Tetrahedron Letters No.46, pp. 4819-4822, 1968. Pergamon Press. Printed in Great Britain.

THE MECHANISM OF THE TROPOLONE REARRANGEMENT (1)

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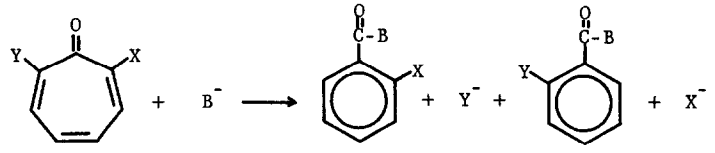
(Received in USA 27 June 1968; received in UK for publication 19 August 1968)

Tropones substituted in the α-position by good leaving groups are converted into benzoic acid derivatives by a wide variety of bases; when two leaving groups are available, a mixture of products is often obtained (3).



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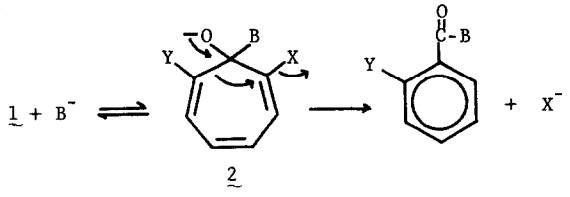
Tracer experiments with carbon-14 (4a), the failure of 2-chlorotropone to react with silver nitrate (4b), and exchange experiments involving $H_2{}^{18}O$ (4c) lead to rejection of all but three mechanisms for the rearrangement. Scheme 1 (6) and the related Scheme 2 were discounted by Doering and Denney (4a) since each fails to take account of the general observation that when X and Y are of different basicity, the poorer leaving group is preferentially expelled. A mechanism consistent with all of these data, Scheme 3 (4a), involves reversible formation of norcaradiene 3, followed by ring-opening to either or both of two cyclohexadienyl anions, 4a and 4b; expulsion of X^- or Y^- yields the aromatic products. The significant feature of this mechanism is that loss of X^- or Y^- is not part of the product-determining transition state; rather, product formation is determined solely by energy differences in the transition states leading from 3 to 4a and 4b. According to Scheme 3, a substituent on the ring which can stabilize a

Scheme 1



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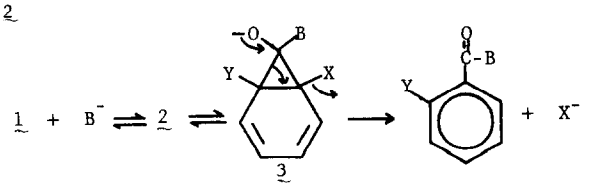
Scheme 2



