrum (m/z): 419, 421 (M^+).

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