Tetrahedron Letters,Vol.27,No.23,pp 2571-2574,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

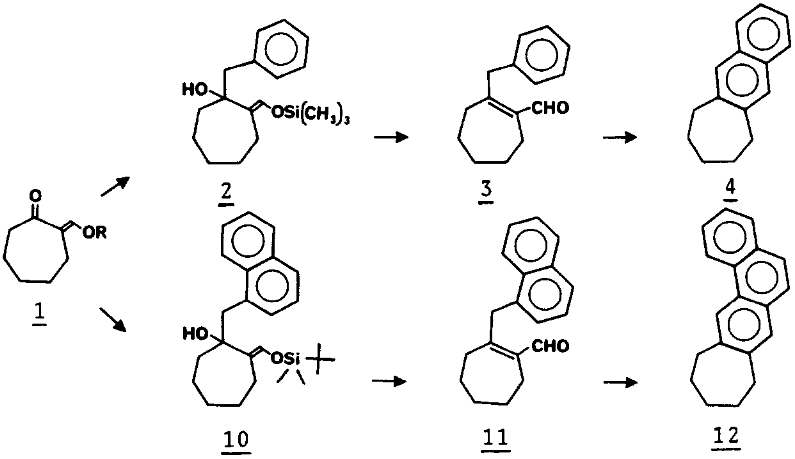
AROMATIC ANNELATION. SYNTHESIS OF NAPHTHALENES

Marcus A. Tius* and Jorge Gomez-Galeno
Department of Chemistry, University of Hawaii,
Honolulu, Hawaii 96822, U.S.A.

Summary: An efficient cationic cyclization reaction has been developed to prepare substituted naphthalenes. The method has been used to prepare a phenanthrene and will be useful for the synthesis of polynuclear aromatic hydrocarbons and C-glycosyl anthraquinones.

The elaboration of aromatic rings from non-aromatic precursors is an area of current research interest.[1] General methods for the preparation of phenols, pyridines and substituted benzene rings have been disclosed.[1] Efforts from our laboratories have led to methods for the elaboration of 2-unsubstituted ketones to phenols, catechol monoethers, pyridines, biphenyls, m-terphenyls, methylphenyls and hydroxy p-quinones[2]. It would be particularly useful to apply this method to the synthesis of C-glycosyl naphthalenes. There is a lack of general methodology for preparing C-glycosyl aromatics.[3] The synthesis of this functional array would be useful for preparing C-glycosidic anthracycline antibiotics.[4]

The elaboration of unsubstituted naphthalenes from 2-unsubstituted ketones was the first objective.[5] Cycloheptanone was condensed with ethyl formate to produce 2-hydroxymethylene ketone 1 (R=H, Scheme I). This compound was treated with a 1/1 (v/v) mixture of chlorotrimethylsilane and triethylamine to produce the hydrolytically labile trimethylsilyl vinylogous ester 1 (R=TMS) which was immediately added to an excess of benzylmagnesium

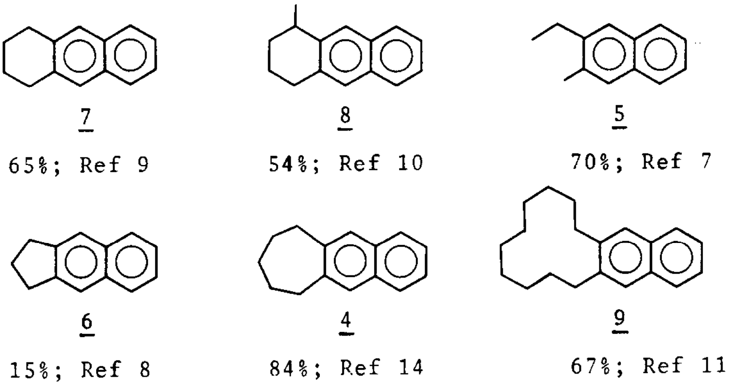


Scheme I

chloride at -55°C. Workup with aqueous sodium dihydrogen phosphate provided tertiary alcohol 2. The acid catalyzed cyclization reaction was expected to require more vigorous conditions than had been used in our earlier work,[2a] because the aromatic stabilization of the benzene ring would be lost in the reaction intermediate. It was most convenient to convert 2 to α,β-unsaturated aldehyde 3 by brief treatment with pyridinium tosylate (PPTS)[6] prior to cyclization. Treatment of 3 with boron trifluoride etherate in anhydrous nitromethane at 23°C produced naphthalene 4 in a clean but slow reaction. The best results were obtained with titanium tetrachloride in dichloromethane. Naphthalenes 4 - 9 were prepared in this manner (Scheme II). It is noteworthy that both geometric isomers of the α,β-unsaturated aldehyde precursor underwent cyclization to 2-ethyl-3-methyl-naphthalene 5. The lowest yield was observed for the cyclization of 6. Low yields had been observed for cyclopentanone in the benzoannelation reaction as well,[2a] perhaps because of a less favorable geometry for overlap between the aldehyde carbonyl carbon and the phenyl ring carbon.

