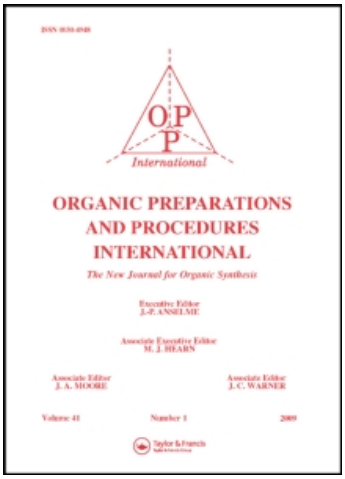


Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A CONVENIENT PREPARATION OF 1-AROYLPIPERAZINES

Mahesh Desai[a]; Jeffrey W. H. Watthey[a]; Marie Zuckerman[a]
[a] Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Ardsley, New York

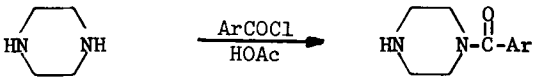
To cite this Article Desai, Mahesh , Watthey, Jeffrey W. H. and Zuckerman, Marie(1976) 'A CONVENIENT PREPARATION OF 1-AROYLPIPERAZINES', Organic Preparations and Procedures International, 8: 2, 85 — 86
To link to this Article: DOI: 10.1080/00304947609355594
URL: http://dx.doi.org/10.1080/00304947609355594

ORGANIC PREPARATIONS AND PROCEDURES INT. 8(2), 85-86 (1976)

A CONVENIENT PREPARATION OF 1-AROYLPIPERAZINES

Mahesh Desai, Jeffrey W. H. Watthey* and Marie Zuckerman
Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation
Ardsley, New York 10502

The preparation of 1-aroylpiperazines, while conceptually very simple, has not been accomplished conveniently by direct acylation of piperazine.[1,2] Indirect procedures are available[1,3] but a satisfactory one-step procedure is obviously desirable. Baltzly et al.[4] prepared 1-acetylpiperazine by the reaction of piperazine with acetic anhydride in glacial acetic acid. Presumably this procedure was successful because the piperazine was mostly present as the monoacetate salt and the product remained in that form after the acetylation. We have found that 1-aroylpiperazines can conveniently be prepared by a similar procedure, namely by treatment of piperazine with an aroyl chloride in glacial acetic acid. The method reliably gives distilled yields of analytically pure material of around 50% and is a practical method for the preparation of these substances. It has been applied to the monobenzoylation of 1,4-diazepine (see Table).



EXPERIMENTAL

1-Aroylpiperazines.- Anhydrous piperazine (43 g, 0.5 mole) was added with stirring during 30 min. to glacial acetic acid (500 ml). The temperature rose to approximately 65° and was maintained at that level until all the solid dissolved. While the temperature was kept at 65°, the aroyl chloride (0.5 mole; dissolved in 200 ml of glacial acetic acid if a solid) was

added during 1 hr. The reaction mixture was allowed to cool to room temperature and was stirred for an additional 18 hr. The solid was filtered off. In most cases this material proved to be the acetate salt of the desired product, otherwise it was piperazine acetate which was discarded. The filtrate was evaporated under reduced pressure, combined with any

TABLE. 1-Aroylpiperazines

Ar	b.p./mm (mp.)°C	Yield (%)	Formula	Analysis (Found) C	H	N
PhCO	145-7/0.05 (73-75[a])	56				
p-BrPhCO	(78-80[b])	50	$C_{11}H_{13}BrN_2O$	49.08 (49.42)	4.86 (5.07)	10.40 (10.48)
2-Cl-4-NO_2PhCO	(149-50[c])	52	$C_{11}H_{12}ClN_3O_3$	48.98 (49.28)	4.48 (4.63)	15.58 (15.32)
2-Furoyl	137-40/0.1	46	$C_9H_{12}N_2O_2$	59.98 (59.97)	6.71 (6.83)	15.55 (15.40)
2-Thienoyl	157-62/0.1	58	$C_9H_{12}N_2OS$	55.07 (55.06)	6.16 (6.49)	14.27 (14.23)
3-Thienoyl	164-8/0.1 (77-79)	60	$C_9H_{12}N_2OS$	55.07 (55.09)	6.16 (6.10)	14.27 (14.14)
PhCO[d]	166-71/0.1	56	$C_{12}H_{16}N_2O$	70.56 (70.83)	7.90 (7.98)	13.72 (13.65)

a. K. R. Jacobi (ref.2) reports 75°; b. Recrystallized from ether; c. Recrystallized from methanol/ether; d. 1-Benzoylhexahydro-1,4-diazepine.

acetate salt obtained by filtration, treated with excess 1ON NaOH and extracted with chloroform (2 x 500 ml). The chloroform solution was dried over anhydrous potassium carbonate, evaporated under reduced pressure and the residue either distilled or recrystallized.

ACKNOWLEDGEMENTS.- We thank Dr. H. B. Renfroe for his encouragement, and the Analytical Research Department for microanalyses.

REFERENCES

1. T. S. Moore, M. Boyle and N. M. Thorn, J. Chem. Soc., 39 (1929).
2. K. R. Jacobi, Ber., 66, 113 (1933).
3. K. Masuzawa, H. Uchida and M. Kitagawa, Bull. Chem. Soc. Japan, 40, 244 (1967); T. Irikura, K. Masuzawa, H. Uchida, K. Nishino, M. Kitagawa, N. Ichinoseki and M. Ito, J. Med. Chem., 11, 801 (1968). B. Dhawan and P. L. Southwick, Org. Prep. Proced. Int., 7, 85 (1975).
4. R. Baltzly, J. S. Buck, E. Lorz and W. Schön, J. Amer. Chem. Soc., 66, 263 (1944).

(Received April 2, 1976)