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Valence Isomers of Aromatic Compounds: On the Mechanism of the Katz Reaction**

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Abstract: Lithium salts of small and medium-sized aromatic anions react with methylene chloride and alkyllithium to afford bridged bicyclobutanes or related polycyclic compounds. We demonstrate that the three new carbon–carbon bonds formed in the course of these title reactions result from a tandem of carbenoid processes. Formation of exocyclic carbenoids precedes intramolecular cheletropic addition and ring enlargement. Neither H-migration nor CH-insertion is observed throughout these processes. Key intermediates have been generated by independent routes.

In the late sixties, *Katz* and his coworkers[1] recognized that monochlorocarbene, generated from CH_2Cl_2 and alkyllithium, can act as a synthetic equivalent of $\ll CH^{\oplus} \gg$ when allowed to react with lithium salts of aromatic anions. Thus, the reaction of cyclononatetraenyllithium (**1**) with CH_2Cl_2/CH_3Li in ether, afforded isobullvalene (**2**) which subsequently underwent a Cope rearrangement to give tricyclo[5.3.0.$0^{4,10}$]deca-2,5,8-triene (**3**)[1,2]. This method of introducing three new carbon–carbon bonds in a single operation was rapidly extended to lithium salts of other aromatic anions, and found its most renowned application in the synthesis of benzvalene (**5**)[3,4]. By now, the reaction of formal chlorocarbene with nearly all of the more readily available lithium salts of aromatic anions has been studied. It should be tacitely understood throughout this communication that the latter are present in solution largely as ion pairs[5]. Table 1, which does not claim to be exhaustive, shows that impressive polycyclic structures have been obtained by this method. Some time ago, we suggested, these reactions to be called «Katz reactions». This proposition has been widely accepted[12].

The present report deals with progress made in understanding the underlying mechanism of these reactions. Three closely related questions needed to be answered. Firstly, in which order are the three new CC-bonds formed? Secondly, are there distinct intermediates and what is their precise nature? And thirdly, what is the final product releasing step?

Ten years ago, we reported that the reaction of indenyllithium (**18**) with $C[^2H_2]Cl_2$/*n*-BuLi gave [1-^{2}H]benzobenzvalene (11%) and both, [1-^{2}H]naphthalene (8%) and [2-^{2}H]naphthalene (13%). The assumption

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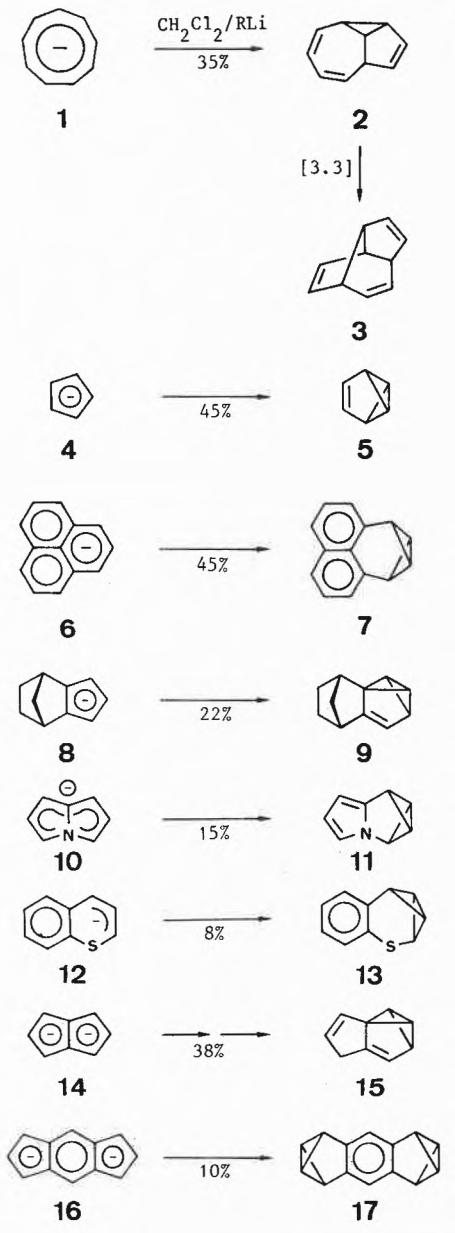
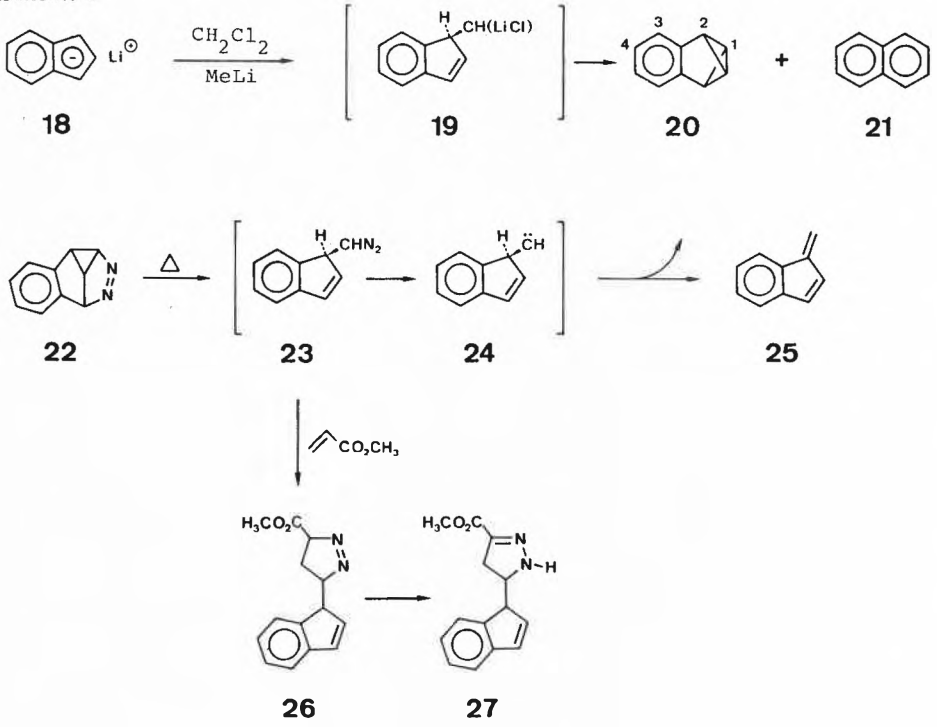
Table 1. Reactions of CH_2Cl_2/RLi with lithium salts of aromatic anions (selected examples).



