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INVESTIGATIONS ON THE QUESTION OF MULTIPLE MECHANISMS IN THE COPE REARRANGEMENT[a]

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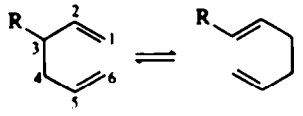
Abstract—The possible occurrence of the ionic Cope rearrangement, and other non-concerted mechanisms is discussed. The synthesis of 2 - (1 - ethyl - 1 - propenyl) - 2 - (3 - *p* - methoxyphenylallyl)malononitrile (**1b**) and its clean thermal 1,3 rearrangement to (1 - ethyl - 5 - *p* - methoxyphenyl - 2 - methyl - 4 - pentenylidene)malononitrile (**4**) are reported. This result contrasts with the rearrangement of 2 - (1,1 - dideuterioallyl) - 2 - (1 - ethyl - 1 - propenyl)malononitrile (**1c**) which isomerizes cleanly in a 3,3 rearrangement. Rearrangement of 2 - (1 - cyclohexenyl) - 2 - (3 - *p* - methoxyphenylallyl)malononitrile (**11**), however, leads sluggishly to [2 - (*p* - methoxy - *α* - vinylbenzyl)cyclohexylidene]malononitrile (**19**) (3,3 shift) and rearrangement of 2 - (1 - isopropyl - 2 - methyl - 1 - propenyl) - 2 - (3 - *p* - methoxyphenylallyl)malononitrile (**12**) leads, also slowly, to (1 - isopropyl - 5 - *p* - methoxyphenyl - 2,2 - dimethyl - 4 - pentenylidene)malononitrile (**14**) (1,3 shift). Rearrangement of **1b** in the presence of sodium borohydride allows interception of the proposed ionic intermediates and isolation of 2 - (1 - ethylpropylidene)malononitrile (**5**) and anethole (**21c**). Ion trapping experiments also gave positive results in the 3,3 rearrangement of **11**. These results are discussed in terms of the ionic Cope rearrangement.

Since its discovery in 1940,[1] the Cope rearrangement (Scheme 1) has been a reaction of interest to



SCHEME 1. The Cope rearrangement.

organic chemists for both synthetic and mechanistic reasons. With the advent of the ideas of the conservation of orbital symmetry in 1965,[2] there has been a resurgence of interest in the rearrangement, redescribed as a [3,3] sigmatropic shift, in the Woodward–Hoffmann terminology, and, as a result, numerous publications have appeared on the theoretical ramifications of this reaction.[3] It is clear, however, that these rules are applicable only if a reaction is concerted; i.e. if the 1,6 bond is constructed simultaneously with the cleavage of the 3,4-bond, although there would not appear to be any requirement for the bond cleavage and bond construction to have progressed to an equal extent in the transition state.

From the point of view of the applicability of the rules of orbital symmetry, it is thus necessary that the concerted or non-concerted nature of the reaction be established. It has been our opinion that, despite the vast majority of Cope rearrangements being concerted (Cope mechanism I), a number of other, non-concerted, mechanisms might be observed, given the right combination of substrates or reaction conditions, and it seemed of interest to conduct some experiments to determine if other mechanisms were feasible, and, if so, under what conditions one might observe them.

Examination of the literature revealed that there were at least four reports of Cope rearrangements for which there was reason to suspect non-concertedness,[4-7] one of them[5] accompanied by the particularly powerful evidence of near zero activation entropy, a result apparently inconsistent with the involvement of a cyclic transition state.† The reactions are considered to proceed by way of a diradical intermediate, as shown in Scheme 2. (Cope Mechanism II).

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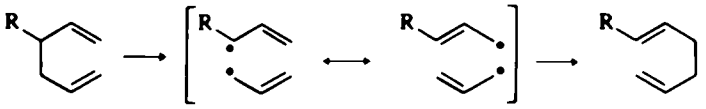
†See, however, the value of $\Delta s^{\ddagger}$ in the "high temperature" Cope rearrangement of 1,5-hexadiene, a reaction considered to be concerted (reference 3e).

