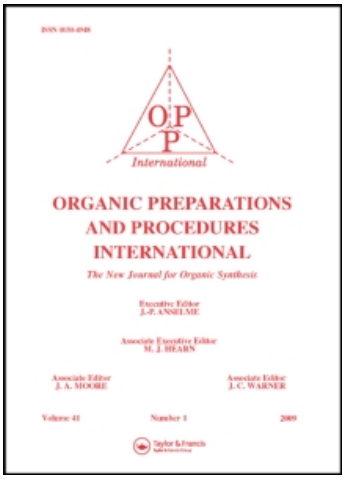


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A FACILE PREPARATION OF 2,3,4,4a,5-6-HEXAHYDROQUINOLINE

Bodo Juhnke[a]; Gerhard Jas[a]; Dieter Schumann[a]
[a] Institut für Organische Chemie, TU Berlin, Berlin, GERMANY

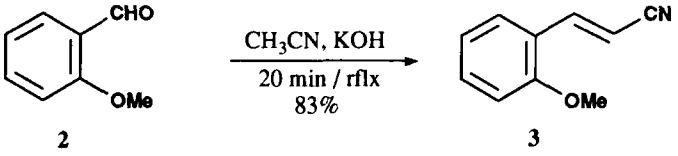
To cite this Article Juhnke, Bodo , Jas, Gerhard and Schumann, Dieter(1992) 'A FACILE PREPARATION OF 2,3,4,4a,5-6-HEXAHYDROQUINOLINE', Organic Preparations and Procedures International, 24: 6, 673 — 675
To link to this Article: DOI: 10.1080/00304949209356243
URL: http://dx.doi.org/10.1080/00304949209356243

A FACILE PREPARATION OF 2,3,4,4a,5,6-HEXAHYDROQUINOLINE

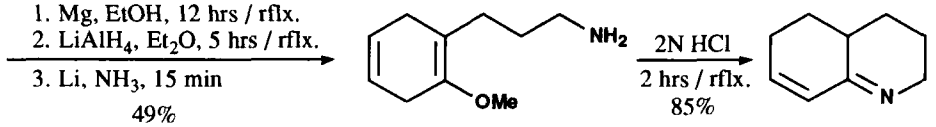
Submitted by Bodo Juhnke, Gerhard Jas and Dieter Schumann*
(11/18/91)

Institut für Organische Chemie, TU Berlin
Straße des 17 Juni 135
W-1000 Berlin 12, GERMANY

In the context of studies on the reactivity[1] of enimines, we needed 2,3,4,4a,5,6-hexahydroquinoline (**1**) in addition to the 2,3,4,6,7,8,-hexahydroquinolines described in the preceding paper. The preparation of the title compound has been previously described only in a doctoral thesis[2] and involved an inconvenient 9-step synthesis. We now describe an efficient new route to **1**.



2 **3**



6 **1**

Commercially available o-methoxybenzaldehyde (**2**) was condensed with acetonitrile under basic conditions[3] to furnish *o*-methoxycinnamonitrile (**3**). To obtain 2-(3-aminopropyl)-1-methoxy-1,4-cyclohexadiene (**6**), nitrile **3** had to be reduced in three steps by using magnesium in methanol,[4] then lithium aluminum hydride and, finally, lithium in ammonia.[5] Hydrolysis and rearrangement was accomplished by refluxing in diluted hydrochloric acid to yield 2,3,4,4a,5,6,-hexahydroquinoline (**1**) in an overall yield of 34%.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on a Bruker WM 400 (400 MHz) spectrometer. ^{13}C NMR spectra were recorded on a Bruker WM 270 (67.5 MHz) spectrometer. Spectra were determined in deuteriochloroform solutions with tetramethylsilane as internal standard. *J*-Values are given in Hz. Mass spectra were recorded on a Varian MAT 711 or MAT 44 S spectrometer with relative intensity in parenthesis. IR spectra were recorded on a Beckmann IR 9 spectrometer and are reported in cm^{-1}. Acetonitrile was distilled over P_4O_{10} under nitrogen; diethyl ether was distilled over sodium benzophenone ketyl under argon; methanol and ethanol were distilled over sodium under nitrogen. *o*-Methoxybenzaldehyde was purchased from Merck. The resulting hexahydroquinoline should be stored under inert gas in a freezer.

