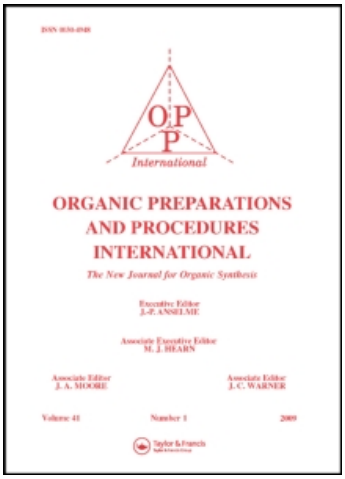

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PREPARATION OF 3-ARYL-3-OXO-2-TOSYLOXYIMINOPROPANENITRILES

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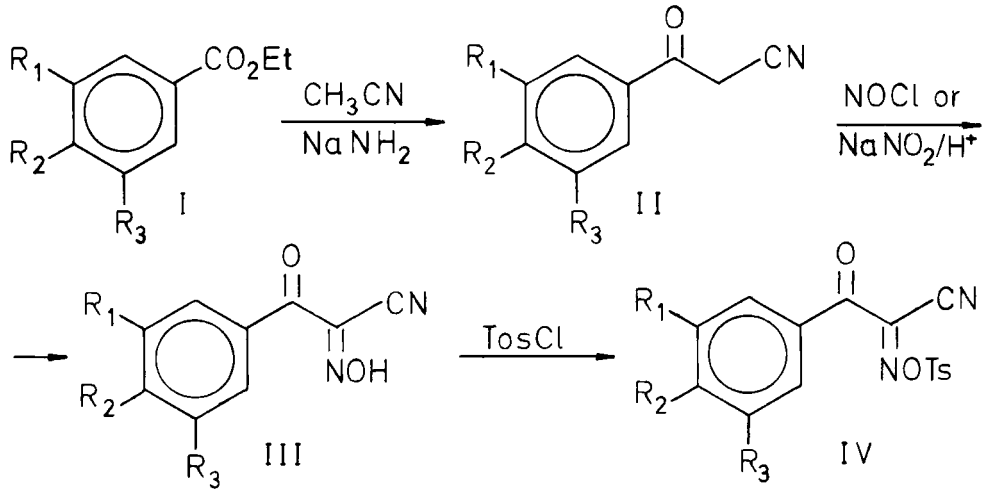
In recent years (O-p-tosylisonitroso)malononitrile, a highly reactive azomethine, has proved to be a useful reagent for the synthesis of a variety of nitrogen heterocycles.[1] In connection with our work on heterocyclic synthesis, we now report the preparation of (O-p-tosylisonitroso)benzoylacetonitrile (3-aryl-3-oxo-2-tosyloxyiminopropanenitrile) and derivatives.



The synthesis involves three steps starting from aromatic esters (I) which, upon reaction with acetonitrile in sodium amide liquid ammonia, affords benzoylacetonitriles (II) in good

yield and purity. Conversion of these compounds into ketoximes (III) by nitrosation at the methylene group can be carried out by treatment with either nitrosyl chloride in chloroform (method A) or sodium nitrite in acetic acid (method B). The yields obtained by both methods are similar. When nitrosyl chloride was used as the reagent, the reaction time was critical and had to be very short in order to avoid further reaction of the oxime. Best results were obtained by bubbling nitrosyl chloride through a benzoylacetonitrile solution for four minutes followed by quenching the reaction by pouring the solution into cold water to hydrolyze any unreacted nitrosyl chloride. Longer reaction times gave less pure products in lower yields. With a reaction time of thirty minutes, for instance, the yields were about halved. The same result was obtained when the reactions were carried out in a sealed tube in a variety of temperatures and reaction times. It must be pointed out that the nitrosation of 3,5-dimethoxybenzoylacetonitrile (IIg) could not be achieved. The physical and spectroscopic data of compounds III are collected in tables I and II. The position of the OH stretching band at 3220-3290 cm^{-1} is in good agreement with the reported values for a variety of oximes;[2,3] the cyano stretching band is very weak, as expected for a β-ketonitrile.[4] In the ^{1}H-NMR spectra, the hydroxyl proton appears as a very broad band at 10-14 ppm, which is near the value reported for simple oximes.[5-7] In some instances, this band is so broad that it is barely noticeable.