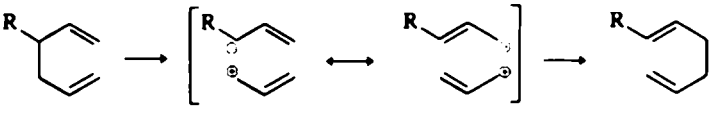


SCHEME 2. Radical mechanism for the Cope rearrangement.

It seemed to us that if this type of mechanism, in which the 3,4-bond completely cleaves prior to radical recombination, were feasible, then there was reason to suspect that another, closely related, mechanism might well have remained undetected, in which the 3,4 bond would be broken heterolytically giving ionic rather than radical intermediates. We term this putative mechanism, shown in Scheme 3, the ionic Cope rearrangement. (Cope mechanism III).

molecule. Another important consideration in the substrate design was the thought that a carefully chosen substrate might give *different products* according to the mechanism followed (i.e. concerted *vs* fragmentation-recombination) and that reaction of such a substrate would give a rapid and convenient method of assessing the success of the design.

With these thoughts in mind, the compound **1b** was selected. The potential carbonium ion is stabil-

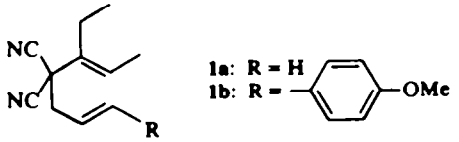


SCHEME 3. The ionic Cope rearrangement.

Further examination of the literature revealed no report of such a mechanism, and our initial experiments, previously reported,[6] showed that it was highly unlikely that Cope rearrangement of any known substrate proceeded by this mechanism.* This paper reports some results on our search for the ionic Cope rearrangement.

RESULTS AND DISCUSSION

The main requirement for the observation of the ionic Cope rearrangement would appear to be the ability of a substrate to form highly stabilized intermediate ions. It was for this reason that our initial work had focussed on compound **1a**, in which the potential carbanion would be stabilized by the two nitrile groups. Cope rearrangement of **1a**, however, proceeded concertedly.[8] Since the potential carbonium ion from **1a** was not stabilized apart

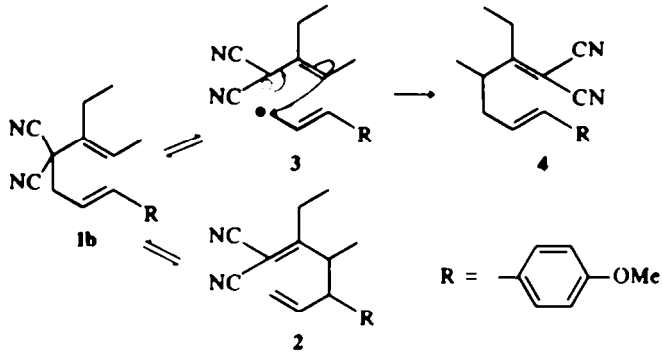


from the intrinsic allylic stability, the next logical step seemed to be a modification in this area of the ized by the *p*-methoxyphenyl group, and the product–mechanism relationship mentioned above is shown in Scheme 4.