***o*-Methoxycinnamonitrile (3).**- To a refluxing suspension of KOH (20.6 g, 0.37 mol) in acetonitrile

(300 mL) was added a solution of *o*-methoxybenzaldehyde (**2**) (50 g, 0.37 mol) in acetonitrile (50 mL) under nitrogen. After refluxing for a further 20 minutes the mixture was poured into ice water (200 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2x100 mL). The combined organic layer was dried (Na_2SO_4), concentrated under reduced pressure and the residue was distilled to yield **3** (48.3 g, 83%) as a slightly yellow liquid, bp. 120° (0.1 mmHg). ^1H NMR: δ 7.62 (d, 1H, *J* = 17), 7.37 (d, 2H, *J* = 8), 6.97 (dd, 1H, *J* = 8; 8), 6.93 (d, 1H, *J* = 8), 6.06 (d, 1H, *J* = 17), 3.89 (s, 3H). ^{13}C NMR: δ 157.9 (s), 146.2 (d), 132.1 (d), 128.7 (d), 122.2 (s), 120.6 (d), 118.9 (s), 111.1 (d), 96.6 (d), 55.3 (q). MS (70 eV) m/z (%): 159 (M^+,80), 131 (100), 89 (75).

Anal. Calcd. for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.28; H, 5.85; N, 8.90

2-(2-Methoxyphenyl)propionitrile (4).- A solution of **3** (31.8 g, 0.2 mol) in methanol (500 mL) was cooled to 0° and magnesium turnings (50 g, 2.1 mol) were added. The *violent* (!) reaction which ensued was moderated with an ice bath. After stirring for 12 hrs the reaction was carefully quenched with conc. HCl and the mixture was brought to pH 2. The aqueous layer was extracted with Et_2O (5x50 mL). After drying ($MgSO_4$) the organic phase was concentrated under reduced pressure and the residue was distilled to furnish **4** (22.4 g, 69%) as a colorless liquid, bp. 75° (0.1 mmHg). IR ($CHCl_3$): ν 2850, 2260, 1600. ^1H NMR: δ 7.27 (ddd, 1H, *J* = 8; 8; 2), 7.18 (dd, 1H, *J* = 8; 2), 6.92 (ddd, 1H, *J* = 8, 8; 1), 6.87 (dd, 1H, *J* = 8; 1),3.84 (s, 3H), 2.96 (t, 2H, *J* = 7.5), 2.63 (t, 2H, *J* = 7.5). MS (70 eV) m/z: 161 (M^+), 121 (78), 91 (100).

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.51; H, 6.89; N, 8.69. Found: C, 74.62; H, 6.95; N, 8.81

2-(3-Aminopropyl)-1-methoxybenzene (5).- A solution of **4** (16.1 g, 0.1 mol) in Et_2O (100 mL) was added dropwise under nitrogen to a suspension of $LiAlH_4$ (5 g, 0.13 mol) in Et_2O (500 mL). After refluxing for 5 hrs the mixture was cooled to 0° and the reaction was quenched with a saturated aqueous Na_2SO_4 solution. The precipitate was filtered and thoroughly washed with Et_2O. After drying (Na_2SO_4) and evaporating off the solvent the residue was distilled to give **5** (15.2 g, 92%) as a slightly yellow oil, bp. 125° (12 mmHg). IR ($CHCl_3$): ν 3490, 1605, 1595. ^1H NMR: δ 7.17 (ddd, 1H, *J* = 8, 8; 2), 7.13 (dd, 1H, *J* = 8; 2), 6.88 (ddd, 1H, *J* = 8, 8; 1), 6.83 (dd, 1H, *J* = 8; 1), 3.82 (s, 3H), 2.70 (t, 2H, *J* = 7.5), 1.73 (tt, 2H, *J* = 7.5, 7.5). MS (70 eV) m/z: 165 (M^+), 148 (94), 91 (100).