Compounds IV (tables 1 and 2) can be prepared by reaction of ketoximes III with tosyl chloride in dry pyridine or in chlo-

roform-triethylamine. Best results were obtained at room temperature with stoichiometric amounts of reagents and reaction times not exceeding 15 minutes. The yields thus obtained are good. Like other O-tosyl derivatives of simple oximes,[8-10] compounds IV are rather unstable compounds. The expected product could not be obtained from tosylation of IIIh and m-nitrobenzoic acid instead of the tosyl derivative is obtained from the tosylation of IIIi. A similar decomposition of simple α-hydroxyiminoketones into aromatic acids has been reported.[11] The cyano stretching band in compounds IV at about 2240 cm^{-1} is somewhat stronger than in compounds III.

TABLE 1. Yields and melting points of compounds II-IV[a]

				II		III[b]			IV[c]	
	R_1	R_2	R_3	mp (°C)	Yield (%)	mp (°C)	Yiel (%) A	B	mp (°C)	Yield (%)
a	H	H	H	79-80	91[d]	121-122	85	80	117-119	75
b	H	CH_3	H	103-104	93	139-141	60	83	118-121[e]	58
c	CH_3	H	CH_3	141-143	90	122-124	55	50	120-122	72
d	H	CH_3O	H	129-130	86	136-137	70	-	119-120	83
e	H	Cl	H	127-129	97[f]	130-132	65	61	115-117	80
f	H	Ph	H	115-116	80	176-178	75	89	146-148	69
g	CH_3O	H	CH_3O	123-125	91	-	-	-	-	-
h	H	Me_2N	H	131-132	77	179-181	52	-	-	-
i	NO_2	H	H	151-152	38[g]	152-154	50	57	-	-

a) Compounds II and III were recrystallized from ethanol and benzene respectively, unless otherwise stated. b) A and B refer to methods A and B (see text). c) Recrystallized from benzene-n-heptane unless otherwise stated. d) Recrystallized from hexane. e) Recrystallized from benzene. f) Recrystallized from methanol. g) This compound was obtained by nitration of benzoylacetonitrile (IIa). Lit. mp. for IIa, IIb, IId, IIe, see ref. 12; lit. mp. for IIg and IIh, see ref. 13; lit. mp. for IIi, see ref. 14; lit. mp. for IIIa-b, see ref. 16; lit. ref. for IVf see ref. 17.

EXPERIMENTAL SECTION

Melting points were determined with a Buchi apparatus in capillary tubes and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 257 and a Perkin-Elmer 580, with scale expansion for the identification of the cyano stretching band of some compounds. The ^{1}H-NMR spectra were measured with a Varian T-60A. A Varian MAT 711 was used for the mass spectra. Microanalysis were performed by Centro Nacional de Química Orgánica del C.S.I.C. of Madrid.

Benzoylacetonitriles (II).- Benzoylacetonitriles (IIa, IIb, IId, IIe) were prepared as reported.[12] p-N,N-Dimethylaminobenzoylacetonitrile (IIh) and 3,5-dimethoxybenzoylacetonitrile (IIg) were obtained as described[13] and m-nitrobenzoylacetonitrile (IIi) was prepared by Long's method.[14] 3,5-Dimethylbenzoylacetonitrile (IIc) and p-phenylbenzoylacetonitrile (IIf), not previously reported in the literature, were obtained by the following general procedure.