The efficacy of this procedure for the preparation of other aromatics has been demonstrated by preparing a phenanthrene (Scheme I). 2-Chloromethylnaphthalene was treated with tributylstannyllithium.[12] The 2-tributylstannylmethyl naphthalene was isolated in 57% yield after flash chromatography on silica gel. Transmetallation with 0.9 equiv of n-butyllithium in THF at -78°C furnished 2-naphthylmethyllithium which was treated with 1 (R=*tert*-butyldimethylsilyl, 0.8 equiv). The reaction product 10 was treated briefly with an excess of PPTS [6] to give 11 in 68-80% overall yield. Cyclization of 11 with $TiCl_4$ in CH_2Cl_2 for 15 min at -40 to -30°C furnished 70% of phenanthrene 12[13] along with 15% of recovered 11. This result demonstrates the utility of the method for the synthesis of polynuclear aromatic hydrocarbons. General experimental procedures follow.

Scheme II


7 65%; Ref 9
8 54%; Ref 10
5 70%; Ref 7
6 15%; Ref 8
4 84%; Ref 14
9 67%; Ref 11

1-Formyl-2-benzylcyclohept-1-ene (3). A solution of 295 mg (2.1 mmol) of 1 (R=H) in 50 mL of ether was treated with 0.45 mL (1.2 equiv) of a 1:1 (v/v) mixture of chlorotrimethlysilane and triethylamine. After 2 min the resulting white suspension was added to 50 mL of a 0.32 M solution of benzylmagnesium chloride in THF (16.0 mmol, 7.6 equiv) at -55°C. The solution was stirred for ca. 1 min, then poured onto ice cold saturated aqueous NaH_2PO_4. The product was partitioned between ether and water. The ethereal phase was washed with brine, dried over K_2CO_3 and evaporated to produce an oil which was dissolved in 5 mL of dichloromethane and added dropwise to 10 equiv of PPTS. After 0.5 h at 23°C, aqueous workup followed by flash chromatography on silica gel afforded 293 mg (65% yield) of 3 as a colorless oil.

2,3-Cycloheptenonaphthalene (4). To a solution of 101 mg (0.47 mmol) of aldehyde 3 in 5 mL of CH_2Cl_2 cooled to -30°C was added 158 μL (1.4 mmol, 3.0 equiv) of $TiCl_4$. The solution was allowed to warm to 23°C during 2.5 h. The reaction mixture was decanted onto saturated aqueous $NaHCO_3$. Extraction with CH_2Cl_2 followed by drying over $MgSO_4$ and flash chromatography furnished 77 mg (84% yield) of naphthalene 4 (mp 104-105°C)[14].

Acknowledgement is made to the National Science Foundation, CHE-83-03495, for generous support. NSF grant CHE-81-00240 supported the purchase of the 300 MHz NMR spectrometer.

References and Notes

1. (a) A. B. Smith, III, and S. N. Kilenyi, Tetrahedron Lett., 4419 (1985); (b) T.M. Sivavec and T. J. Katz, Tetrahedron Lett., 2159 (1985); (c) R. K. Dieter and Y. J. Lin, Tetrahedron Lett., 39 (1985); (d) T. R. Kelly and H-t. Lin, J. Am. Chem. Soc., 107, 4998 (1985); (e) W. D. Wulff, R. W. Kaesler, G. A. Peterson and P-C. Tang, J. Am. Chem Soc., 107, 1060 (1985); (f) T. J. Katz and T. M. Sivavec, J. Am. Chem Soc., 107, 737 (1985); (g) J. N. Freskos and J. S. Swenton, J. Chem Soc., Chem. Commun., 658 (1985); (h) M. Yamaguchi, K. Shibato and I. Hirao, Chemistry Lett., 1145 (1985); (i) D. L. Boger and M. D. Mullican, J. Org. Chem., 49, 4033 (1984); (j) R. L. Danheiser and S. K. Gee, J. Org. Chem., 49, 1672 (1984), and references cited therein.
2. (a) M. A. Tius and S. Ali, J. Org. Chem., 47 3163 (1982), and references cited therein; (b) M. A. Tius and S. Savariar, Synthesis, 467 (1983).
3. A. O. Stewart and R. M. Williams, J. Am Chem. Soc., 107, 4289 (1985).
4. For a recent example of the synthesis of an anthraquinone antibiotic with a C-glycosidic linkage, and a discussion of the importance of this class of compounds, see: S. J. Danishefsky, B. J. Uang and G. Quallich, J. Am. Chem. Soc., 107, 1285 (1985).
5. (a) H. J. J. Loozen, J. Org. Chem., 40, 520 (1975); (b) M. P. Reddy and G. S. K. Rao, J. Org. Chem., 46, 5371 (1981); (c) M. P. Balu, G. Singh, H. Ila and H. Junjappa, Tetrahedron Lett., 117 (1986).
6. M. Miyashita, A. Yoshikoshi and P. A. Grieco, J. Org. Chem., 42, 3772 (1977).
7. 5: ir (neat) 2932, 1603, 876, 745 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ7.70-7.80 (2H, m), 7.59 (2H, bs), 7.30-7.50 (2H, m), 2.78 (2H, q, J = 7 Hz), 2.46 (3H, s), 1.30 (3H, t, J = 7 Hz); ^{13}C nmr ($CDCl_3$, 75 MHz) δ 141.12, 134.85, 132.44, 132.16, 127.76, 127.02, 126.76, 125.53, 124.98, 124.91, 26.26, 19.64, 14.29; mass spectrum (m/e) 170

(m^+), 155, 141; calcd for $C_{13}H_{14}$ 170.1096, found. 170.1097. J. M. Duswalt, T. J. Mayer, *Anal. Chem.*, 42, 1789 (1970).

