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ACID CATALYZED REARRANGEMENTS OF 4-METHYL-4-CYANOCYCLOHEXADIENONE

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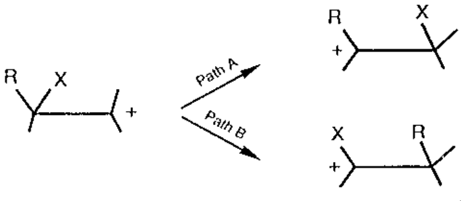
Abstract. *Acid-catalyzed dienone-phenol rearrangement reactions of 4-methyl-4-cyanocyclohexadienone occur very slowly and give either fragmentation or methyl group migration, not cyano group migration, under non-nucleophilic strongly acidic conditions.*

Substantial theoretical and experimental work suggests that a cyano group can stabilize an adjacent positive charge by resonance, partially offsetting the destabilization expected from the inductive effect. Other electron-withdrawing groups, such as ketone, ester, etc. also provide some such stabilization.[1] Recent work involving equilibria in a bicyclohexane system suggests that a β-cyano substituted cation is slightly more stable than an α-cyano substituted one[2]. The major experimental approaches to determination of the stability of α-cyano cations have been by solvolysis studies and by generating such species in super acid media. Much less work has been carried out in which the cation was generated via a rearrangement pathway.[2,3]

For some time, we have been involved in rearrangement studies in which electronegative substitients, X, are pitted against alkyl or other normally very good migrating groups[4]. In these cases, the electronegative group usually migrates (path A in Eq 1), since the X-substituted cation (path B), and hence the transition state leading to it, is substantially destabilized by the inductive effect[4,5].

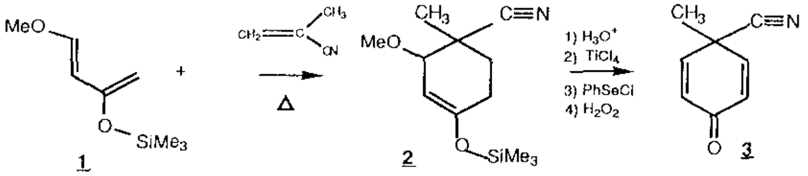


(Eq 1)

The intriguing possibility exists, if X = CN, that the stabilizing influence of the cyano group on the adjacent charge might be sufficient to allow the group R to migrate (path B) or the forces might be nearly enough balanced such that the cyano group might migrate in properly chosen systems in which R is a cationic stabilizing substituent. Previous attempts to observe migration of a cyano group in a cationic rearrangement have led to other types of reactions instead[7,8].

The dienone-phenol reaction, whose mechanism is well established, is one of the most straightforward and cleanest systems for study of such rearrangements.[6] We have prepared the simplest cyano-substituted dienone, 4-methyl-4-cyano cyclohexadienone, 3, by the method shown in Scheme I. Diels-Alder reaction between Danishefsky's diene[9], 1, and excess methacrylonitrile in refluxing toluene gave the adduct 2, along with some polymeric material. Hydrolysis, first with 5% HCl then with $TiCl_4$ in $CHCl_3$ to eliminate methanol from the intermediate β-methoxy cyclohexanone, gave the cyclohexenone derivative in 44% yield. A phenylselenenylation-selenoxide elimination sequence then gave the crystalline dienone 3, mp 62-63°, in 42% yield.

