ACTA CHEMICA SCANDINAVICA 4 (1950) 710–717

Short Communications

The Preparation of 3-Nitro-*p*-Toluic Acid from *p*-Cymene

J. N. OSPENSON

Stockholms Högskola och Svenska Träforskningsinstitutet, Stockholm, Sweden

In the course of other experimental work, it became necessary to prepare 3-nitro-*p*-toluic acid from *p*-cymene. The literature advocates the use of fuming nitric acid, a nitric-sulfuric acid mixture, or oxidation to *p*-toluic acid (with dilute HNO_3) followed by nitration [1].

In view of the results of Senseman and Stubbs [2] in the catalytic oxygen oxidation of *p*-cymene, in the liquid phase, to *p*-toluic acid, a study of the effect of manganese dioxide on the nitric acid oxidation of cymene was undertaken.

The products obtained from conc. nitric acid (d. 1.40), cymene, and MnO_2 varied widely with the HNO_3-cymene ratio. With a ratio of 50 ml HNO_3 per ml cymene, quite pure crystalline 3-nitro-*p*-toluic acid (M. P. 186°, Eq. wt. 175 for the raw product) was obtained in a yield of 50–60 %. The pure acid could be easily obtained by a single recrystallization from boiling water. If the ratio were increased to 100 : 1, the yield was sharply reduced, probably due to the formation of dinitro products. Ratios of 10 : 1 and 25 : 1 yielded heterogeneous products from which alkali insoluble aldehydes and ketones, *p*-toluic acid, terephthalic acid, in addition to nitro-*p*-toluic acid, were isolated. The yields of pure nitro acid from these ratios were small.

The reaction was generally complete after one hour. Increasing the reaction time had little effect on either the yield or the composition of the products obtained.

A comparison test, using the optimium HNO_3-cymene ratio but no MnO_2, yielded a product (in 19 % yield) which showed a melting point of 160 to 180° (pure 3-nitro-*p*-toluic acid melts at 189°).

Thus it can be seen that the use of MnO_2 increases the yield of the nitro acid and decreases the formation of oxidation by-products.

However, in the oxidation of cymene to *p*-toluic acid with dilute HNO_3 (d. 1.19), the MnO_2 appears to act in an adverse manner, since the yields obtained (approx. 35 %) are inferior to those reported by Tuley and Marvel [3] (approx. 50 %).

An attempt was made to replace the MnO_2 with mercury salts, but the results were unsatisfactory. No precipitate at all was obtained after cooling the refluxed solution.

The following table summarizes the results:

Density of HNO_3 used	Time of reflux hr.	Ratio ml HNO_3 : Cymene	Product	Average Yield*	Remarks
1.40	1	50:1	3 nitro-*p*-toluic acid	53 %	
1.40	2	50:1	»	51 »	
1.40	1	100:1	»	15 »	
1.40	1	10:1	»	24 »	
1.40	1	25:1	»	26 »	
1.40	1	50:1	»	19 »	no MnO_2
1.19	1	50:1	*p*-toluic acid	35 » **	
1.19	1	250:1		40 » **	
1.19	1	250:1	—	—	$HgNO_3$ used

* Yield calculated from weight of raw product and quotient of found equivalent weight and true equivalent weight of product.

** Solubility of *p*-toluic acid in water (0.034 g/100 ml at 5° C) taken into account.

Inability of Guanosine to Act as a Precursor of Polynucleotides

EINAR HAMMARSTEN and
PETER REICHARD

Biochemical Department, Karolinska Institutet, Stockholm, Sweden

Recent work from this laboratory [1] has shown that the pyrimidineribosides, which contain ribose bound to cytosine or uracil are metabollically different from free pyrimidines. Isotope experiments with the latter [2, 3] proved that these compounds cannot be utilized for the synthesis of polynucleotides while isotopic cytidine and also to some extent uridine can be used by the rat for the synthesis of pyrimidines of both ribonucleic acid and desoxyrinucleic acid [1]. It was thought that perhaps in the same way guanine coupled to ribose might be a precursor for purines while free guanine is not [2]. For that reason guanosine containing N^{15} was prepared by allowing *B. coli* to grow in a $N^{15}H_4^+$ containing medium. After isolation of PNA from the bacteria [4] guanosine was prepared and purified by starch chromatography [5]. It had an excess of N^{15} of 4.20 atom per cent. After cristallisation from water the N^{15}-guanosine was injected subcutanously into rats at a level of 10 mg/100 g of body weight per day. The injections were carried out twice daily and over a period of 3 days. After that the rats were killed, the polynucleotides prepared and separated. Purines and pyrimidines were prepared from each fraction and analyzed for N^{15} (5). None of the fractions contained any significant amount of N^{15}. It is thus concluded that guanosine does not act as a precursor for the synthesis of polynucleotides.

1. Hammarsten, E., Reichard, P., and Saluste, E., *J. Biol. Chem.* **183** (1950) 109.
2. Plentl, A. A., and Schoenheimer, R. *J. Biol. Chem.* **153** (1944) 203.
3. Bendich, A., Getler, H., and Brown, G. B. *J. Biol. Chem.* **177** (1949) 565.
4. Hammarsten, E. *Acta Med. Scand.* Suppl. **196** (1947) 134.
5. Reichard, P. *J. Biol. Chem.* **179** (1949) 763.

Received June 2, 1950.

The general procedure used is as follows:

30 ml of pure *p*-cymene (B. P. 175.5—176.5°) were added to a mixture of 1500 ml conc. HNO_3 (d. 1.40) and 18 g MnO_2. This mixture was then refluxed for approximately one hour. Care must be taken to dispose of the oxides of nitrogen liberated during the reaction. The clear yellow solution was allowed to cool, whereupon pale yellow crystals separated. These were removed by filtration through a sintered glass filter and washed with cold water. If this wash water is added to the filtrate a further amount of slightly less pure 3-nitro-*p*-toluic acid separates.

The precipitate was then dissolved in dilute ammonia, filtered, and reprecipitated by neutralization with conc. HCl. This precipitate was removed, after cooling, and recrystallized from boiling water.

M. p. (lit.)	189°
M. p. (found)	188°—189°
N (calc.)	7.73 %
N (found)	7.70 »

The methyl ester was prepared by means of methanol and hydrochloric acid.

M. p. (lit.)	49°
M. p. (found)	48°—49°

1. Noad, H. *Ann.* **63** (1847) 297; Fittica, F. *Ann.* **172** (1874) 309; Kermack, W. O. *J. Chem. Soc.* **125** (1924) 2827; King, H. *J. Chem. Soc.* **127** (1925) 2639; Alfthan, J. *Ber.* **53** (1920) 83; Fittig, R., and Ramsay, W. *Ann.* **168** (1873) 251.
2. Senseman, C. E., and Stubbs, J. J. *Ind. Eng. Chem.* **24** (1932) 1184.
3. Tuley, W. F., and Marvel, C. S. *Org. Syn.*, Vol. 27 (1947) 86.

Received May 8, 1950.