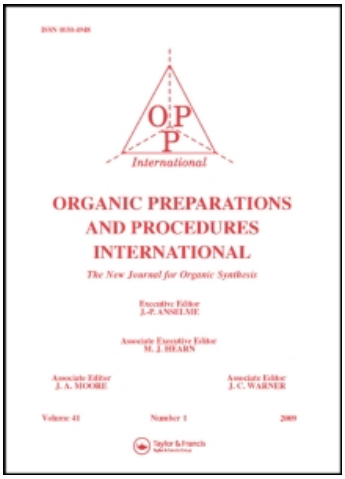



## Organic Preparations and Procedures International

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

# SYNTHESIS OF 3-METHYL- AND 3-tert-BUTYLPHENANTHRENE

R. C. Bansal[a]; S. A. Samad[a]; J. S. Thomson[b]; E. J. Eisenbraun[a]
[a] Department of Chemistry, Oklahoma State University, Stillwater, OK [b] National Institute for Petroleum and Energy Research, Bartlesville, OK

**To cite this Article** Bansal, R. C. , Samad, S. A. , Thomson, J. S. and Eisenbraun, E. J.(1988) 'SYNTHESIS OF 3-METHYL- AND 3-tert-BUTYLPHENANTHRENE', Organic Preparations and Procedures International, 20: 3, 305 — 311
**To link to this Article: DOI:** 10.1080/00304948809355829
**URL:** http://dx.doi.org/10.1080/00304948809355829

temperature, an orange precipitate formed and was collected and recrystallized from absolute ethanol to give the iodide salt 2.

Acknowledgement.- The present study was supported by the Basic Science Research Institute Program, Ministry of Education, 1985. We thank Professor Maurice M. Kreevoy of University of Minnesota for his helpful support.

REFERENCES

1. There is no report of the preparation of N-benzylpyridinium or N-benzylquinolinium iodide. For N-benzylacridinium iodide, see F. Krohnke and H. L. Honig, Chem. Ber., 90, 2226 (1957).

2. M. M. Kreevoy and I.-S. H. Lee, J. Am. Chem. Soc., 106, 2550 (1984).

3. R. M. G. Roberts, D. Ostovic, and M. M. Kreevoy, J. Org. Chem., 48, 2053 (1983).

4. D. Ostovic, I.-S. H. Lee, R. M. G. Roberts, and M. M. Kreevoy, ibid., 50, 4206 (1985).

* * * * *



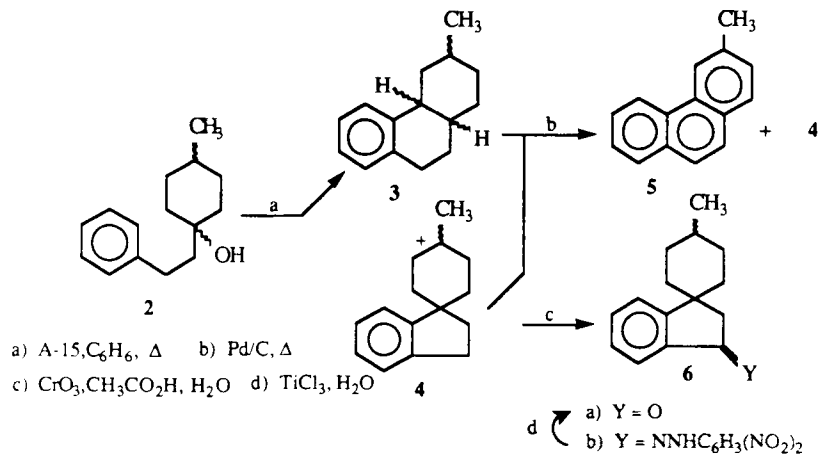
## SYNTHESIS OF 3-METHYL- AND 3-tert-BUTYLPHENANTHRENE

Submitted by (02/23/87) R. C. Bansal[†], S. A. Samad[†], J. S. Thomson[††], and E. J. Eisenbraun*[†]

[†]Department of Chemistry, Oklahoma State University, Stillwater, OK 74078
[††]National Institute for Petroleum and Energy Research, Bartlesville, OK 74005

3-Methylphenanthrene (5) was needed as an analytical standard and for precise thermodynamic studies as a model monomethyl tricyclic fossil-fuel constituent.[1] The Bogert-Cook synthesis shown below is a well-known route

to alkyl substituted phenanthrenes but the influence of the spiro hydrocarbon 4 as a side product has not been reported.[2] The purpose of the current synthesis made even a minor conversion of 4 to 2-methylphenanthrene by ring expansion unacceptable since 5 was required in 99.9+% purity.