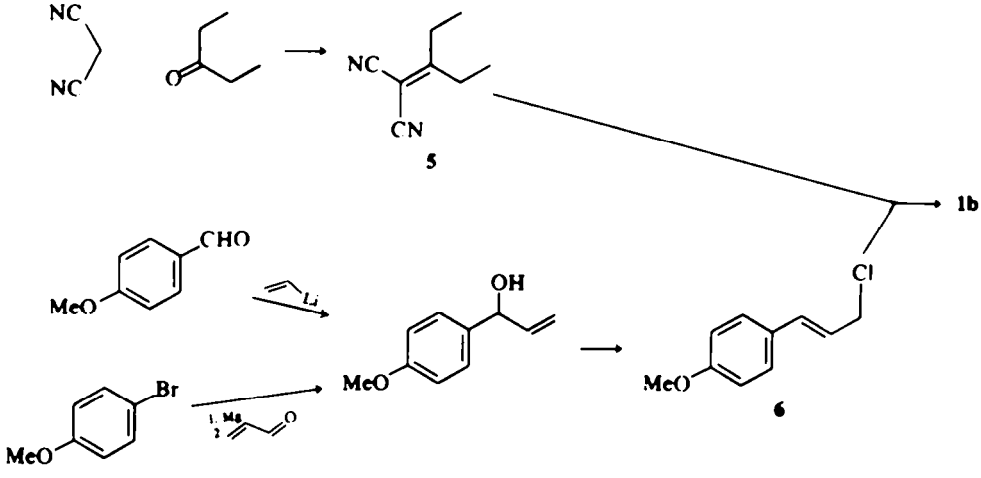
Concerted [3,3]-Cope rearrangement of **1b** can cause only the interconversion of **1b** and **2** whereby conjugation with the nitrile groups is gained at the expense of loss of conjugation with the aromatic ring. If the ionic Cope rearrangement operates, however, and the ions **3** have sufficient lifetime, recombination could give rise, in addition to **1b** and **2**, to compound **4**, in which conjugation with both the nitrile groups and the aromatic ring is achieved (an overall 1,3-shift). This compound, presumably more stable than either **1b** or **2**, might be expected, therefore, to be a significant product in the *Ionic* Cope rearrangement of **1b**.

The synthesis of compound **1b** was achieved by the condensation of the anion of 2 - (1 - ethylpropylidene)malononitrile (**5**) with *p*-methoxycinnamyl chloride (**6**) as shown in Scheme 5, these reagents being prepared from malononitrile and 3-pentanone[9,10] and from either anisaldehyde or *p*-bromoanisole[11] respectively by known routes. Considerable difficulty and irreproducibility was encountered in the preparation of alcohol **7** by the reaction of *p*-anisaldehyde with vinyl magnesium bromide.[11] This difficulty was overcome either by using the *p*-broamoanisole-acrolein route[11] which gave, in our hands, a 32% yield of alcohol **7**, or by using the first route, but replacing the vinyl magnesium bromide by vinyl lithium, in which case a 73% yield of alcohol was achieved. The final condensation, which in principle could give rise to a complex mixture owing to the potential ambidence of both reagents gave, as hoped for, compound **1b**

*Recently Dewar and Wade have presented evidence[7] for a 4th type of mechanism *via* 1,4-cyclohexylene intermediates. Conceivably, given the appropriate substituents on the 2 and 5 positions of the 1,5-hexadiene, a 5th mechanism, with ionic rather than radical intermediates, but otherwise similar to the 4th mechanism, might be observable.



SCHEME 4. Potential rearrangement of compound 1b.



SCHEME 5. Synthetic scheme.

as the major product, the only serious contaminant being identified as compound 4, presumably arising as a consequence of the ambidence of the substituted malononitrile anion 3. Chromatography on alumina, however, afforded pure samples of 1b.

Thermal isomerization of compound 1b was now considered. As mentioned above, it was felt that the formation of compound 4 in the rearrangement mixture of 1b and/or 2 would constitute encouraging evidence of the involvement of the ionic Cope rearrangement mechanism. The pyrolysis experiment was, therefore, extraordinarily gratifying. *Mild heating* (80°) *of diene* 1b *caused rapid* ($t_{1/2} \simeq$ 2 h) *and quantitative conversion to the more conjugated compound* 4. Such a rearrangement* is unlikely concertedly,† but is in harmony with the idea of a mechanism proceeding *via* ionic (or radical) intermediates.

Having obtained this encouraging result, two lines of advance clearly presented themselves. These were (a) to investigate how general the rearrangement might be, and (b), to gather more experimental evidence to confirm or deny the ionic nature of the reaction. Before proceeding with these questions, however, one other point regarding the rearrangement of 1a seemed worth clarifying. The strikingly different mechanisms suggested for rearrangement of 1a (concerted) and 1b (ionic) had arisen by different types of evidence, the concerted suggestion for 1a from kinetics,[8] and the ionic suggestion for 1b from product analysis. With the rapid and convenient product analysis method now at hand, it seemed of interest to analyse the [1,3]-or

*Since this reaction is now no longer a [3,3] sigmatropic shift, one could question whether it should be termed a Cope rearrangement at all. Although the definition suggested by Hammond and DeBoer[8] does, in fact, specifically include this type of rearrangement, the important point, perhaps, is that if it can be established that this particular rearrangement is ionic, then an ionic [3,3] shift on a similar type of substrate is presumably also feasible.

