BECKMANN REARRANGEMENT OF 5-ARYLFURFURAL OXIMES

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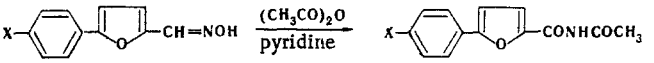
The acylation of 5-arylfurfural oximes with acetic anhydride in the presence of pyridine is accompanied by Beckmann rearrangement and gives 5-arylpyromucic acid acetamides. Under the same conditions, 5-arylpyromucic acid nitriles are obtained from aldoxime anti-acetates.

In an investigation of various conditions for the acetylation of 5-arylfurfural oximes we observed that the acetylation of oximes with acetic anhydride gives their O-acetyl derivatives, whereas the use of a mixture of acetic anhydride and pyridine as the acylating agent gives 5-arylfuran-2-carboxylic acid acetamides (Ia-e), i.e., the products of a Beckmann rearrangement.



Ia-e

Both the syn and anti isomers of arylfurfural oximes were subjected to conversion to acetamides. Acetamides (Ia-e) of pyromucic acid were obtained from them in high yields, and the described conversion can be proposed as a method for the synthesis of amides of this type.

The presence in the IR spectra of carbonyl absorption at 1675-1686 and 1705-1710 cm^{-1} and of an NH group at 3240-3260 cm^{-1} and the presence in the PMR spectra of signals of NH protons at 10.94-11.40 ppm and protons of an acetyl group at 2.4 ppm and the absence of signals of aldehyde protons confirm the proposed structure of Ia-e (see Table 1).

TABLE 1. Data from the PMR Spectra of the Synthesized Compounds

Compound	δH_{ald}	$\delta COCH_3$	δ3-H	δ4-H	δ of the aromatic ring protons	δCH_3 or OCH_3	δNH	Solvent
Ia	—	2,40	7,60	7,10	7,25—7,85	2,35	10,96	$(CD_3)_2SO$
Ib	—	2,40	7,59	7,02	6,99—7,93	3,82	10,94	$(CD_3)_2SO$
Ic	—	2,39	7,62	7,18	7,30—8,05	—	11,01	$(CD_3)_2SO$
Id	—	2,41	7,61	7,24	7,63—7,96	—	11,40	$(CD_3)_2SO$
Ie	—	2,40	7,61	7,22	7,51—8,02	—	11,05	$(CD_3)_2SO$
IIa	7,74	2,26	7,31	6,71	7,10—7,64	2,34	—	$CDCl_3$
IIb	7,76	2,26	7,29	6,66	6,82—7,71	3,77	—	$CDCl_3$
IIc	7,78	2,26	7,32	6,79	7,05—7,68	—	—	$CDCl_3$
IId	7,74	2,27	7,32	6,79	7,40—7,65	—	—	$CDCl_3$
IIIa	—	—	7,09	6,59	7,12—7,64	2,32	—	$CDCl_3$
IIIb	—	—	7,07	6,51	6,81—7,67	3,79	—	$CDCl_3$
IIIc	—	—	7,06	6,62	7,19—7,71	—	—	$CDCl_3$
IIId	—	—	7,13	6,68	7,54	—	—	$CDCl_3$
IVa	7,58	—	7,34	6,99	7,23—7,86	2,29	—	$(CD_3)_2NCOD$
IVb	7,54	—	7,34	6,85	6,86—7,79	3,79	—	$(CD_3)_2NCOD$

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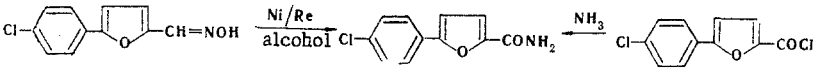
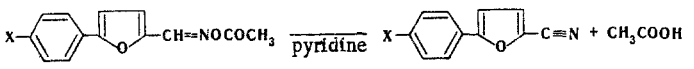
TABLE 2. 5-Arylfuran-2-carboxylic Acid Acetamides

