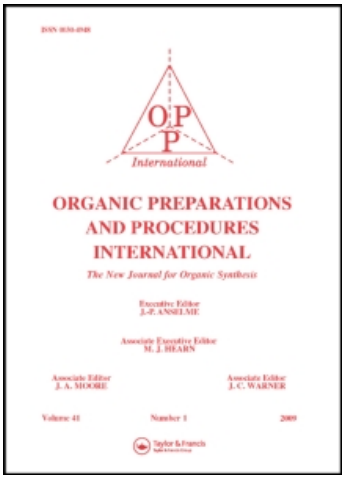

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A HIGH-YIELD SYNTHESIS OF 3-PENTADECYLPYRIDINE

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2,6-H), 6.72 (4H, d, J = 8 Hz, 3,5-ArH), 7.3 (4H, d, J = 8 Hz, 2,6-ArH), 7.6 (2H, d, J = 16 Hz, 1,7-H); M^+: 336.

Anal. Calcd for $C_{21}H_{20}O_4$: C, 74.97; H, 5.99. Found: C, 74.87; H, 6.14

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A HIGH-YIELD SYNTHESIS OF 3-PENTADECYLPYRIDINE

Submitted by (04/04/94)

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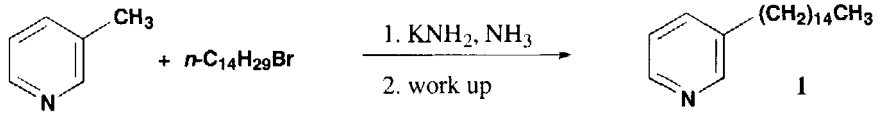
Long chain and fused-ring heteroaromatic compounds which have been identified as major constituents in oil shale and lower rank bituminous and lignite coals[1] are believed to play a major role in their liquefaction properties; however, their influence during thermolyses is unknown.[2] It is estimated that nitrogen-containing compounds constitute 40% of the shale crude and GC/MS analyses shows a preponderance of these to be alkylpyridines.[3] A number of studies have shown that model compounds can give good extrapolations to the natural products under pyrolysis conditions; however,

the current literature[4] specifically states that understanding the pyrolysis parameters of model compounds containing oxygen, nitrogen and sulfur functionalities has major gaps in the data base that need to be filled. Thus, a project studying the pyrolysis reactions of the isomeric pentadecylpyridines has been initiated in our lab. Of the isomers, only 2-pentadecylpyridine has been previously synthesized for checking its emulsifying and antibacterial properties.[5]



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The synthesis of alkylpyridines has been accomplished most readily by metallating the corresponding picolines followed by treatment with alkyl halides. By this procedure first reported by Chichibabin[6] and Bergstrom,[7] it is possible to alkylate 2- and 4-picoline but not 3-picoline. In 1951, Brown and Murphey reported the alkylation of 3-picoline using sodium amide as a base;[8] however, even after this publication, reports continue to appear describing the inability of different base systems to metallate 3-alkylpyridines.[9] In our experience the Brown and Murphey procedure has been quite successful for preparing 2-, 3-, and 4-alkyl and alkenylpyridines in high yields, typically in the 70-98% range.[10] Our attempts to extrapolate that procedure to 3-pentadecylpyridine (**1**), however, resulted in yields of approximately 35-40%. A review of the literature shows that this is common for the long-chain alkyl pyridines as 2-tridecylpyridine was isolated in a 25% yield,[5] 2-pentadecylpyridine in a 44% yield,[5] 2-heptadecylpyridine in a 53% yield,[5] and 4-nonadecylpyridine in a 43% yield.[11] Our first attempts at improving the yield consisted of changing the base-solvent system. Attempts with lithium diisopropylamide and *n*-butyllithium failed to improve the yield. Consideration of the original system again made it clear that two problems were responsible for the lowered yields; first the *n*-tetradecyl bromide solidified upon addition to the liquid ammonia media and second it was difficult to separate 1-tetradecylamine and 1-tetradecyl bromide from the product by distillation. These problems were mostly overcome by adding the bromide in ether as this decreased solid formation upon addition and by changing the work-up solvent from dichloromethane, in which the *n*-pentadecylpyridine hydrochloride salt was soluble, to ether which did not dissolve the salt, thus allowing the separation of the product from unreacted bromide. A subsequent extraction of the aqueous phase with dichloromethane allowed the extraction of the product from 1-tetradecylamine which remained in the aqueous phase. These changes led to an improved yield (~65%). Finally, changing the base to potassium amide further resulted in a significant improvement in the yield to 91%. This counterion effect on yields when changing from sodium to potassium has been noted previously.[9d]