†Concerted, symmetry-allowed suprafacial [1,3] sigmatropic shifts with inversion at the migrating centre are not unknown,[12] but in the all-carbon series are not known to take place in preference to a [3,3] sigmatropic shift, and occur at much higher temperature.

[3,3]-nature of the shift in the rearrangement of **1a** by the use of the deuterated substrate **1c**. This substrate had previously been synthesized and the kinetics of its isomerization studied by Sunko *et al*,[13,14] and although, in a parallel study of 1,5-hexadiene itself, these workers had investigated the possibility of a [1,3]-shift,[14,15] no such evidence was mentioned in the case of the isomerization of substrate **1c**. In view of this lack of data, and also a puzzling feature of the reported NMR spectra of deuterated and non-deuterated **1c**,* we felt it desirable to unambiguously establish this point. The preparation was accomplished as previously described[16] from diene **5** and deuterated allyl chloride, the latter being prepared from acrylic acid *via* reduction of acryloyl chloride with lithium aluminum deuteride. The sample of **1c** obtained showed an NMR spectrum identical with that measured previously for the undeuterated analogue **1a**,§ with the exception of the complete absence of the 2 proton doublet at δ2·65 ppm. Pyrolysis of **1c** in refluxing isopropanol gave quantitative conversion to the system (**8** or **9**) where conjugation with the nitrile groups was achieved, and careful integration of the NMR spectrum was consistent with the regiospecific formation of isomer **8**, and the absence of any detectable **9**. This evidence showed that although rearrangement of **1b** is clearly a [1,3]-shift, rearrangement of **1a** is a [3,3]-shift, with no apparent scrambling of the unsubstituted allylic group, (in agreement with our own previous conclusions[8] and those of Sunko *et al*[13-15]) *thus confirming the abrupt mechanistic change between pyrolysis of compounds* **1a** *and* **1b**.

1c **8** **9**

Having established this point, we returned to the two lines of advance mentioned above. In order to test the possibility of ionic intermediates in the rearrangement of **1b**, the two methods of ion trapping and of rate dependence on solvent polarity immediately suggested themselves. The generality of the rearrangement was, however, first investigated partly for its own sake, but mainly because of reservations we had concerning the suitability of compound **1b** as a substrate for kinetic measurements. These reservations concerned ambiguity in the double bond stereochemistry.

A **B**

Numbering the hexadiene system as shown in the diagram,† the stereochemistry around the 5–6 double bond appears to be unambiguously *trans*. This stereochemistry is not involved in the final step of the synthesis and decoupling the protons at δ4·22 ppm adjacent to chlorine in the chloride precursor **6**‡ resolves the olefinic protons into a pair of doublets with $J = 15{\cdot}5$ Hz, indicative of a *trans* orientation.[16] Furthermore, this stereochemistry arises in the thionyl chloride conversion of **7** to **6**, a reaction known to give rise to *trans* configurations.[17,18] In contrast to this clear situation, the stereochemistry around the 1,2-double bond remains obscure. Stereochemical assignments around trisubstituted double bonds are frequently difficult and in the cases where successful assignments have been made, eg[19-26] sometimes on the basis of allylic coupling but mostly from the relative chemical shifts of groups, it has been necessary to possess *both* stereoisomers, the assignment being made on the comparison between them. In the case of compound **1b**, although we believe it to be in the configuration A, and despite the fact that we have no chromatographic or NMR suggestions of a mixture of isomers, there can be no certainty in this belief in the absence of access to both stereoisomers A and B.§

*Considering that the Yugoslavian work was initiated to study isotope effects of "mechanistically unambiguous" reactions,[14] and that our work was searching for multiple mechanisms in reactions, it is amusingly ironic that we both became involved in studying the same reaction of the same substrate. Although other peaks reported in the NMR spectrum of **1c** are in accord with those in our spectra, the olefinic protons (at positions 5 and 6 of their attractive (but non-IUPAC) nomenclature for this compound) are referred to as giving signals at the unusual position of τ6·9–7·7 ppm. In our spectra, previously described,* these proton signals are in the expected olefinic region δ5·0–6·1 ppm.

