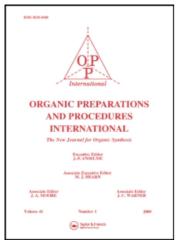
This article was downloaded by: On: *27 January 2011* Access details: *Access Details: Free Access* Publisher *Taylor & Francis* Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International

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

N-ACETYL-L-TYROSINE ETHYL ESTER

M. Dymicky^a ^a Eastern Regional Research Center, Philadelphia, Pennsylvania

To cite this Article Dymicky, M.(1976) 'N-ACETYL-L-TYROSINE ETHYL ESTER', Organic Preparations and Procedures International, 8: 5, 219 — 222

To link to this Article: DOI: 10.1080/00304947609355628 URL: http://dx.doi.org/10.1080/00304947609355628

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

ORGANIC PREPARATIONS AND PROCEDURES INT. 8(5), 219-222 (1976)

N-ACETYL-L-TYROSINE ETHYL ESTER

M. Dymicky

Eastern Regional Research Center¹ Philadelphia, Pennsylvania 19118

In connection with our studies of the mode of reactivity of polyfunctional epoxides with tyrosine and its derivatives, we noted a number of shortcomings pertaining to the syntheses of N-acety1-L-tyrosine ethy1 ester. First of all, as pointed out by Barnes and his group², the literature data on melting points of this compound differ widely, ranging from 78-97°. Secondly, the known methods of synthesis of this compound appear rather complicated, time-consuming, and give low yields. If one considers that the known methods²⁻⁸ utilize N-acetyl-L-tyrosine⁹ as the starting material, the overall yields of the ester would range from 25-50%, based on tyrosine. Also, as pointed out by du Vigneaud and Meyer⁹, acetylation of optically active tyrosine with acetic anhydride in the presence of sodium acetate, causes racemization and diacylation. These by-products lower the yield of the N-mono acyl ester and introduce difficulties in the processes of purification of the product'. Considering all these shortcomings, we felt it of interest to reinvestigate the preparation of N-acetyl-L-tyrosine ethyl ester. As a result, we developed a very convenient and highly efficient procedure for the synthesis of this compound, utilizing tyrosine ethyl ester (or its salt) as the starting material.

 $HO - CH_2 CH \cdot COOEt + CH_3 COC1 \xrightarrow{Et_3N} HO - CH_2 CH \cdot COOEt + Et_3N \cdot HC1$ $HO - CH_2 CH \cdot COOEt + Et_3N \cdot HC1$ $HO - CH_2 CH \cdot COOEt + Et_3N \cdot HC1$ $HO - CH_2 CH \cdot COOEt + Et_3N \cdot HC1$

219

© 1976 by Organic Preparations and Procedures, Inc.

The ester can be prepared very conveniently, with the quantitative yields, using the procedure of Dymicky, Mellon, and Naghski¹⁰.

Our studies indicate that N-acetyl-L-tyrosine ethyl ester forms a monohydrate very easily, which can be dehydrated in vacuum at $56^{\circ}/0.1$ mm. The monohydrate, when dried in vacuum at room temperature melts at 60° , with gradual dehydration and a gradual increase of the melting point. The dehydrated, very pure N-acetyl-L-tyrosine ethyl ester melts sharply at 96-97° $[\alpha]_D^{25} = +25.2$, (c.2, ethanol). Products with melting points between 60 and 96° represent a mixture of partially dehydrated materials. The purity of the dehydrated product has been confirmed by elemental analyses, IR and NMR spectra.

It is of interest to note that recrystallized material from benzene melts at 96-97°. Correct analyses require pure benzene and drying at $56^{\circ}/0.1 \text{ mm}$.

EXPERIMENTAL

N-Acetyl-L-Tyrosine Ethyl Ester Monohydrate.

<u>Procedure A</u>. - To a solution of 10.46 g (0.05 mole) of tyrosine ethyl ester,¹⁰ and 5.05 g (0.05 mole) of triethylamine in 200 ml dry ethyl acetate contained in a 500 ml three-necked reaction flask, equipped with a condenser, stirrer, addition funnel, and mounted in an oil bath, controlled at about 50° was added dropwise with stirring 3.93 g (0.05 mole) of acetyl chloride, in 100 ml dry ethyl acetate. Within about one hour the addition was completed, and the reaction mixture was allowed to react further for two hours. The white precipitate of triethylamine hydrochloride was filtered and washed with ethyl acetate. The combined filtrates were then concentrated in vacuum, at $25^{\circ}/0.1$ mm, until a dry residue is obtained, giving 12.39 g (99%) of the crude product. The mate-

2011

Downloaded At: 12:51 27 January

220

rial is then recrystallized from water, 25 ml/g, and dried in vacuum at $25^{\circ}/0.1$ mm, giving about 90% of pure product, mp \approx 60-65°; $\{\alpha\}_{D} = +23.53$, (c.2, EtOH).

<u>Anal</u>. Calcd. for C₁₃H₁₇NO₄·H₂O: C, 57.98; H, 7.11; N, 5.19. Found: C, 57.86; H, 7.17; N, 5.14.

N-Acetyl-L-Tyrosine Ethyl Ester.

The material obtained above was dried in vacuum, at 56°/0.1 mm, to constant weight, yielding quantitative amount of dehydrated product, mp. 96° $[\alpha]_{\eta}^{25}$ = + 25.2, (c.2, EtOH).

<u>Anal</u>. Calcd. for C₁₃H₁₇NO₄: C, 62.13; H, 6.68; N, 5.57. Found: C, 62.05; H, 6.80; N, 5.53.

<u>Procedure B.</u> - If tyrosine ethyl ester hydrochloride is used as the starting material, then one uses a two molar ratio of triethylamine and follows the same method as given above. The yield of the product is the same, as given under A.

<u>Acknowledgements</u>. - The author wishes to express his thanks to Mrs. Annete S. Kravitz for elemental analyses, and to Mr. James M. Purcell for determination of NMR spectra.

REFERENCES

- 1. Agricultural Research Service, U.S. Department of Agriculture.
- J. H. Barnes, R. C. Cookson, G. T. Dickson, J. Elks, and V. D. Poole, J. Chem. Soc., 1448 (1953).
- 3. C. Niemann and G. E. McCasland, J. Am. Chem. Soc., 66, 1870 (1944).
- 4. E. Cherbulies and H. Plattner, Helv. Chim. Acta, 12, 317 (1929).
- 5. D. W. Thomas, R. V. McAllister, and C. Niemann, J. Am. Chem. Soc.,

2011

Downloaded At: 12:51 27 January

73, 1548 (1951).

- S. Kaufman, H. Neurath, and G. W. Schwert, J. Biol. Chem., <u>177</u>, 793 (1949).
- A. Taurog, S. Abraham, and I. L. Chaikoff, J. Am. Chem. Soc., <u>75</u>, 3473 (1953).
- 8. W. A. Bolhofer, ibid., 75, 4469 (1953).
- 9. V. du Vigneaud and C. E. Meyer, J. Biol. Chem., 98, 295 (1932).
- M. Dymicky, E. F. Mellon, and J. Naghski, Anal. Biochem., <u>41</u>, 487 (1971).

(Received June 22, 1976; in revised form August 16, 1976)