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# NUCLEOPHILIC AROMATIC SUBSTITUTION - A ROUTE TO THE NAPHTHALENE SYSTEM FROM α-CYCLOPROPYLSTYRENE

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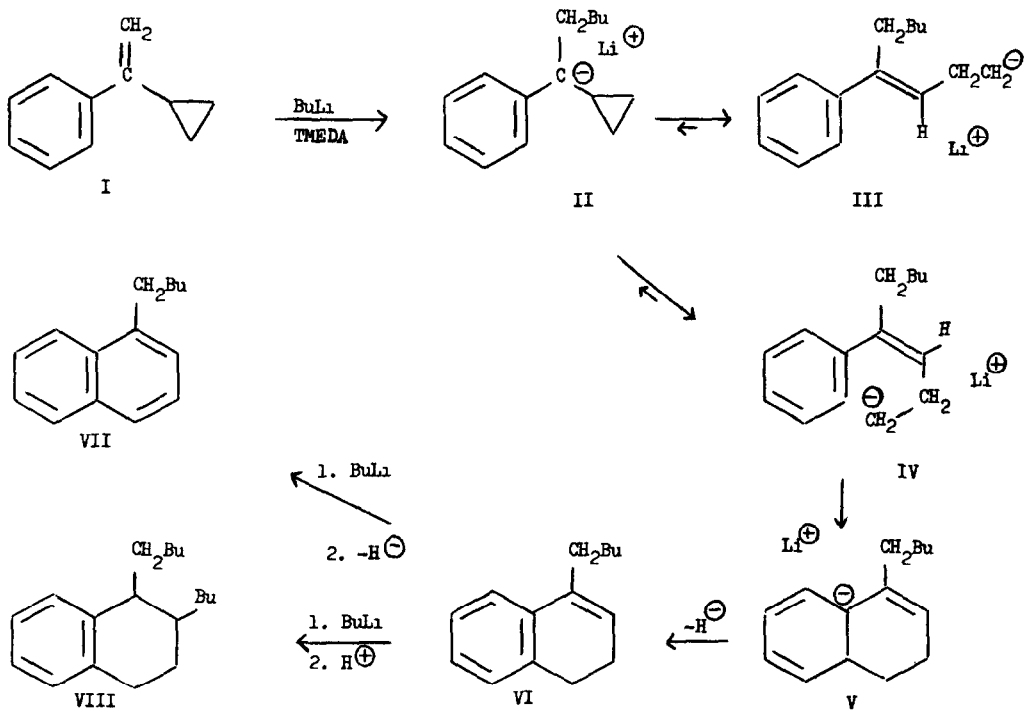
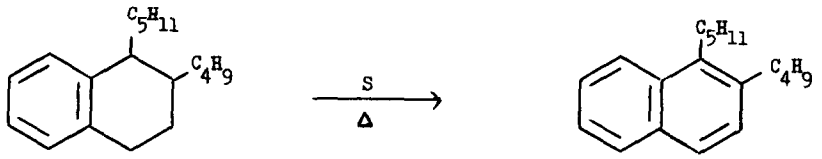
Alkyllithium reagents add to α-cyclopropylstyrene (I) to produce cyclopropylcarbinyllithium derivatives which undergo ring-opening to the corresponding styrenes[1,2]. These additions were achieved either by using isopropyllithium in ether[1] or with BuLi-TMEDA (tetramethylethylenediamine) complex in hexane[2]. We have shown that the intermediate carbanion II ring-opens rapidly to produce the isomeric cis and trans anions III and IV, in an approximate ratio of 1:1, which could be trapped by protonation or silylation[2].

We now wish to report on the intramolecular cyclization of anion IV leading to the formation of naphthalene derivatives.