References: **2**, **3**[1,2]; **5**[3]; **7**[6]; **9**[7]; **11**[8]; **13**[9]; **15**[10]; **17**[11].

was made that benzobenzvalene (**20**) and naphthalene (**21**) have a common precursor. This finding ruled out chlorocyclopropanation as the initial CC-bond forming step, since this cannot account for the formation of [1-^{2}H]naphthalene[13]. *Per exclusionem* we deduced that in the initial step only one CC-bond is formed. Nucleophilic attack of the indenyl anion (**18**) at chlorocarbene or dichloromethyllithium[14] was suggested to give an indenylcarbene or a corresponding carbenoid (**19**) as the key intermediate. Intramolecular 1,2-addition and concomitant ring enlargement could then account for the products **20** and **21**, respectively (Scheme 1).

Scheme 1



Recently, we found[15] that the thermolysis of 1,2-diazabenzo[*e*]semibullvalene (**22**) in dilute chloroform solution gave mainly benzofulvene (**25**) (83%) and only minor amounts of benzobenzvalene (11%) and naphthalene (6%). Similar observations have been made by *Kjell* and *Sheridan* for the gas phase pyrolysis of **22**[16]. We interpreted this finding in terms of a 1,3-dipolar cycloreversion of **22**. The ensuing diazomethyl-indene (**23**) rapidly loses nitrogen to give **24** and thus was not observed as an intermediate in the thermolysis experiments. Our interpretation is strongly supported by the fact that the formation of $C_{10}H_8$ compounds **20**, **21**, and **25** is completely suppressed when the thermolysis of **22** is run in the presence of excess methyl acrylate. This powerful 1,3-dipolarophile[17] intercepts diazomethyl-indene (**23**) to afford the tautomeric dihydropyrazoles **26** and **27** in a total yield of > 93%[18].