†The numbering that arises from the correct IUPAC name adds unnecessary confusion.

‡The decoupling experiment on the chloride is preferable to that on **1b** because of the additional vinyl proton present in the latter.

§The same problem presumably exists in compound **1a** on which numerous kinetic investigations have been made,[27,8,10,11] but for which first order kinetics are reported. It is noteworthy, however, that Cope, *et al.*[27] (footnote 6) reported their best kinetic data with compound **10**, a compound *devoid of this stereochemical ambiguity*.

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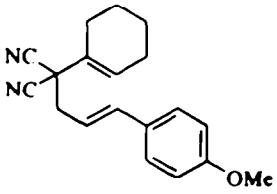
In view of this stereochemical ambiguity, we turned our attention to the synthesis of alternative substrates that would possess the structural features apparently necessary for the rearrangement, but which would not have the stereochemical ambiguity. To this end we made efforts to synthesize compounds **11** and **12**.



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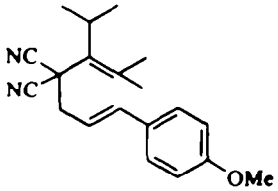
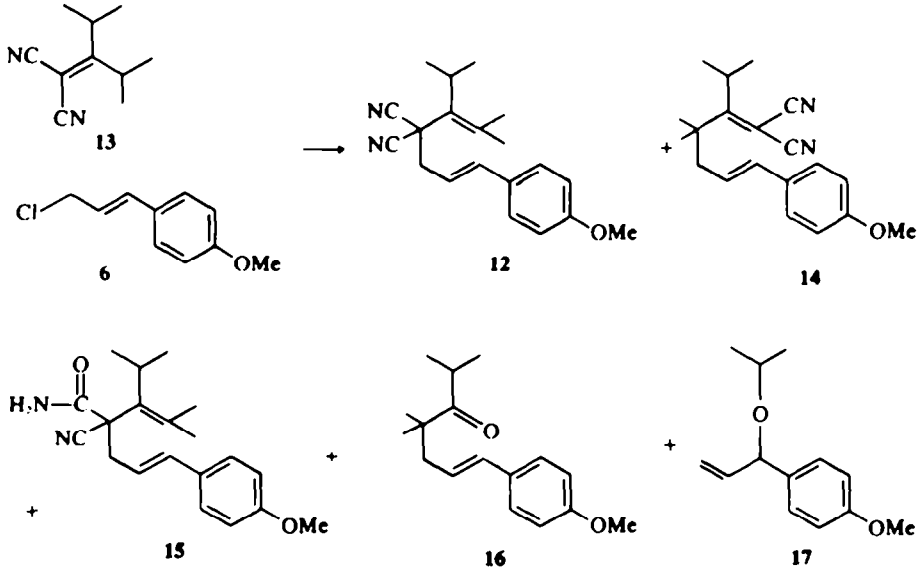


12

Both syntheses followed the route used for the preparation of compound **1b** (Scheme 5), the 3-pentanone being replaced by cyclohexanone for the route to **11**, and by diisopropyl ketone for the route to **12**. The synthesis of compound **11** presented no difficulties, and the final product was a crystalline solid. The final step of the synthesis of compound **12**, however, gave a mixture of five compounds in addition to both unreacted starting materials.

analogous preparations of **1b** and **11**. To ensure that the formation of **16** had not occurred due to diisopropyl ketone impurity in dinitrile **13**, the sample of dinitrile **13** was rechecked for purity and was shown to have no detectable diisopropyl ketone present. Thus the formation of ketone **16** appears to arise by a retro-aldol process during the reaction. The formation of the isopropyl ether (isopropanol being the solvent) **17** (0·98 g) also caused surprise, again because this compound had not been observed previously in analogous preparations.

