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THE REACTIONS OF 2,4- AND 2,5-CYCLOHEXADIENE-1-CARBOXYLATES WITH BASE. STUDIES RELATED TO THE MECHANISM OF THE TROPOLONE REARRANGEMENT (1)

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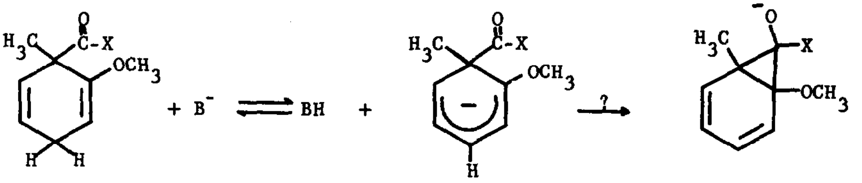
In an effort to gain insight into the mechanism of the base-catalyzed aromatization reaction of tropones and tropolones, and to develop a new synthetic route to such systems, we have investigated the action of a wide variety of bases on 2,4- and 2,5-cyclohexadiene-1-carboxylic acid derivatives. The results of these experiments are described in this paper and their relevance to the mechanism of the tropolone rearrangement is discussed in the following communication.

The first compounds studied were the 2-methoxy-1-methyl-2,5-cyclohexadiene-1-carboxylates [1]. The reaction which we sought was abstraction of one of the doubly allylic protons followed by closure of the carbanion on the carbonyl group, a process related to homoenolate formation in various ketones (3).



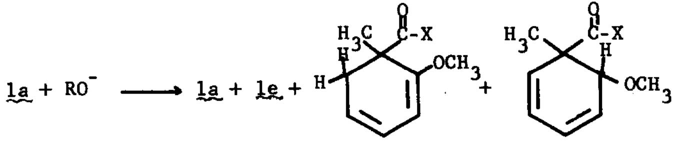
1a $X = OCH_3$
1b $X = O\text{i-Pr}$
1c $X = Cl$
1d $X = OC_6H_5$
1e $X = O^-$

2

3

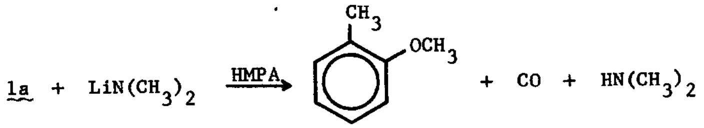
A number of bases (sodium hydride in ether, mesityl Grignard in ether and in dibutyl ether, and triphenylmethylsodium in ether, all at reflux, and potassium carbonate in dimethylformamide at 140°) with 1a lead either to no reaction or to conversion of the ester into carboxylate anion 1e (presumably by Bunnett reaction (4) of 1a with alkoxide ion from basic decomposition of the solvent).

Sodium methoxide in methanol at reflux was similarly discouraging, but at 110° for 20 hr, substantial double-bond isomerization occurs yielding conjugated dienes 4a and 5a; Bunnett reaction and/or hydrolysis by traces of moisture was also observed in the formation of 1e, 4c, and 5c. Potassium *t*-butoxide in dimethyl sulfoxide (DMSO)(5) at 75° leads completely to salts 1e, 4c, and 5c; *t*-butyl methyl ether from the Bunnett reaction was isolated (6).



4a X = OCH_3 5a X = OCH_3
4b X = O*i*-Pr 5b X = O*i*-Pr
4c X = O^- 5c X = O^-

Lithium dimethylamide in hexamethylphosphoramide (HMPA) (5) at 100° for 13.5 hr or at room temperature for 18 hr produces quantitative conversion of 1a into *o*-methoxytoluene [6], carbon monoxide (103%)and dimethylamine (81%). After 1 hr at 85°, 6 is obtained in 85% yield, the remainder of starting material appearing as a mixture of 1a, 4a, and/or 5a. Several