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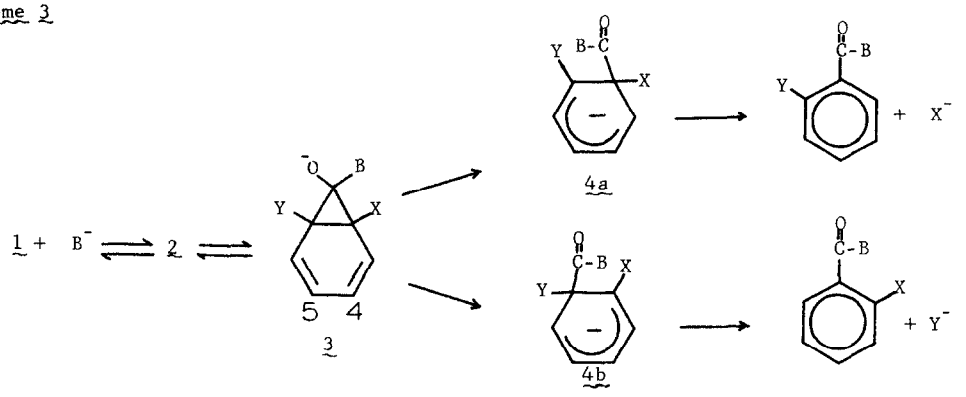
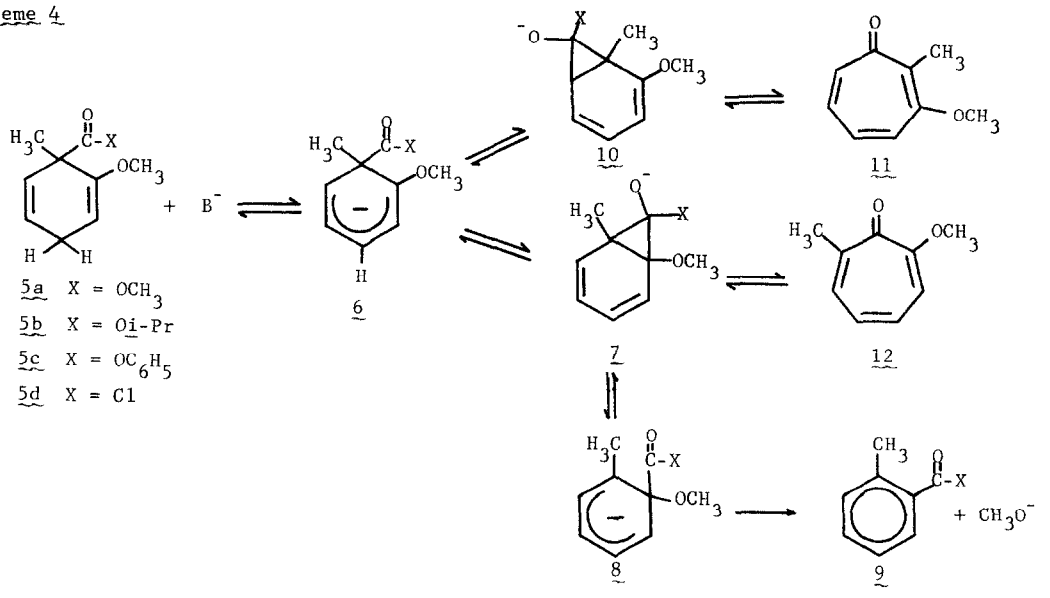
Scheme 3



negative charge through resonance should, by suitable placement, be able to direct the ring-opening of 3 in the direction of either 4a or 4b. In fact, for the case X = OCH_3 and Y = Br, a nitro group at C-5 gives loss of X^- exclusively (7), and a carbomethoxy group at C-4 leads completely to loss of Y^- (5).

We began our study of the tropolone rearrangement with the hope of determining whether or not the ring-opening step (3 → 4) is reversible. Closure of an anion such as 4 on the carbonyl group is formally a homoenolization reaction although, to date, the only cases reported involve ketones (8). We have investigated the reactions of cyclohexadiene 5, hoping to find a base which would convert it into anion 6 (Scheme 4). Unlike 4a and 4b, 6 cannot yield an aromatic compound directly, but by ring-closure to 7, followed by cleavage in the opposite direction to 8, a derivative of o-toluic acid 9 can be formed. Alternatively, closure of 6 to 10 could generate tropone 11, and loss of X^- from 7 could yield tropone 12, but both 11 and 12 would be expected to yield

Scheme 4



5a X = OCH_3
5b X = Oi-Pr
5c X = OC_6H_5
5d X = Cl

9 in the presence of B^-. Finally, norcaradiene 10 might open in the opposite direction to give an anion which, by a series of such cyclizations and openings [formally like the thermal rearrangements of norcaradienes (9)], would eventually give anion 8 and then aromatic compound 9.