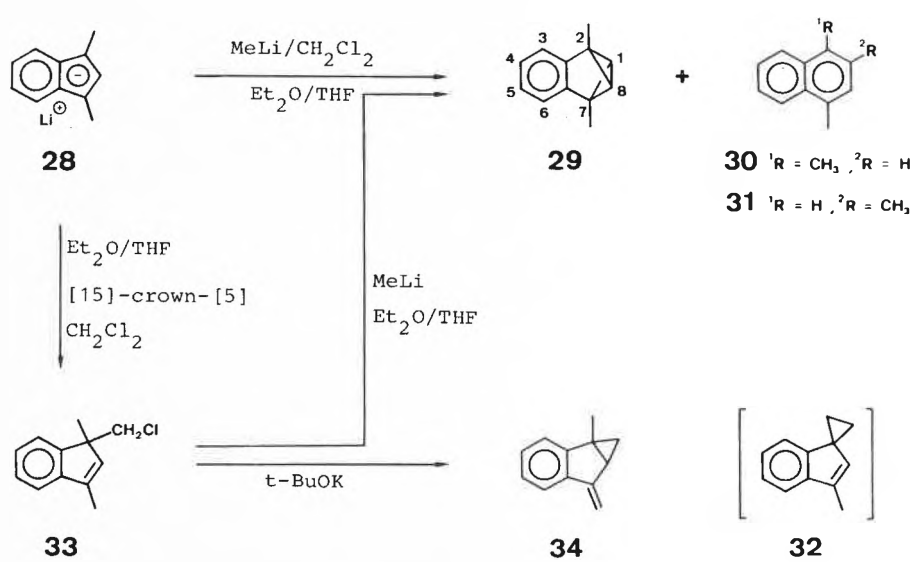
It should be mentioned, that low temperature photolysis of **22** affords **23**, and both **20** and **21** in comparable amounts[16]. *Kjell* and *Sheridan* have elegantly demonstrated that in these photolysis experiments **20** and **21** result from direct loss of nitrogen from **22**, eluding the 1,3-dipolar cycloreversion pathway. Further irradiation of **23** gave only **25**[16].

In the light of these findings, it is unlikely that the key intermediate in the Katz reaction of indenyllithium (**18**) leading to benzobenzvalene (**20**) is a free indenylcarbene[19], at best it could be a carbenoid. Unfortunately, benzofulvene (**25**) does not survive the conditions of the Katz reaction, so we have no information whether hydrogen migration occurs in competition to bicyclobutane formation and ring enlargement.

To gain more information on the precise nature of the key intermediate, the reaction of 1,3-dimethyl-indenyllithium (**28**)[20] with formal chlorocarbene was investigated. The methyl groups serve both, as a label and, by virtue of possible CH-insertion, as a mechanistic probe. 1,3-Dimethyl-indenyllithium (**28**) in Et_2O/THF (10:1) gave upon reaction with CH_2Cl_2/MeLi at −15°C to 25°C three isomeric hydrocarbons, namely 2,7-dimethyl-benzobenzvalene (**29**), 1,4-dimethyl-naphthalene (**30**), and 1,3-dimethyl-naphthalene (**31**); absolute yields based on **28** are 25%, 40%, and 12%, respectively. In addition, 1,3-dimethyl-1-ethyl-indene was isolated in 14% yield from the reaction mixture. This compound which is not shown in Scheme 2, is of no mechanistic interest to our question, since it results most probably from direct reaction of **28** with ethyl chloride, the latter being a notorious by-product of the reaction of MeLi with CH_2Cl_2 in tetrahydrofuran (THF) containing solutions[21]. No 3′-methyl-spiro[cyclopropane-1,1′-indene] (**32**), which would result from an intramolecular carbene insertion, was detected by GC or ^{1}H-NMR analysis in the crude reaction mixture. We have synthesized this compound from 1-methylindene and 1,2-dibromoethane[22] and found it to be stable under the conditions of the Katz reaction.

The structural proof of the new compounds by ^{1}H-NMR, ^{13}C-NMR, elemental analysis, and mass spectrometry is straightforward. Only compound **29** deserves special comment. Due to its C_{2v}-symmetry, this hydrocarbon shows a very simple and at first glance non informative ^{1}H-NMR spectrum. When recorded in $CDCl_3$ at 360 MHz it consists of a narrow aromatic [AA′BB′] spin pattern centered at $\delta = 6.95$ and just two singlets at $\delta = 3.85$ (2H) and 1.45 (6H). However, careful examination of the ^{13}C-satellites of the proton resonance at $\delta = 3.85$ revealed both, a huge $^1J_{C(1)-H}$ coupling constant of 210 Hz and a $^3J_{H-H}$ coupling constant of 9.5 Hz. This data clearly attests to a bicyclobutane skeleton. Spin saturation of the methyl resonance moreover, resulted in a 12% nuclear Overhauser effect (NOE) for the low-field part of the aromatic [AA′BB′] pattern.