Compound	X	mp, °C (from ethanol)	Empirical formula A	Found, %				Calc., %				IR spectrum, cm⁻¹		UV spectrum		Yield, %
				C	H	halogen	N	C	H	halogen	N	CO	NH	halogen	lg ε	
Ia	CH_3	163,5—166	$C_{14}H_{13}NO_3$	69,0	5,3			69,1	5,3			1678	3260	322	4,43	64
												1707		222	4,21	
Ib	OCH_3	178—179,5	$C_{14}H_{13}NO_4$	64,5	5,1			64,9	5,0			1675	3240	334	4,44	67
												1705		220	4,21	
Ic	H	187—189	$C_{13}H_{11}NO_3$	68,6	4,8		6,1	68,1	4,8		6,1	1685 1708	3258	315 220	4,41 4,22	70
Id	Br	213—214	$C_{13}H_{10}BrNO_3$	50,8	3,2	25,9	4,6	50,7	3,3	25,8	4,5	1686 1710	3252	330 222	4,50 4,25	70
Ie	Cl	207,5—209,5	$C_{13}H_{10}ClNO_3$	59,1	3,9			59,2	3,8			1682	3250	318	4,28	59
												1708		222	4,03	

An attempt to carry out the Beckmann rearrangement of the arylfurfural oximes under different conditions (by refluxing an alcohol solution of the oxime over a Raney nickel catalyst) was successful in only one case: 5-(p-chlorophenyl)furfural oxime was converted to 5-(p-chlorophenyl)pyromucic acid amide. The structure of the amide was confirmed by comparison with the amide synthesized from 5-(p-chlorophenyl) pyromucic acid chloride and ammonia.



The difficulty in the conversion of unsubstituted 5-arylfurfural oximes to the corresponding amides would seem to constitute evidence that the Beckmann rearrangement that we observed occurred via prior acetylation of the oximes. However, an attempt to obtain arylpyromucic acid acetamides by refluxing the oxime acetates in pyridine and also in pyridine–acetic anhydride did not give positive results. In the case of the aldoxime anti-acetate the corresponding nitriles were formed in this reaction, and the aldoxime syn-acetates remained unchanged under the conditions that we used.*



II a–d III a–d

II, IIIa X = CH_3; b X = OCH_3; c X = H; d X = Br

The observed conversions of the aldoxime anti-acetates to the nitriles of the corresponding acids are in good agreement with the literature data on this problem [1].

EXPERIMENTAL METHOD

The PMR spectra were recorded with JNM 4H-100 and C-60HL spectrometers with tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with Perkin-Elmer 457 and UR-10 spectrometers.

5-(p-Tolyl)pyromucic Acid Acetamide (Ia). A 4-ml sample of acetic anhydride was added to a solution of 1.5 g (7.5 mmole) of 5-(p-tolyl)furfural oxime [2] in 6 ml of anhydrous pyridine, and the mixture was heated for 2 h on a boiling-water bath. It was then cooled, and the resulting crystals were removed by filtration and washed with water. Acetamides Ib-e (Table 2) were similarly obtained.

O-Acetyl Derivative of 5-(p-Tolyl)furfural Oxime (IIa) (anti isomer). A mixture of 1.5 g (7.5 mmole) of the anti isomer of 5-(p-tolyl)furfural oxime (IVa) [2] (see Table 1 for data on the sterochemical struc-

*The stereochemical structures of the oximes and their acetates were established by means of the PMR spectra on the basis of a comparison of the H_{ald} chemical shifts [3]: IIa-d and IVa-b proved to be the anti isomers.

ture of oxime IVa) and 8.4 ml of acetic anhydride was heated at 60° for 20 min, after which it was poured into water, and the resulting precipitate was removed by filtration to give 1.45 g (80%) of IIa with mp 120-122 (from alcohol). Found: C 69.0; H 5.3%. $C_{14}H_{13}NO_3$. Calculated: C 69.1; H 5.3% (See Table 1 for data on the sterochemical structure of IIa).

O-Acetyl Derivative of 5-(p-Methoxyphenyl)furfural Oxime (IIb) (anti isomer). This compound was obtained as in the preceding experiment from the anti isomer of 5-(p-methoxyphenyl)furfural oxime (IVb) (see Table 1 for data on the stereochemical structure of oxime IVb). The yield of IIb, with mp 140-142° (from alcohol), was 72.%. Found: C 64.7; H 5.1%. $C_{15}H_{13}NO_4$. Calculated: C 64.9; H 5.0% (See Table 1 for data on the stereochemical structure of IIb).