Excess (4 equivalents) of BuLi-TMEDA complex in hexane was reacted with I for 24 hr. at room temp. Decomposition with water and dilute HCl gave a product mixture (ca. 75%) b.p. 145-160°/0.4 mm (ball oven). GLC analysis (SE 30, 15%, 2 m at 170°) showed the presence of three major fractions which constitute 90% of the mixture. The first fraction (15%) was an equimolar mixture of cis- and trans-1-pentyl-1-phenylbutenes derived from III and IV as proven before[2]. The second fraction (40%) was identified as 1-pentylnaphthalene (VII) based on the following spectroscopic data. NMR ($CCl_4$): 7.98-6.69/m, 7H (aromatic); 2.99/t (J ≅ 8), 2H (benzylic); 1.91-0.79, 9H ($-(CH_2)_3CH_3$). UV: $\lambda_{max}^{CH_3CN}$ (nm) 274 (ε 5400); 284 (ε 6090) and 291 (ε 4000). MS: 198 ($M^+$, 50%); 141 (100%) and 115 (25%) m/e. The third fraction (35%) was identified as 1-pentyl-2-butyl-1,2,3,4-tetrahydronaphthalene (VIII) (with unknown stereochemistry). NMR ($CCl_4$): 6.83/bs, 4H (aromatic); 2.82-2.20/m, 3H (benzylic); 2.1-0.8, 23H (aliphatic alicyclic). UV: $\lambda_{max}^{EtOH}$ (nm) 262 (ε 610); 268 (ε 780) and 275 (ε 830); MS: 258 ($M^+$, 15%) and 187 (100%). In order to confirm the structure of VIII, a sample was heated with sulphur at 230-240° for 1 hr.[3] and



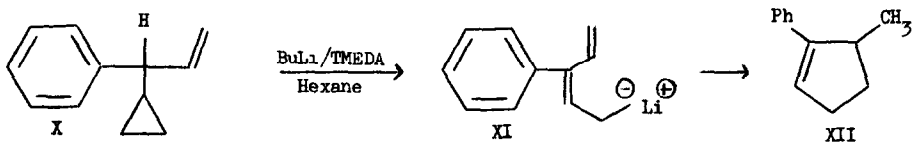

VIII IX

then sublimed at 140-160°/0.2 (ball oven). Crude 1-pentyl-2-butylnaphthalene (IX) was obtained; MS: $M^+$ 254 m/e and UV: $\lambda_{max}^{EtOH}$ (nm) 275, 283 and 297.

When I was reacted with a smaller amount (2 equivalents) of BuLi 1-pentyl-3,4-dihydronaphthalene (VI) could also be isolated (GLC). NMR ($CCl_4$): 7.0/bs, 5H (aromatic); 5.75/t (j = 3.6), 1H (olefinic); 2.69/t (J = 7), 2H (benzylic); 2.50-2.02, 4H (allylic); 1.61-0.76, 9H ($-(CH_2)_3CH_3$) UV: $\lambda_{max}^{EtOH}$ (nm) 262 (ε 14,000). MS: 200 ($M^+$, 54%), 144 (100%), 141 (54%), 129 (99%), 115 (46%).

The formation of the naphthalene derivatives can be rationalized by the following mechanism: The two anions III and IV[2] are probably in equilibrium through a small concentration of II[4]. The intramolecular cyclization IV ⟶ V shifts the equilibrium in the direction of IV, thus keeping the ratio of III:IV practically constant. The intermediate carbanion V loses rapidly a hydride to produce VI. After VI is formed it reacts with a second mole of BuLi to give either VII by proton abstraction and loss of hydride or VIII by addition and protonation.

Only a few cases of nucleophilic cyclization on the benzene ring were reported in the literature[4,5,6]; however, in all of them potassium was the counterion. Magid and Wilson[7] have reported on the metalation of α-cyclopropylallylbenzene (X) with BuLi. The resulting anion XI cyclized to produce XII only - thus demonstrating the difficulty of aromatic nucleophilic substitution.



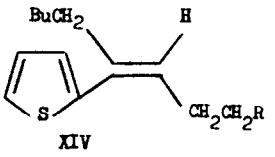

X XI XII

In our system anion IV, lacking a double bond in an appropriate position, cyclizes via aromatic nucleophilic substitution to produce VI in high yield (based on the yield of VII + VIII).

