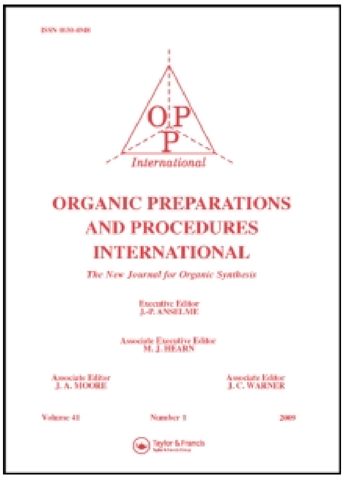

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

PREPARATION OF 3-TETRADECYLINDOLE

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To cite this Article Wynne, James H. , Mushrush, George W. and Stalick, Wayne M.(1999) 'PREPARATION OF 3-TETRADECYLINDOLE', Organic Preparations and Procedures International, 31: 4, 447 — 450

To link to this Article: DOI: 10.1080/00304949909355737

URL: http://dx.doi.org/10.1080/00304949909355737

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PREPARATION OF 3-TETRADECYLINDOLE

Submitted by (05/27/99)

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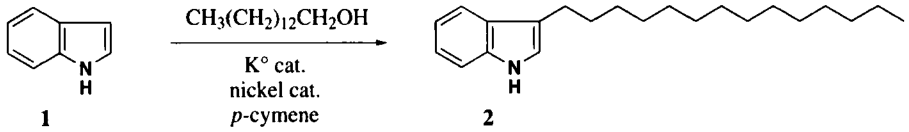
To date, no comprehensive synthetic technique has been developed for the synthesis of 3-substituted long chain alkyl indoles. However, two reports for the synthesis of 3-octylindole do exist in the literature.[1,2] Since we required a number of examples of these alkyl indoles for testing their effect on sediment formation in fuels, we made a study of feasible synthetic techniques.[3]

Numerous attempts to synthesize short chained 3-alkylindoles have been reported.[4] Most involved the use of an organometallic species in varying yields, one of which includes the use of a nickel-phosphine complex to aid the cross-coupling of indole with an alkyl halide.[5] Alkylation of indole has also been reported to occur when $ZnCl_2$ and $Zn(OAc)_2$ are employed, albeit in low yields.[6] Other approaches include the use of iron complexes[7] and copper complexes.[8] Reports of reactions such as the Stephans-Castro and Heck coupling make use of various Pd (0) species; however, these reactions proved unsuccessful in our case.[9] The use of magnesium in the form of a Grignard reagent has also been reported to promote alkylation in the 3-position; however, low yields are obtained.[4,10]

We thus investigated many synthetic routes in hopes of finding a good general method of synthesis. It was found that modifications of the method reported by Pratt and Botimer,[1] as used in the synthesis of 3-octylindole proved most successful. We report here a seemingly general, one step synthesis employing catalytic amounts of nickel metal and potassium metal, in the presence of indole and tetradecanol, or other long chain alcohol, in rapidly refluxing *p*-cymene.

The role of the nickel is not yet known; however, preliminary investigations indicate that it serves as a catalyst for the oxidation of the primary alcohol to the corresponding aldehyde. This theory is supported by the successful substitution of a catalytic amount of tetradecanal in place of nickel and potassium catalysts, with no sign of diminished yield.[11]



3-Octyl, 3-decyl, 3-dodecyl, 3-hexadecyl, and 3-octadecylindole were also synthesized by this method in greater than 60% yield. Some of these, however, were not easily recrystallized from methanol, and required flash chromatography for purification. Further purification will be required to obtain analytically pure samples.

EXPERIMENTAL SECTION

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were taken on a Bruker 300 MHz spectrometer. FTIR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer. GC analyses were performed on a Hewlett-Packard 6890 capillary chromatograph with FID (0.32 mm x 30 m HP-5, 0.25 µm, column programmed to hold 100° for 1 min with a 20° ramp to 250°). Mass spectra data was recorded at 70 eV on a GC/MS system consisting of a Hewlett-Packard HP-6890-Plus GC (Grestel Large Volume Cool Injector System CIS-4, HP 5 MS, 30 m x 0.25 mm x 0.25 mm film thickness, 50° to 280° at 15°/min, held for 15 min.) coupled to a HP 5973 quadrupole mass spectrometer (tranferline 280°, ion source 200°, quad 150°). Elemental analysis was performed by Atlantic Microlab, Inc. Norcross, GA 30091.