O-Acetyl Derivative of 5-Phenylfurfural Oxime (IIc) (anti isomer). A mixture of 8 g (43 mmole) of the anti isomer of 5-phenylfurfural oxime [3] and 50 ml of acetic anhydride was heated at 60° for 20 min, after which it was cooled, and the resulting precipitate was removed by filtration to give 5 g (51%) of a product with mp 94-96° (from alcohol). Found: C 68.2; H 4.8; N 6.2%. $C_{11}H_9NO_2$. Calculated: C 68.1; H 4.8; N 6.1%. (See Table 1 for data on the stereochemical structure of IIc).

5-(p-Tolyl)pyromucic Acid Nitrile (IIIa). A solution of 1 g (4.1 mmole) of the anti-acetate of 5-(p-tolyl)furfural oxime (IIa) in 5 ml of dry pyridine was heated on a boiling-water bath for 2 h, after which it was cooled and poured into water. The resulting precipitate was removed by filtration and washed with water to give 0.46 g (62%) of nitrile IIIa with mp 85-87° (from alcohol); IR spectrum: 2233 cm^{-1} (CN). Found: C 78.9; H 4.8; N 7.9%. $C_{12}H_9NO$. Calculated: C 78.7; H 4.9; N 7.7%.

5-(p-Anisyl)pyromucic Acid Nitrile (IIIb). This compound, with mp 83-84° (from hexane), was obtained in 84% yield as in the preceding experiment. IR spectrum: 2232 cm^{-1} (CN). Found: C 72.1; H 4.5; N 7.0%. $C_{12}H_9NO_2$. Calculated: C 72.3; H 4.5; N 7.0%.

5-Phenylpyromucic Acid Nitrile (IIIc). This compound, with mp 72-74° (from petroleum ether), was similarly obtained in 74% yield. Found: C 78.2; H 4.3; N 8.3%; $C_{11}H_7NO$. Calculated: C 78.1; H 4.1; N 8.3%.

5-(p-Bromophenyl)pyromucic Acid Nitrile (IIId). This compound, with mp 87-88° (from alcohol), was similarly obtained in 90% yield. IR spectrum: 2232 cm^{-1} (CN). Found: C 53.3, H 2.7; Br 32.7; N 5.4%. $C_{11}H_6BrNO$. Calculated: C 53.3; H 2.4; Br 32.2; N 5.6%.

5-(p-Chlorophenyl)pyromucic Acid Chloride. A solution of 5 g (42 mmole) of thionyl chloride in 5 ml of dry benzene was added to a solution of 7.8 g (35 mmole) of 5-(p-chlorophenyl)pyromucic acid [4] in 15 ml of dry benzene, after which the mixture was refluxed or 3 h. It was then evaporated to half its original volume, and the resulting precipitate was removed by filtration to give 5.8 g (69%) of a product with mp 81-82° (from benezene). Found: C 54.5; H 2.6; Cl 29.3%. $C_{11}H_6Cl_2O_2$. Calculated: C 54.8; H 2.5; Cl 29.5%.

5-(p-Chorophenyl)pyromucic Acid Amide. A suspension of 1.1 g of freshly prepared Raney nickel in 30 ml of absolute alcohol was added to a solution of 3.2 g (14 mmole) of 5-(p-chlorophenyl)furfural oxime [3] in 60 ml of absolute ethanol, and the mixture was refluxed with stirring for 6 h. The catalyst was then removed by filtration, and the filtrate was vacuum evaporated to give 3 g (93%) of 5-(p-chlorophenyl)pyromucic acid amide with mp 195-197° (from benzene). IR spectrum: 1650 (CO) and 3340 cm^{-1} (NH). Found: C 59.5; H 3.6; N 6.3%. $C_{11}H_8ClNO_2$. Calculated: C 59.6; H 3.6; N 6.3%.

This same amide was obtained by mixing a solution of 1 g (4.1 mmole) of 5-(p-chlorophenyl)pyromucic acid chloride in 10 ml of ether with 30 ml of 25% ammonium hydroxide. This procedure gave 0.83 g (90%) of 5-(p-chlorophenyl)pyromucic acid amide with mp 195-197° (from benzene). No melting-point depression was observed for a mixture of this product with the amide obtained by rearrangement.

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