Ammonia gas (600 ml) was condensed in a two-necked flask cooled in Dry Ice and equipped with a Dry Ice condenser. Then 600 ml of dry diethyl ether were added followed by one mole of sodium in several portions, together with a small amount of ferric chloride (~50-100 mg); the mixture was stirred until the sodium was dissolved. Then a solution of 2 moles of acetonitrile in 50 ml of dry ether was added. After five minutes, one mole of the appropriate ethyl benzoate in 70 ml of dry ether was added. The solution was stirred under reflux (Dry Ice condenser) for 1 hr. and then the ammonia was allowed to evaporate slowly and 250 ml of ether were added. The mixture was extracted with water and the aqueous phase was washed several times with ether and filtered with Hyflo Super-Cel to remove suspended, colloidal material. The filtrate was precipitated with 6N hydrochloric acid and the solid benzoylacetonitrile was collected; the product thus obtained was pure enough for use without further purification.

3,5-Dimethylbenzoylacetonitrile (IIc).- This compound was obtained in 90% yield from 0.12 mole of ethyl 3,5-dimethylbenzoate and 0.24 mole of acetonitrile, mp. 142-143° (from ethanol).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 3.08.

Found: C, 76.01; H, 6.38; N, 7.82
IR (KBr pellet): 3010, 2960, 2920, 2255, 1685, 1605, 1595, 1445 cm^{-1}. NMR (DMSO-d_6: δ 2.25 (s, 6H, CH_3), 4.55 (s, 2H, CH_2) 7.40 (s, 2H, arom.), 7.15 (s, 1H, arom.).

p-Phenylbenzoylacetonitrile (IIf).- This compound was obtained in 80% yield from 0.03 mole of ethyl p-phenylbenzoate and 0.06 mole of acetonitrile. mp. 115-116° (from ethanol). A small amount of p-phenylbenzoic acid was obtained from the mother liquor.
Anal. Calcd. for $C_{15}H_{11}NO$: C, 81.46; H, 4.97; N, 6.33.
Found: C, 81.37; H, 4.82; N. 6,25.
IR (KBr pellet): 2960, 2920, 2260, 1690, 1405 cm^{-1}. NMR (DMSO-d_6): δ 4.63 (s, 2H, CH_2), 7.1-7.9 (m, 9H, arom).

3-Aryl-2-hydroxyimino-3-oxopropanenitriles (III). General Procedures. Method A).- To a solution of the appropriate benzoylacetonitrile (II) (0.01 mole) in 40 ml of chloroform was bubbled a stream of nitrosyl chloride[15] (purified just prior to use by low temperature distillation using a Dry Ice condenser) for 4 minutes. The solution was poured inmediately into water and ether was added until the organic phase floats over the water. The organic phase was washed several times with water and extracted with several portions of 5% sodium bicarbonate. The combined aqueous extracts were acidified with 6N hydrochloric acid. Compounds III either precipitated and were filtered or were extracted into ether and the extract evaporated in vacuum. From the chloroform-ether solution can be recovered a small amount of impure III.

Method B).-To a solution of 0.01 mole of the appropriate benzoylacetonitrile in the minimum amount of acetic acid cooled in an ice bath was added 0.01 mole of sodium nitrite dissolved in 10 ml of water. Stirring was continued at room temperature for 1 hr. and the solution was then poured into ice water. The solid thus formed was collected and washed well with cold water. In some instances, the product remained in solution and the solution had to be concentrated by vacuum evaporation before precipitation began. In the case of IIIc and IIIi, the acetic acid solution was neutralized with 10% sodium bicarbonate and