Scheme 1



The cyano dienone 3 proved to be exceptionally stable under a variety of acidic conditions. For example, no change occurred in trifluoroacetic acid (TFA) at 25° during a period of several months. By comparison, 4-methyl-4-carbethoxycyclohexadienone rearranges with carbethoxy migration with a half life of 20 minutes under these conditions.[4a]

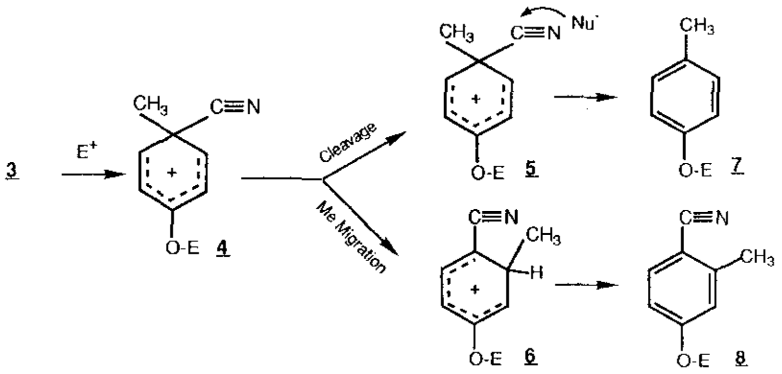
Treatment of 3 with conc. H_2SO_4 at 38° gave immediate formation of ion 4 (E=H), detectable in this medium by PMR[10], but only cyano hydrolysis occurred, followed by decarboxylation (half life ca. 4 min.), and then sulfonation of the p-cresol, 7 (E=H), formed. No migration reaction was observed.

A clean reaction occurred between dienone 3 and TFA at elevated temp (sealed tube, 90°, 12 hr). The only product derived from the dienone 3 was p-cresol trifluoroacetate, 7, ($E=CF_3CO$). Cleavage of the cyano group by attack of TFA on 5 ($Nu = CF_3COO^-$) is assumed to give trifluoroacetyl cyanate, CF_3COOCN, an unknown and doubtlessly highly reactive compound, which evidently trimerized to tris-trifluoroacetyl cyanurate. Cyanuric acid was detected after hydrolysis, but all attempted syntheses of authentic samples of the assumed intermediates failed.

The rate of rearrangement of 3 in TFA was markedly increased if some trifluoroacetic anhydride, TFAA, was added. Also, the rate of the rearrangement of 3 to p-cresol trifluoroacetate in TFA/TFAA was much faster than p-cresol was esterified under the reaction conditions, suggesting that trifluoroacetyation to ion 5, $R=CF_3CO$, was initiating the reaction.

A number of reactions were carried out, in which the strength of the electrophile was increased and that of any potential nucleophiles was decreased. Thus, dienone 3 reacted with BF_3OEt_2 slowly (half life 24 hr at 90°, $CDCl_3$, sealed tube). Exclusive methyl migration occurred under these conditions, to give 4-ethoxy-2-methylbenzonitrile, 8, ($E=C_2H_5$) (65%), identical to a sample synthesized by ethylation of the corresponding phenol[11]. The other primary product was evidently a BF_3 complex of the nitrile group, since the amide and acid derivatives of 8 were obtained upon hydrolysis. No product of cyano group migration was detected.

Scheme 2



The unusual formation of an ethyl ether in this reaction suggests that reversible BF_3 complexation with the dienone carbonyl group is not productive and that ion 4 ($E=C_2H_5$) is formed irreversibly, which forces a migration reaction to occur. In this case, methyl migration occurs instead of cyano migration. This generates the stabilized α-cyano cationic intermediate 6, which leads to the product.

Although it is difficult to make quantitative comparisons since the reaction conditions are so different, the slow rate of this reaction, several orders of magnitude slower than methyl migration in 4,4-dimethylcyclohexadienone[4a], suggests that the cation 6 is substantially destabilized relative to the corresponding methyl-substituted cation.

In accord with these results, methyl triflate ("magic methyl") also caused methyl migration from 3, but the product, 8, (E = Me), underwent rapid further methylation, to give complex mixtures of aromatic methylated products.