To test for skeletal rearrangement of 4, the mixture of 4 and 5 was first treated with picric acid in methanol to remove 5 as the picrate. The filtrate, containing 4 (4 does not form a picrate), was concentrated and extracted with hexane through basic alumina contained in a Soxhlet extractor[3] to remove picric acid. Preparative high pressure liquid chromatography[4] (HPLC, silica/hexane) removed remaining traces of 5 and other impurities to give 4 which appeared as a single HPLC (analytical, silica/hexane) peak and a single GC peak using a 6' x 1/8" OV-101 packed column. Capillary GC on this material separated it into two peaks having retention times of 43.21 and 43.63 min.[5] This sample of spiro hydrocarbon 4, with 2- and 3-methylphenanthrenes absent, was resubjected to the same treatment with hot Pd/C as was used to convert 3 to 5. NMR ($^{1}H$ and $^{13}C$) showed that recovered 4 was unchanged.

To further test the identity and sterochemistry of structure 4, it was oxidized with chromic acid to the liquid ketone mixture **6a**. A single

carbonyl peak in the $^{13}C$ NMR spectrum but extra $^{13}C$ NMR signals indicated an isomeric mixture. The capillary GC trace showed two peaks at 72.83 and 72.92 min. in the ratio 1:1.5.[5] The red 2,4-dinitrophenylhydrazone (2,4-DNP), **6b**, mp. 245-247°, was prepared, recrystallized, and hydrolyzed[3] with aqueous $TiCl_3$ to **6a**.[6] The $^{13}C$ NMR spectrum of **6a** retained the extra peaks and thus ketone **6a** is a mixture of isomers with fortuitously identical carbonyl chemical shifts in their $^{13}C$ NMR spectra.

Since spiro hydrocarbon **4** is not altered by the aromatizing conditions used to produce **5**, the reaction sequence may reliably serve to synthesize phenanthrenes substituted at C-3. The sequence was used to prepare 3-tert-butylphenanthrene as well in 32% yield.



## EXPERIMENTAL SECTION

4-Methyl-1-phenethylcyclohexan-1-ol(**2**).- 4-Methylcyclohexanone (**1**) (112 g, 1 mol in 200 mL ether), purified via the semicarbazone, was added dropwise to phenethylmagnesium bromide in 600 mL anhydrous ether. The Grignard reagent was prepared from 212 g (1.15 mol) of phenethyl bromide and 28.5 g (1.15 equiv) of magnesium. After 1 hr of reflux, the reaction mixture was cooled, poured onto a mixture of ice and hydrochloric acid, extracted with ether, dried ($MgSO_4$), filtered, and concentrated to 163 g of yellow oil. Distillation gave 111 g (50%) of **2**, bp. 110-115°/0.1 mm, lit.[7] bp. 113°/0.1 mm.

$^{13}C$ NMR ($CDCl_3$): $\delta$ 142.9, 128.3, 128.2, 125.5, 70.3, 46.3, 36.8, 32.3, 30.2, 29.6, 22.3.

Cyclization of Alcohol **2** to a Mixture of 3-Methyl 1,2,3,4,4a,9,10,10a-Octahydrophenanthrene (**3**) and Spiro Hydrocarbon (**4**).- The alcohol **2** (332 g, 1.5 mol) was dehydrated with 70 g of Amberlyst-15[8] (A-15) in 1.5 L of refluxing benzene, the water produced by the reaction was removed using a Dean Stark trap. When the azeotrope was no longer produced, the reaction

mixture was filtered, a fresh batch of A-15 (60 g) was added, and reflux was continued for 72 hrs until GC analysis (5% Carbowax 20 M on Chromosorb W contained in a 1/8" x 6' stainless steel tube) showed a mixture of 3 and 4 (88:12). Addition of fresh A-15 (10 g) and heating for 2 hrs did not change this ratio. The reaction mixture was cooled, filtered, concentrated, and distilled to give 221 g (74%) of colorless oil, bp. 80-90°/0.2 mm, lit.[8] bp. 86°/0.1 mm.