TABLE 2. Combustion Analyses and spectral data of III and IV

	Combustion Analysis (Found) C	H	N	S	NMR[a]	IR[b]
IIIa	62.06 (61.98)	3.44 (3.51)	16.09 (16.32)		7.2-7.9(m,5H, ArH)	3280, 2238 1650[c]
IIIb	63.85 (64.05)	4.25 (4.22)	14.88 (15.07)		7.1-7.9(m,4H,ArH) 2.3(s,3H,CH_3)	3290, 2240 1650[d]
IIIc	65.47 (65.72)	4.94 (4.77)	13.85 (14.00)		7.4(s,2H,ArH) 7.1(s,1H,ArH) 2.3(s,6H,CH_3)	3220, 2260 1665
IIId	58.85 (58.87)	3.92 (3.85)	13.72 (13.86)		6.8-7.9(m,4H,ArH) 3.8(s,3H, CH_3O)	3200, 2234 1630
IIIe	51.79 (51.49)	2.39 (2.52)	13.52[e] (13.77)		7.2-7.8(m,4H, ArH)	3220, 2250 1670
IIIf	72.02 (71.79)	3.99 (4.05)	11.19 (11.49)		7.20-7.95(m, 9H, ArH)	3260, 2234 1685
IIIh	60.30 (60.58)	5.02 (5.01)	19.35 (19.48)		6.4-7.8(m,4H,ArH) 3.0(s,6H,CH_3)	3240, 2231 1625
IIIi	49.34 (49.63)	2.27 (2.33)	19.17 (19.17)		7.2-8.6(m, 4H, ArH)	3250, 2236 1670
IVa	58.55 (58.34)	3.65 (3.74)	8.53 (8.51)	9.76 (9.69)	7.2-7.8(m,9H,ArH) 2.4(s,3H,CH_3)	2240, 1675[f]
IVb	59.64 (59.69)	4.12 (4.29)	8.18 (8.37)	9.36 (9.64)	6.90-7.76(m,8H, ArH), 2.35(d,6H, CH_3)	2240, 1680
IVc	60.67 (60.93)	4.49 (4.72)	7.86 (7.94)	8.98 (9.10)	7.17-7.72(m,7H, ArH), 2.43(s,3H, CH_3), 2.26(s,6H, CH_3)	2240, 1660
IVd	57.00 (56.74)	3.90 (3.99)	7.81 (8.05)	8.95 (9.18)	6.8-7.83(m,8H,ArH) 3.82(s,3H,CH_3O), 2.43(s,3H,CH_3)	2239, 1660
IVe	52.96 (53.03)	3.03 (3.19)	7.72 (7.25)	8.82[g] (8.69)	7.08-7.7(m,8H,ArH) 2.45(s,3H,CH_3)	2238, 1680
IVf	65.33 (65.33)	3.99 (4.06)	6.93 (6.87)	7.93 (8.15)	7.23-7.85(m,13H, ArH), 2.40(s,3H, CH_3)	2240, 1665

a) All the NMR spectra were recorded at 60MHz in DMSO-d_6. b) The IR spectra were obtained in KBr pellet. c) Mass spectrum of IIIa 174(M^+,64), 129(18),105(100), 77(90). d) Mass spectrum of IIIb: 188(M^+,27), 172(100), 171(75), 119(61), 91(32). e)Cl:17.02(17.26). f) Mass spectrum of IVa: 328(M^+,2), 172(5), 156(9), 155(100), 105(37). g) Cl: 9.79(10.11).

extracted with ether, dried over magnesium sulphate and evaporated in vacuum.

3-Aryl-3-oxo-2-tosyloxyiminopropanenitriles (IV). General Procedure.

Method A.- To a solution of 0.02 mole of the appropriate 2-hydroxyimino-3-oxopropanenitrile (III) in the minimal amount of dry pyridine (about 3-10 ml) was added at room temperature with stirring, a solution of 0.02 mole of tosyl chloride in about 4 ml of dry pyridine. After stirring for five minutes, the reaction mixture was poured into ice water. The solid thus formed was collected and washed well with 6N hydrochloric acid and then with water. Method B.- To a solution of the appropriate III (0.004 mole) in about 20 ml of chloroform was added a solution of 0.004 mole of tosyl chloride in 4 ml of chloroform together with 0.004 mole of triethylamine. After stirring for about five minutes, the reaction mixture was poured into ice water and transferred to a separatory funnel. The organic phase was washed several times with water and dried over magnesium sulfate. Evaporation of the solvent under vacuum afforded the corresponding compound IV. These compunds were purified by dissolving the sample at room temperature (or by gentle warming) followed by cooling the solution.

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