When $\alpha$-(2-thienyl)vinylcyclopropane (XIII)[8] was submitted to the same reaction conditions as I, addition of BuLi followed by ring-opening occurred, however no indication of intramolecular cyclization could be traced after 24 hr. Addition of water to the reaction mixture produced mainly the two isomers XIVa and XVa, b.p. 120-150°/0.2 (ball oven) in 55% yield. The two isomers[9] in a 1:4 ratio were separated by GLC (SE 30, 15%, 2m at 150°).

1-Pentyl-cis-1-(2-thienyl)butene (XIVa); NMR ($CCl_4$): 7.10-6.68/m, 3H (thienyl); 5.35/t (J = 6), 1H (vinyl); 2.49-1.97/m, 4H (allylic); 1.95-0.77, 12H $[-(CH_2)_3CH_3 + CH_3-]$; UV: $\lambda_{max}^{EtOH}$ (nm) 248 ($\varepsilon$ 6,800), 263 (7,100) and MS: $M^+$ 208 m/e.

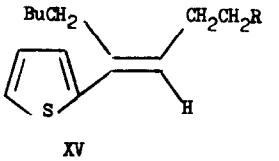
1-Pentyl-trans-1-(2-thienyl)butene (XVa); NMR ($CCl_4$): 7.1-6.65/m, 3H (thienyl); 5.70/t (J = 6), 1H (vinyl); 2.64-1.98/m, 4H (allylic); 1.8-0.76, 12H $[-(CH_2)_3CH_3 + CH_3-]$; UV: $\lambda_{max}^{EtOH}$ (nm) 265 (7,550), 279 (7,700) and MS: $M^+$ 208 m/e.




XIV

a, R = H

b, R = $-Si(CH_3)_3$




XV

a, R = H

b, R = $-Si(CH_3)_3$

In order to establish whether extensive metalation of the thiophene ring prevented cyclization to benzthiophene derivatives, decomposition of the reaction mixture with trimethylsilylchloride was performed. A mixture of silyl derivatives was obtained in 60% yield. These were separated by GLC (SE 30, 15%, 2m at 150°) into three fractions in a ratio of 1.2:5:1.

The first fraction was characterized as the cis isomer[9] XIVb; NMR ($CCl_4$): 7.05-6.62/m, 3H (thienyl); 5.3/t (J = 7), 1H (vinyl); 2.55-1.85/m, 4H (allylic); 1.6-0.72 $[-(CH_2)_3CH_3 + -CH_2-Si\equiv]$; 0.19/s, 9H (trimethylsilyl); UV: $\lambda_{max}^{EtOH}$ (nm) 251 (7,000), 278 (7,400) and MS: $M^+$ 280 m/e.

The second fraction was identified as the trans[9] isomer XVb; NMR ($CCl_4$): 7.02-6.73/m, 3H (thienyl); 5.8/t (J = 7), 1H (vinyl); 2.60-2.0/m, 4H (allylic); 1.55-0.79 $[-(CH_2)_3CH_3 + -CH_2-Si\equiv]$; 0.39/s, 9H (trimethylsilyl); UV: $\lambda_{max}^{EtOH}$ (nm) 255 (6,600) 293 (6,000) and MS: $M^+$ 280 m/e.

Only the third fraction (15% of the mixture) consisted of dimetalation products according to its NMR and mass spectra. It contained at least two compounds (GLC) - however their exact structure was not established. Metalation of thiophene in the 2-position by BuLi is known to be an easy process[10], but the presence of a double bond in XIII brought about addition of BuLi rather than metalation.

Apparently - accumulation of the negative charge in the carbanion, after the addition of one mole of BuLi to XIII, made the attack of a second mole of BuLi on the thiophene ring extremely difficult.

The fact that no cyclization to benzthiophene derivatives could be observed, in contrast to the high yield of cyclization to produce naphthalene derivatives in the benzo analog, can be ascribed to the lack of reactivity of the 3-position in thiophene - thus diminishing the chances for nucleophilic attack on that position.

## References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9) The cis-trans configuration was established by NMR and UV spectra, see ref. 2 and references therein.

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