As is reported in the preceding communication, compounds 5a-d with a number of bases never yielded 9. Consideration of the following summary of the pertinent reactions of 5a-d leads not only to the conclusion that the ring-closure reaction (e.g. 4 → 3) does not occur, but also to the realization that Scheme 2 and not Scheme 3 is the more plausible mechanism for the tropolone rearrangement:

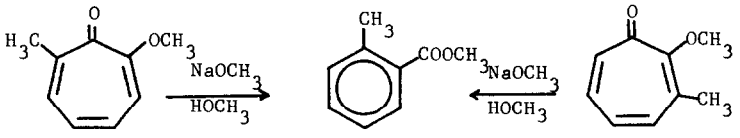
1. A number of bases are capable of converting 5 into 6 as evidenced by double-bond isomerization of 5a with sodium methoxide in methanol, potassium t-butoxide in DMSO, and lithium dimethylamide in HMPA, and of 5b with sodium isopropoxide in isopropanol and potassium t-butoxide in DMSO.

2. The most reasonable mechanism for the formation of o-methoxytoluene and carbon monoxide from 5a or 5b with lithium dimethylamide in HMPA, from 5a with phenyllithium, and from 5b or 5c with potassium t-butoxide in DMSO is via anion 6. While a concerted loss of proton, carbon monoxide, and alkoxide is conceivable, the fact that double-bond isomerization is found in recovered cyclohexadiene argues for a two-step mechanism.

3. The related compound, dimethyl 1-methyl-2,4-cyclohexadiene-1,2-dicarboxylate (compound 7 of the previous communication) is similarly converted into methyl o-toluate and a double-bond isomer with either potassium t-butoxide in t-butanol or potassium carbonate in dimethylformamide.

Thus, in both protic and aprotic solvents, the only fate we have observed for 6 is either protonation or loss of carbon monoxide. Closure of 6 to 7 or 10 does not occur.

We have studied the tropolone rearrangement of 12 and of its isomer 13 and have found both reactions to be normal. Sodium methoxide in refluxing methanol converts both 12 and 13 into 14 and a water-soluble fraction consisting of sodium o-toluate and sodium 3-methyltropolonate. No trace of 5 (or its double-bond isomers) or o-methoxytoluene could be found. If 12 rearranges by the mechanism of Scheme 3, it must pass through intermediate 7; to fit the data, 7 must open



12 14 13

exclusively towards 8 and not at all towards 6. This is unreasonable since the only difference between the transition states leading to 6 and 8 is the stability of a carbanion substituted by a methoxyl or a methyl group, respectively; that the two transition states should be of comparable stability (if anything, that leading to 6 should be of lower energy) is shown by the nearly equal rates of nucleophilic aromatic substitution by methoxide ion on 4-methyl- and 4-methoxy-2-nitrobromobenzene (10) and by the greater rate of proton abstraction by methoxide from methyl α-methoxyacetate than from methyl propionate (11).

We conclude, therefore, that 12 yields 14 directly from 7, by-passing intermediate 8, and that 7 opens as it does because only one leaving group is available. Further evidence that the

leaving group must depart as the cyclopropane ring opens is the observation that 2-methyltropone with methanolic sodium methoxide yields neither toluene nor cyclohexadienes, but only tar.

Scheme 2, concerted ring-opening, aromatization, and loss of X^- or Y^- is, therefore, preferred for simple tropones such as 12 (i.e., the reaction is more like an E2 than an El_{CB} elimination). In the way of analogy, concerted base-promoted ring-opening with loss of halide has been demonstrated for a pair of isomeric α-bromocyclopropanones (12). The original reason (4a) for invoking Scheme 3 was to explain the preferential expulsion of the poorer leaving group. This can be accommodated by Scheme 2, if it is realized that substantial carbanion character develops on the β carbon atom in an E2 elimination (13). Thus, in the expulsion of X^- from 3 (Scheme 2), negative charge is developed in the transition state at the carbon bearing Y. When, for example, X = OCH_3 and Y = Br, placing a partial negative charge near Y rather than near X leads to a lower energy transition state despite the fact that the stronger base is being expelled. It is, of course, possible that in those cases cited earlier (5,7) in which a powerful electron-withdrawing substituent directs the course of the rearrangement, the two-step (El_{CB}) mechanism is favored and the reaction passes through a resonance stabilized intermediate such as 4a or 4b.

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