Reaction of 3 with trimethylsilyl triflate ($CDCl_3$, sealed tube, 90°, 24 hr) did give a smooth reaction to give only the trimethylsilyl ether 8, ($E = Me_3Si$), which was hydrolyzed upon work-up to the phenol 8, (E = H), identical to an authentic sample.[11]

Thus, when 3 is treated with strong Lewis acids under relatively non-nucleophilic conditions, such that the cyano group is not destroyed, a slow methyl migration occurs. Two major factors appear to contribute to the sluggishness of the rearrangement reaction, the initial formation of the ion 4, and its rearrangement to ion 6. The primary factor must be the relative destabilization of the transition state on the pathway between ions 4 and 6, since ion 4 can be detected by NMR spectra.[10,12] However, some α-cyano stabilization of the cationic intermediate is evident, since the methyl group migrated instead of the cyano group. The major structural difference between the cyano group and substituents with similar electron-withdrawing character which are known to migrate well[4,5], such as esters and ketones, is the hybridization at the carbon atom. We believe that the major reason that cyano does not migrate is because of its SP hybridization, which would give a transition state that has vinyl cation character. Experiments are underway to compare the cyano with the ethynyl substituent (which has SP hybridization but lacks the unfavorable polarity) in such rearrangements.

Comparison of the cyano group with another electron-withdrawing substituent which also does not migrate, the trichloromethyl group, is instructive[4c]. The trichloromethyl group has unfavorable polarity, and has no compensating resonance stabilization of the carbocation possible. The CCl_3 group shows no tendency to migrate, but also has a dramatic rate retardation (ca. 10^8 times for methyl migration in a methyl-trichloromethyl substituted dienone compared to a dimethyl substituted dienone). The rate retardation of methyl migration in an α-cyano substituted cation is much less, which we believe reflects some stabilization of the adjacent charge by resonance.

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REFERENCES

† Present address: Department of Chemistry, Kyung Hee Univ., South Korea.

1. Review: Gassman, P. G.; Tidwell, T. T. *Accts. Chem. Res.*, **1983**, *16*, 279-285.
2. Kirmse, W.; Goer, B. *J. Am. Chem. Soc.*, **1990**, 112, 4556-4557.
3. Gassman, P. G.; Saito, K.; Talley, J. J. *ibid.*, **1980**, *102*, 7613-7615.
4. (a) Marx, J. N.; Argyle, J. C.; Norman, L. R. *ibid.*, **1974**, 96, 2121-2129. (b) Marx. J. N.; Bombach, E. J. *Tetrahedron Lett.*, *1977*, 2391-2394. (c) Vitullo, V. P.; Cashen, M. J.; Marx, J. N.; Caudle, L. J.; Fritz, *J. Am. Chem. Soc.*, **1978**, 1205-1210.
5. Review: Shubin, V. G. in Rees, C., ed. "Topics in Current Chemistry", Springer Verlag, Berlin, **1984**, Vol 117, pp 267-341.
6. Vitullo, V. P.; Grossman, N. *J. Am. Chem. Soc.*, **1972**, *94*, 3844-3848.
7. McDonald, R. N.; Hill, D. C. *J. Org. Chem.* **1970**, *35*, 2942-2948.
8. Miller, T. G. *J. Org. Chem.*, **1969**, *34*, 3710-3713.
9. Danishefsky, S.; Kitahara, T. *ibid.*, **1974**, *96*, 7807-7808.
10. Deshielding of the α and β vinyl proton signals in the PMR from 6.38 and 6.90 ($CDCl_3$) respectively to 7.43 and 8.26 (H_2SO_4) corresponds to ca. 100% protonation in H_2SO_4[4a].
11. Synthesis of an authentic sample of 8 (R=H) was accomplished via a Gatterman reaction on m-cresol, followed by oxime formation and dehydration. (Gross, H.; Reiche, A.; Mattey, G. *Chem. Ber.*, **1963**, 308-313; Van Es, T. *J. Chem. Soc.*, 1965, *1564-1568*.
12. Ion 6 can not be detected by NMR spectra, since its irreversible formation from 4 is followed by a rapid deprotonation to the phenol.[6]

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