EXPERIMENTAL SECTION

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were taken on a Varian Gemini 300 MHz spectrometer. IR spectra were recorded on a Perkin Elmer model 1310 spectrophotometer. GC analyses were made on a Hewlett-

Packard 5790A capillary chromatograph with FID (0.32 mm x 30 m Alltech Econo-Cap SE-30, film thickness 0.25 μm, column programmed to hold at 70° for 5 min with a 8° ramp to 260°). Mass spectra data was recorded at 70 eV on a GC/MS system consisting of a Hewlett-Packard HP-5980A GC coupled to a Finnegan ITD 40 ion trap mass spectrometer. Elemental analysis was performed by Atlantic Microlab, Inc. Norcross, GA 30091.

3-Pentadecylpyridine (1).- To a 500 mL three-necked round-bottomed flask, equipped with a mechanical stirrer and a Dry-Ice condenser, was added 250 mL of anhydrous liquid ammonia and 0.2 g of $Fe(NO_3)_3 \cdot 9H_2O$, with stirring, to produce an orange solution. Freshly cut potassium (9.8 g, 0.25 mole) [CAUTION[12]] was added to the stirred solution, in small pieces, over a 25 min period producing the blue solvated electron, stirring was continued until the blue color disappeared indicating the complete formation of KNH_2. To the stirred potassium amide mixture, was added 23.3 g (0.25 mole) of 3-picoline over a 5 min period, producing a dark red color. Freshly distilled *n*-bromotetradecane (45.7 g, 0.165 mole) dissolved in 50 mL of diethyl ether was added over a 10 min period. The solution was stirred for 2 hrs and the ammonia allowed to evaporate overnight. Cautious addition of 10 g of solid ammonium chloride with stirring was followed by the addition of distilled water (200 mL) to discharge any remaining potassium amide. The reaction mixture was extracted with 75 mL of ether, and two subsequent extractions with 100 mL of ether each. The product was separated from the combined ethereal layer (and *n*-tetradecyl bromide) by extraction with three 100 mL portions of 1M HCl. The combined aqueous acid layer was extracted with three 100 mL portions of dichloromethane, leaving any excess 1-tetradecylamine hydrochloride behind. The combined dichloromethane layers were washed with three 100 mL portions of 1M NaOH, a 100 mL portion of water and dried over $MgSO_4$. The solution was suction filtered and evaporated *in vacuo*. The dark oily residue was purified by vacuum distillation to yield 43.35 g (91%) 3-pentadecylpyridine as a light yellow liquid, bp. 155°/0.5 mm, mp. 18.5°; n_D^{25} 1.4785; picrate, mp. 100.5°. IR (neat): 3040, 2920, 2845, 1575, 1460, 1420, 715 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.8 (t, 3H), 1.3 (s, 24H), 1.6 (t, 2H), 2.6 (t, 2H), 7.15 (s, 1H), 7.45 (s, 2H), 8.45 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 15.103, 23.704, 30.181, 30.3862, 30.4334, 30.575, 30.6809 (6 C, overlapped), 32.114, 32.950, 34.036, 124.139, 136.638, 138.895, 148.172, 150.995; MS (m/Z): 289 (M^+, 14%), 106 (100%).

Anal. Calcd. for $C_{20}H_{35}N$: C, 82.98; H, 12.19; N, 4.83. Found: C, 82.77; H, 12.14; N, 4.78

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12. Extreme caution should be exercised when working with potassium; small unreacted pieces coming in contact with water will cause a fire. We found that cutting the potassium under pentane and destroying it in methanol worked the best in our lab.

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AN IMPROVED ELECTROSYNTHETIC PREPARATION OF THE FEMALE HOUSEFLY SEX PHEROMONE

Submitted by (03/11/94)

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The housefly *(Musca domestica)* pheromone, (Z)-9-tricosene (**1**), has been prepared in a number of different ways. Most of the chemical syntheses suffer from being multistep processes.[1] In Brazil, this compound is sold in two commercial formulations associated with traditional insecticide to control flies in household and poultry applications. Gribble and co-workers[2] described a one step synthesis of this pheromone using a mixed Kolbe electrolysis of oleic acid (**2**) and heptanoic acid (**3**),