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48: Found: C, 72.92; H, 9.30; N, 8.41

2-(3-Aminopropyl)-1-methoxy-1,4-cyclohexadiene (6).- Amine **5** (25.4 g, 0.15 mol) was dissolved in liquid ammonia (300 mL) and lithium (10.8 g, 1.56 mol) was added carefully within 10 min. After stirring for an additional 30 min ethanol was added until the solution discolored. Then Et_2O (100 mL) was added and the ammonia was evaporated. The residue was poured into H_2O (100 mL). The aqueous layer was extracted with Et_2O (5x50 mL). The combined organic layer was dried (Na_2SO_4), concentrated under reduced pressure and distilled to yield **6** (19.7 g, 77%) as a yellow oil, bp. 128° (12 mmHg). ^1H NMR: δ 5.65 (s, 2H), 3.50 (s, 3H), 2.80 (t, 2H, *J* = 7.5), 2.69 (d, 2H, *J* = 7), 2.67 (d, 2H, *J* = 7), 2.12 (t, 2H, *J* = 7.5), 1.50 (tt, 2H, *J* = 7.5; 7.5). ^{13}C NMR: δ 145.4 (s), 124.4 (d), 123.1 (d), 114.2 (s), 55.7 (q), 41.7 (t), 31.4 (t), 30.2 (t), 25.8 (t), 25.7 (t). MS (70 eV) m/z: 167 (M^+), 121 (95), 91 (100).

Anal. Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.61; H, 10.43; N, 8.58

2,3,4,4a,5,6-Hexahydroquinoline (1).- A solution of the enolether **6** (12 g, 72 mmol) in 2N HCl (50 mL) was refluxed under nitrogen for 2 hrs, then allowed to cool to room temperature and was made basic by adding 2N NaOH (pH>10). The aqueous phase was extracted with Et_2O (4x50 mL); the combined organic layer was dried (Na_2SO_4), concentrated under reduced pressure and the residue distilled to give the desired hexahydroquinoline **1** (8.3 g, 85%) as a slightly yellow liquid, bp. 50° (0.1 mmHg). IR (CCl_4): ν 1670,1630. ^1H NMR: δ 6.29 (m, 1H), 6.02 (dd, 1H, J = 10; 3), 3.81 (m, 1H), 3.57 (m, 1H), 3.53 (m, 1H), 2.38 (m, 1H), 2.25 (m, 1H), 2.11 (m, 1H), 1.83 (m, 1H), 1.74 (m,1H), 1.63 (m, 1H), 1.47 (m, 1H), 1.27 (m, 1H). ^{13}C NMR: δ 167.5 (s), 137.8 (d), 130.5 (d), 49.9 (t), 36.8 (d), 29.8 (t), 27.0 (t), 25.9 (t), 22.7 (t). MS (70 eV) m/z: 135 (M^+,100), 134 (66), 107 (50).
Anal. Calcd. for $C_9H_{13}N$: C, 79.95; H, 9.69; N, 10.36. Found : C, 79.84; H, 9.89; N, 10.61

REFERENCES

1. G. Jas, E. Schuster, B. Juhnke, C. Hesse and D. Schumann, *Ann.*, Submitted for publication.

2. G. Schmidt, Dissertation, TU Berlin (1979).

3. S. A. DiBiase, B. A. Lipisko, A. Haag, R. A. Wolak and G. W. Gokel, *J. Org. Chem.*, **44**, 4640 (1979).

4. J. A. Profitt, D. S. Watt and E. J. Corey, *ibid.*, **40**, 127 (1975).

5. A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5360 (1953).

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A CONVENIENT SYNTHESIS OF SOME NEW PYRANO[2,3-d]PYRIMIDINES

Submitted by (12/26/91)

V. K. Ahluwalia*†, Rakesh Kumar and Renu Aggarwal

Department of Chemistry
University of Delhi, Delhi-110007, INDIA

Pyranopyrimidines are associated with diverse physiological activities[1] and a number of methods have been developed for their synthesis[2]. The present communication describes a convenient synthesis of some new types of pyrano[2,3-d]pyrimidines, by the condensation of 2-thiobarbituric acids **1a-h** with *o*-hydroxybenzylideneacetone (**2**) under basic as well as acidic conditions.

The reaction of 1,3-bis(4-methylphenyl)-2-thiobarbituric acid (**1a**) with *o*-hydroxybenzylideneacetone (**2**) was carried out in the presence of pyridine at reflux. The product obtained (mp. 250-251°) gave a positive 2,4-dinitrophenylhydrazine (DNP) test and a negative ferric