Scheme 2



When we attempted to run this Katz reaction in presence of a crown ether, we observed, that 1,3-dimethyl-indenyllithium (**28**) in Et_2O/THF (10:1) with 1.0 molar equivalent of [15]-crown-[5] added, reacted rapidly with CH_2Cl_2 to afford the chloromethyl compound **33** in > 93% yield. In absence of the crown ether and in the corresponding temperature range (−15°C to 25°C), this reaction was extremely sluggish. Treatment of chloride **33** with 1.5 equivalent each of potassium *tert*-butoxide and [18]-crown-[6] in boiling THF resulted in an ε-elimination affording benzohomofulvene **34** (96%). This mode of reaction has ample precedence[23]. However, when we treated the chloride **33** with 1.5 equivalent of MeLi or *n*-BuLi in Et_2O/THF (10:1) at −15°C to 25°C, we obtained the same hydrocarbons, i.e. **29** (21%), **30** (48%), and **31** (19.6%) that we isolated from the Katz reaction of 1,3-dimethyl-indenyllithium (**28**). Although the yields and product ratios are somewhat different, again, the spirocompound **32** was not formed.

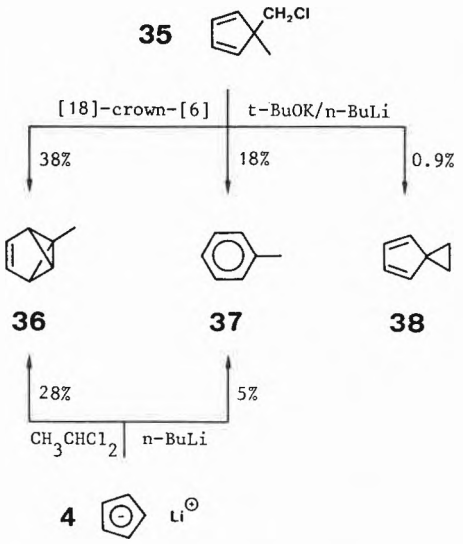
The chloride **33** is certainly not a real intermediate in the Katz reaction nor is it expected to be one. Firstly, its formation in absence of a crown ether is far too slow, and secondly, when we performed the Katz reaction of unsubstituted indenyllithium **18** in presence of chloride **33**, the latter did not cross in, but was recovered almost quantitatively. Nevertheless, the availability of chloride **33** allows us to enter the mechanistic pathway of the Katz reaction *via* subsequent α-lithiation, i.e. at a stage where one of the new bicyclobutane bonds of **29** is already formed. This confirms nicely our earlier conclusions. The final and product releasing step is clearly an intramolecular 1,2-carbenoid addition, the non-intervention of free carbene being attested by the absence of CH-insertion.

These results should be compared with the known behaviour of 1-chloromethyl-1-methylcyclopenta-2,4-diene (**35**)[24]. This compound, unlike chloride **33**, turned out to be nearly inert to *n*-BuLi in Et_2O/THF (10:1) at room temperature (3 h). However, when solutions of **35** in ether were allowed to react at room temperature with a modified Schlosser base[25], two mole-equivalents each of potassium *t*-butoxide, *n*-butyllithium, and [18]-crown-[6] for three hours, three isomeric hydrocarbons were obtained, namely 1-methyl-benzvalene **36** (38%), toluene **37** (18%), and spiro[2.4]hepta-4,6-diene **38** (0.9%) (Scheme 3).

At first glance, this transformation resembles the bicyclobutane formation **33**→**29** of Scheme 2. It must be noted however, that in compound **35** the central bicyclobutane bond, and not a lateral one, is already present. Consequently, in this process we are dealing with an intramolecular 1,4-cheletropic addition. The small amount of spirane **38** formed reveals that at least some leakage to free carbene had occurred under the strongly ionizing conditions[26].

Christl et al.[27] reported very recently, that the Katz reaction is not limited to the use of CH_2Cl_2 but can be extended to 1,1-dichloroethane. Starting from cyclopentadienyllithium **4** these authors have obtained the same hydrocarbon **36** we had prepared from **35**. Once again, products resulting from hydrogen migration, such as 6-methylfulvene or vinylcyclopentadienes, were not observed in these experiments.

Scheme 3



From the ensemble of these findings we can safely conclude that the mechanism of the Katz reaction consists of a sequence of carbenoid reactions. What is found here for our model compounds probably holds for all of the examples shown in Table 1. In the first instance, one new CC-bond is formed by nucleophilic attack of the aromatic anion at chlorocarbene or dichloromethyllithium. The ensuing exocyclic carbenoid can undergo an intramolecular cheletropic addition, or ring enlargement. Corresponding by-products, though not explicitely shown, are found in all the reactions mentioned in Table 1. The intramolecular addition can be a 1,4-cheletropic process if geometric and electronic factors allow, but in most cases, 1,2-addition prevails.

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