8. 6: m.p. 84-85°C; ir (KBr) 2955, 741, 702 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 7.75 (q, 2H, J = 6 Hz), 7.65 (1H, bs), 7.37 (2H, q, J = 6 Hz), 3.06 (4H, t, J = 7 Hz), 2.14 (q, 2H, J = 7 Hz); ^{13}C nmr ($CDCl_3$, 75 MHz) δ 143.37, 132.87, 127.41, 124.79, 122.05, 32.61, 26.19; mass spectrum (m/e) 168 (m^+), 152, 139, 115; calcd for $C_{13}H_{12}$ 168.0939, found 168.0943. H. Christol, D. D. Koulodo, M. Mousseron and F. Plenat, *Bull. Soc. Chim. Fr.*., 1576 (1960).
9. 7: m.p. 92-94°C; ir (KBr) 2900, 832, 719 cm^{-1}; ^1H nmr ($CDCl_3$, 300 MHz) δ 7.68 2H, q, J = 6 Hz), 7.51 (2H, bs), 7.33 (2H, q, J = 6 Hz), 2.94 (4H, bs), 1.85 (4H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 136.16, 132.07, 126.91, 126.58, 124.82, 29.77, 23.38; mass spectrum (m/e) 182 (m^+), 167, 165, 154, 141; calcd for $C_{14}H_{14}$ 182.1096, found 182.1108.
10. 8: ir (neat) 2925, 843, 772 cm^{-1}; ^1H nmr (300 MHz. $CDCl_3$) δ 7.60-7.80 (2H, m), 7.53 (2H, bs), 7.30-7.40 (2H, m), 3.08 (1H, bq) 2.95 (2H, t, J = 6 Hz), 1.5-2.1 (4H, m), 1.40 (3H, d, J = 7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ 141.35, 136.08, 132.20, 131.91, 121.18, 126.81, 126.38, 125.59, 124.98, 124.78, 32.77, 31.71, 30.25, 22.74, 20.90; mass spectrum (m/e) 196 (m^+), 181, 178, 171, 165, 152; calcd for $C_{15}H_{16}$ 196.1253, found 196.1246 F. G. Morin, W. J. Horton, D. M. Grant, D. K. Dalling and R. J. Pugmire, *J. Am. Chem. Soc.*, 105, 3992 (1983).
11. 9: m.p. 55-56°C; ir (KBr) 2900, 880, 859, 730 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 7.74-7.71 (2H, q, J = 6 Hz), 7.64 (2H, bs), 7.34-7.38 (2H, q, J = 6.3 Hz), 2.81 (4H, t, J = 8 Hz), 1.50-2.00 (14H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 140.16, 132.14, 127.69, 126.90, 124.93, 30.37, 30.00, 26.86, 26.00, 23.14; mass spectrum (m/e) 266 (m^+) 231, 223, 209, 195, 183, 169; calcd for $C_{20}H_{26}$ 266.2072, found 266.2022.
12. (a) W. C. Still, *J. Am. Chem Soc.*, 100, 1481 (1978); (b) W. C. Still, *J. Am. Chem. Soc.*, 99, 4836 (1977).
13. 12: ir (hexane) 889, 806, 745 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 8.65 (1H, d, J = 8 Hz), 8.40 (1H, s), 7.85 (1H, d, J = 8 Hz), 7.70-7.50 (m, 5H), 3.09-3.05 (2H, bt), 3.01-2.98 (2H, bt), 1.95-1.85 (2H, m), 1.83-1.70 (4H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 142.54, 131.86, 130.56 130.10, 128.56, 128.45, 127.99, 126.37, 126.19, 126.03, 125.90, 125.48, 122.41, 122.30, 37.88, 36.65, 32.58, 28.91, 28.90; mass spectrum (m/e) 246 (m^+), 217, 215, 205, 202, 141; calcd for $C_{19}H_{18}$ 246.1408, found 246.1406.
14. 4: m.p. 104-105°C; ir (KBr) 881, 824, 737 cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ 7.24 (2H, q, J = 5.7 Hz), 7.55 (2H, bs), 7.38 (2H, q, J = 6 Hz), 2.95 (4H, m), 1.6-2.0 (6H, m); ^{13}C nmr (75 MHz, $CDCl_3$) δ 142.08, 132.33, 126.92, 126.67, 125.04, 36.81, 32.42. 29.14; mass spectrum (m/e) 196 (m^+), 167; calcd for $C_{15}H_{16}$ 196.1253, found 196.1296. P. Grice and C. B. Reese, *Tetrahedron Lett.*, 2563 (1979).

(Received in USA 19 March 1986)