3-Tetradecylindole (2).- 1-Tetradecanol (10.98 g, 51.22 mmol) was combined with freshly cut potassium metal (0.32 g, 8.19 mmol) and 50 mL of *p*-cymene in a 100 mL round bottom flask equipped with a magnetic stirrer and a Dean-Stark trap with condenser. The mixture was heated at reflux for 30 min., then allowed to cool slightly before beginning the rapid addition of indole (3.00 g, 25.61 mmol) and a nickel metal catalyst (0.75 g, 12.8 mmol).[12] The resulting solution was once again heated to rapid reflux, the point where the condenser was nearly flooded, and thus allowed to reflux for 24 h. Upon completion, the reaction mixture was allowed to cool slowly before being diluted with 50 mL of Et_2O. The solid nickel catalyst was removed by vacuum filtration. The organic layer was washed with

1M HCl (3 x 30 mL) followed by water (2 x 15 mL). The resulting organic layer was dried over $MgSO_4$ and reduced in volume by rotary evaporation. The resulting oil was placed in a Kugelrohr distillation apparatus and the resulting fractions were collected under reduced pressure (2 mmHg) while heating (100-150°). Four fractions were collected consisting of: *p*-cymene, tetradecanol, indole, and desired product with trace impurities. The recovered unreacted starting materials were of high enough purity to be immediately reused without further purification. The product was slightly contaminated but was easily purified by recrystallization from methanol. It was dried for 5 h on a vacuum pump to remove any traces of solvent, affording 5.78 g of crude 3-tetradecylindole. Recrystallization gave two crops of highly pure crystals, which were combined to give 5.70 g (72%) of colorless solid, mp. 56.5-57°. IR (neat): 3404, 2906, 2833, 1550, 1451, 1083, 1000, 735 cm^{-1}; ^1H NMR: δ 7.87 (b, N-H), 7.61 (d, J = 7.5, 1H), 7.35 (d, J = 8.0, 1H), 7.20-7.10 (m, 2H), 6.97 (s, 1H), 2.75 (t, J = 7.8, 2H), 1.73-1.68 (m, 2H), 1.37-1.24 (m, 22H), 0.88 (t, J = 5.7, 3H). ^{13}C NMR: δ 136.38, 127.68, 126.81, 121.81, 120.93, 119.03, 117.29, 110.97, 31.93, 30.18, 29.69, 29.36 (7 C, overlapped), 25.16, 22.69, 14.10; MS (m/Z): 313 (M^+, 79%), 130 (100%).

Anal. Calcd For $C_{22}H_{35}N$: C, 84.28; H, 11.25; N, 4.47. Found: C, 84.13; H, 11.22; N, 4.43

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11. Unpublished results from our laboratory.

12. Fisher reduced nickel powder, Cat. No. N-40 was employed.

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A NOVEL METHOD FOR THE SYNTHESIS OF TELLUROESTERS

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Organotellurium compounds have attracted considerable interest as reagents and intermediates in organic synthesis recently.[1] From a number of methods, a convenient and general method to introduce a tellurium moiety into organic molecules is the reaction of metal tellurides with appropriate electrophiles.[2] The use of ditellurides and samarium diiodide in THF/HMPA has also been reported recently to give telluride anions.[3] As a powerful, versatile and ether-soluble one-electron transfer reducing agent, SmI_2 has played an ever-increasing role in organic synthesis[4] since its introduction by Kagan and his group.[5] Though SmI_2 is a useful reagent, its storage is difficult because it is very sensitive to air oxidation. On the other hand, metallic samarium is stable in air and its strong reducing power ($Sm^{3+}/Sm = -2.41V$) is comparable to that of magnesium ($Mg^{2+}/Mg = -2.37V$), superior to that of zinc ($Zn^{2+}/Zn = -0.71V$). These properties prompted us to use it directly instead of samarium (II) iodide.[6] Herein, we report that reductive cleavage of Te-Te bond in ditellurides by $Sm/ZrCl_4$ system led to telluride anion species, which react with acyl halides or anhydrides to give telluroesters in good yields under mild and neutral conditions.

$$\underset{\mathbf{1}}{\mathbf{RTeTeR}} \xrightarrow{Sm/ZrCl_4} \mathbf{[RTeSmCl_2]} \xrightarrow{R^1COX} \underset{\mathbf{2}}{\mathbf{RTeCOR^1}}$$

a) $R = C_6H_5, R^1 = C_6H_5$ b) $R = C_6H_5, R^1 = p\text{-}ClC_6H_4$ c) $R = C_6H_5, R^1 = p\text{-}BrC_6H_4$
d) $R = C_6H_5, R^1 = o\text{-}BrC_6H_4$ e) $R = p\text{-}MeC_6H_4, R^1 = C_6H_5$ f) $R = p\text{-}MeC_6H_4, R^1 = p\text{-}ClC_6H_4$
g) $R = C_6H_5, R^1 = CH_3$ h) $R = C_6H_5, R^1 = CH_3CH_2$ i) $R = C_6H_5, R^1 = CH_3$
j) $R = C_6H_5, R^1 = CH_3(CH_2)_{10}$ k) $R = n\text{-}C_4H_9, R^1 = C_6H_5$ l) $R = n\text{-}C_4H_9, R^1 = o\text{-}BrC_6H_4$

The formation and reaction of samarium aryltellurolates generated *in situ* from the cleavage of the corresponding ditellurides with $Sm/ZrCl_4$ reductive system, are shown in the Scheme. The