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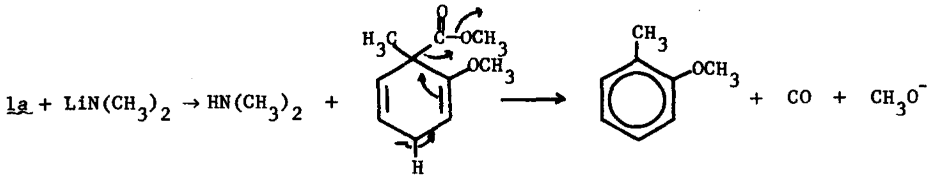
mechanisms for the formation of 6 can be envisaged, but the fact that carbon monoxide is isolated suggests that the oxidation of 1a involves proton and not hydride loss; the observation that double-bond isomerization of 1a occurs suggests that the reaction is a two-step process proceeding *via* 2a which then expels carbon monoxide and methoxide. Analogous formation of the elements of the formyl anion in a number of reactions has previously been reported (7). In similar fasion, 1a with phenyllithium in refluxing ether leads to 46% of 6; the major course of the reaction, apparently, is addition of phenyllithium to the carbonyl group.



2a

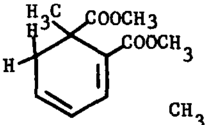
6

Since methyl ester 1a is so readily transformed into carboxylate anion 1e which would not be expected to undergo the desired ring closure, we turned our attention to the reactions of isopropyl ester 1b. Treatment of 1b with sodium isopropoxide in refluxing isopropanol results in the recovery of a small amount of 1b, 4b, and 5b; the major portion of starting material appears as a mixture of salts 1e, 4c, and 5c. Since diisopropyl ether is not among the products, we believe that formation of the carboxylates occurs by E2 elimination on 1b. Potassium *t*-butoxide in DMSO at 100° leads to 60% of 6, and 40% of a mixture of salts 1e, 4c, and 5c. Quantitative conversion of 1b into 6 occurs with lithium dimethylamide in HMPA.

Acid chloride 1c undergoes no reaction with 2,4,6-trimethylpyridine at 110° for 9 hr; starting material is recovered in high yield. Phenyl ester 1d, which can undergo neither Bunnett reaction nor easy E2 elimination, is completely transformed into *o*-methoxytoluene [6] by potassium *t*-butoxide in DMSO.

From the double-bond isomerizations and the formation of 6 under a variety of conditions, we are confident that anion 2 has been formed, but that closure to 3 does not occur. In an effort to effect cyclization under milder conditions, we investigated the reactions of the substantially stronger carbon acid, dimethyl 1-methyl-2,4-cyclohexadiene-1,2-dicarboxylate [7].

Sodium methoxide in refluxing methanol gives no evidence of proton abstraction. A mixture of neutral (80%) and water soluble (20%) materials is obtained; the neutral fraction consists of a mixture of 7 and the *cis* and *trans* isomers of Michael product 8; the salts, after esterification, yield 7 and 8 in approximately the same proportions. Potassium *t*-butoxide in refluxing *t*-butanol yields only water soluble products which, upon esterification, give 38% of 7, 4% of its double-bond isomer 9, and 58% of methyl *o*-toluate [10]. Potassium carbonate in dry dimethylformamide at 130° for 18 hr gives 90% of a neutral fraction (95% **10**, 3% **7**, and 2% **9**) and 10% of a mixture of salts (8) which are esterified to give a similar mixture of esters (98% **10** and 2% **7** and **9**). No evidence of ring closure (analogous to **2** → **3**) was obtained and the simplest



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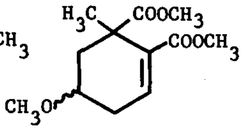

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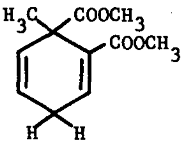

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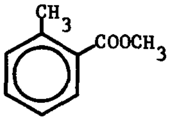

10

mechanism for the formation of **9** and **10** is proton abstraction from **7**, followed by expulsion of carbon monoxide and methoxide (as postulated for **1** → **6**)

REFERENCES

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