Pd/C-catalyzed Dehydrogenation of a Mixture of 3 and 4 to 3-Methylphenanthrene (5) and 4.- A mixture of 3 and 4 (20 g, 0.1 mol) was dehydrogenated to a mixture of 5 and unreacted spiro hydrocarbon 4 by heating at 245° for 8 hrs in the presence of 1 g of 10% Pd/C. The reaction mixture solidified on cooling. It was dissolved in benzene, filtered through Dicalite, and concentrated to 19.5 g of dark product, then dissolved in 200 mL methanol and added to a solution of 30 g of picric acid in 200 mL of methanol. The resulting yellow picrate of 5 was collected, recrystallization from hot methanol to give 19 g of yellow needles, mp. 136°, lit.[7] mp. 138-139.5°, lit.[9] mp. 137-138°. This picrate was decomposed[3] on a column of basic alumina (1" diameter x 3") using hexane to give 9.0 g (50%) of 5, mp. 61-62°, lit.[7] mp. 61.5-62.5°, lit.[9] mp. 62-63°.

$^1$H-NMR ($CDCL_3$): $\delta$ 8.64 (d, 1H), 8.44 (s, 1H), 7.82 (d, 1H), 7.74 (d, 1H), 7.68-7.50 (m, 4H), 7.36 (3, 1H), 2.56 (s, 1H); $^{13}$C-NMR ($CDCl_3$): $\delta$ 136.3, 132.3, 130.2, 130.1, 128.6, 128.5, 128.4, 126.8, 126.5, 126.4, 126.2, 126.0, 122.7, 122.5, 22.2.

The filtrate from above was concentrated and freed of picric acid by passing its solution in hexane through a column (1" diameter x 4") of basic alumina.[3] The hexane extract was concentrated and Kugelrohr distilled to give 4 g of yellow oil rich in 4 and 5 as a minor GC component.[10] Similarly 193.5 g of mixture of 3 and 4 was dehydrogenated

and processed as described above to yield 93 g of **5** and 35 g of an oil rich in **4**.

The purity of **5** was independently verified by capillary GC/MS studies,[11] which showed that 1- and 2-methylphenanthrene were both absent in the final sample of **5** (99.99% purity).

Purification of Spiro Hydrocarbon (4).- Preparative HPLC[4] gave 17.5 g of **4** as a colorless oil, bp. 85-90°/0.1 mm.

$^{13}C$ NMR ($CDCl_3$): $\delta$ 152.1, 151.7, 143.3, 142.7, 126.1, 126.0, 125.9, 125.6, 124.3, 124.2, 123.4, 121.9, 47.7, 47.4, 39.2, 39.1, 34.9, 34.1, 32.4, 32.2, 30.1, 29.9, 29.8, 29.4, 22.7, 19.9.

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06

Found: C, 89.87; H, 10.15

Chromic Acid Oxidation of 4 to Spiro Ketone **6a**.- An 8 g (0.04 mol) sample of **4** was oxidized as described[13] to give 8.2 g of green oil. Kugelrohr distillation at 105-110°/0.4 mm gave 6.8 g (80%) of **6a** as a pale yellow oil.

$^{13}C$ NMR ($CDCl_3$): $\delta$ 204.9, 163.6, 163.2, 135.6, 135.5, 134.5, 134.3, 127.3, 124.5, 123.7, 123.1, 123.0, 49.3, 48.0, 42.5, 42.4, 38.2, 33.6, 32.4, 31.7, 29.4, 27.0, 22.3, 18.1.

Ketone **6a** (4.0 g) was converted to its 2,4-DNP which after three crystallizations from boiling nitroethane gave 1.8 g of **6b** as red needles, mp. 245-247°. Thin layer chromatography of this 2,4-DNP on silica (toluene) showed a single spot. To 1.77 g of the 2,4-DNP in 200 mL of dimethoxyethane was added 45 mL of a 20% aqueous solution of $TiCl_3$.[6] The reaction mixture was heated to reflux for 45 min under nitrogen, cooled, diluted with water, and extracted with ether. The ethereal extract was washed with water, dried ($MgSO_4$), and filtered. Concentration gave 1 g of dark yellow oil which was passed through a column (1" diameter x 6") of silica with a 1:1 mixture of ether:hexane. Distillation (Kugelrohr) gave

0.5 g of **6a** as a pale yellow viscous liquid. Capillary gas chromatography showed two peaks at 72.83 and 72.92 min in the ratio 1:1.15.[5] The $^{13}C$ NMR spectrum of **6a** was unchanged after hydrolysis of its 2,4-DNP.

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47

Found: C, 83.94; H, 8.52

Synthesis of 3-tert-Butylphenanthrene.- Using the procedure described for the synthesis of **5**, with substitution of 4-tert-butylcyclohexanone for **1**, gave 3-tert-butylphenanthrene, mp. 49-50°, lit.[12] mp. 45-55°; picrate mp. 140-141°, lit.[12] mp. 142-143°, in 32% overall yield.

$^{13}C$ NMR ($CDCl_3$): $\delta$ 149.2, 132.1, 130.4, 129.9, 129.8, 128.5, 128.1, 126.4, 126.2, 124.8, 122.4, 118.1, 35.1, 31.5.

Acknowledgement.- The Oklahoma State University authors are grateful for financial support from the National Institute for Petroleum and Energy Research, Bartlesville, OK 74005.



REFERENCES

1. The results of thermodynamic and spectroscopic studies of **3** will be reported by personnel of the National Institute for Petroleum and Energy Research, Bartlesville, OK 74005.
2. M. T. Bogert, Science 77, 289 (1933); J. W. Cook, C. L. Hewett and A. M. Robinson, J. Chem. Soc., 1168 (1939).
3. C. E. Browne, W. L. Buchanan and E. J. Eisenbraun, Chem. Ind. (London), 35 (1977).
4. Waters Prep LC/System-500 using PrepPak-500 silica cartridge and hexane eluent.
5. Hewlett-Packard 5890 GC/FID using 30 M x 0.25 mm I.D. x 0.25 $\mu$ film thickness Supelcowax 10 column. Program: 70°C initial, 2°/min to 280°C.
6. J. E. McMurray and M. Silvestri, J. Org. Chem., 40, 1502 (1975).
7. M. F. Ansell and G. T. Brooks, J. Chem. Soc., 4518 (1956).

8. Amberlyst-15, sulfonated, bead-form resin, was a gift from Rohm and Haas Co., Philadelphia, PA 19105.

9. R. D. Haworth, J. Chem. Soc., 1125 (1932).

10. 5% Carbowax 20 M on Chromosorb W, 1/8" x 6' at 200°C, with 4 preceding 5.

11. 3-Methylphenanthrene (5) was subjected to GC/MS using a 60-m DB-5 capillary column operated from 70° to 120° 10°/min, from 120 to 200° at 2°/min, and from 200 to 350° at 12°/min. We thank D. R. I. McNeil, Shell Development Company for these studies.

12. L. F. Fieser and C. C. Price, J. Am. Chem. Soc., 58, 1838 (1936).

13. W. M. Harms and E. J. Eisenbraun, Org. Prep. Proced. Int., 4, 67 (1972).



* * * * *

## SYNTHESIS OF 2-[4-METHOXY-2-[2-(METHYLSULFINYL)ETHOXY]PHENYL]-1H-IMIDAZO[4,5-b]PYRIDINE, A POTENT NONGLYCOSIDE INHIBITOR OF $Na^+$, $K^+$-ATPASE

Submitted by (05/06/87) David W. Robertson* and Joseph H. Krushinski

Lilly Research Laboratories
Eli Lilly and Company
Indianapolis, IN 46285

AR-L 100 (compound 5, 2-[4-methoxy-2-[2-(methylsulfinyl)ethoxy]-phenyl]-1H-imidazo[4,5-b]pyridine) is one of the few potent, nonglycoside inhibitors of $Na^+$, $K^+$-ATPase.[1,2] We now describe our synthesis of this important pharmacological tool as shown below. Since acid-catalyzed