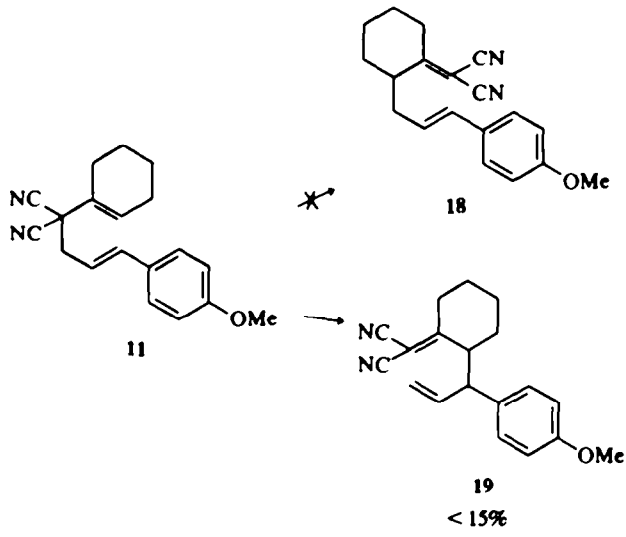
Having compounds **11** and **12** at hand, their pyrolytic rearrangements were studied. Considering that the modifications to substrate **1b** had been designed to leave intact what we considered to be the crucial structural features for the rearrangement, the chemistry of compound **11** came as another surprise. None of the expected compound **18** was found, and what little reaction did take place ($< 15\%$ in 36 h at 140°) gave rise to the formation of the product expected from the direct concerted Cope rearrangement of **11**, compound **19**, the first and only rearrangement in our investigations where conjugation with the aromatic ring has been lost. Pyrolysis of compound **12** was also disappointing; although conversion to the anticipated rearrangement product **14** did occur, the rearrangement was

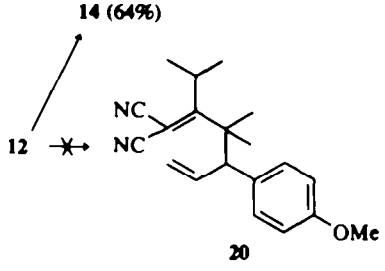


13 **6** **12** **14** **15** **16** **17**

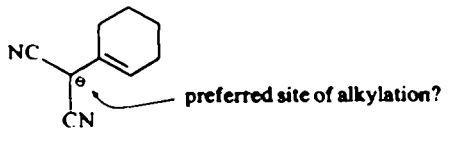
Purification of each compound by column and preparative plate chromatography followed by elemental and spectral analysis revealed the structures of the compounds to be **12**, **14**, **15**, **16**, and **17**. In a preparation on a 0·025 mole scale (4·05 g **13** and 4·55 g **6**), 0·83 g of purified **12** was isolated, together with 0·17 g of the not unexpected **14**. The formation of the apparently hydrolysed products **15** (0·10 g) and **16** (0·09 g) was surprising, particularly since this type of product had not been observed in extremely slow (64% conversion after 7 days at 118°). In contrast to rearrangement of compound **11**, no detectible quantity of compound **20** was formed.

These unexpected results demanded considerable rethinking of the project. Our original intent in investigating the generality of the rearrangement had been to gradually move to less strongly electron-withdrawing groups than the two nitriles, and to less strongly electron-donating groups than





the *p*-methoxyphenyl, but in view of the non-rearrangement of compound **11** and the sluggish rearrangement of **12**, the two types of compound with no stereochemical ambiguity, this exercise became pointless, and it became of even greater urgency to obtain further experimental evidence to test the idea of ionic intermediates in the rearrangement of **1b**. Nevertheless, the surprisingly different chemistry of compounds **1b**, **11** and **12** deserves some comment. Examination of space-filling models of these compounds certainly shows that *concerted* rearrangement of **11** might indeed be expected to proceed considerably more easily than either compound **1b** or **12**. However, the fact that concerted (i.e. [3,3]-shift → **19**) rearrangement may be facilitated does not explain the *prevention* of the [1,3]-shift occurring (i.e. **11** → **18**). It is difficult to see any reason why ion formation should be any more difficult from compound **11** than for either of the others, but a possible rationale of the non-formation of compound **18** arises on considering the possibility that the intermediate anion may

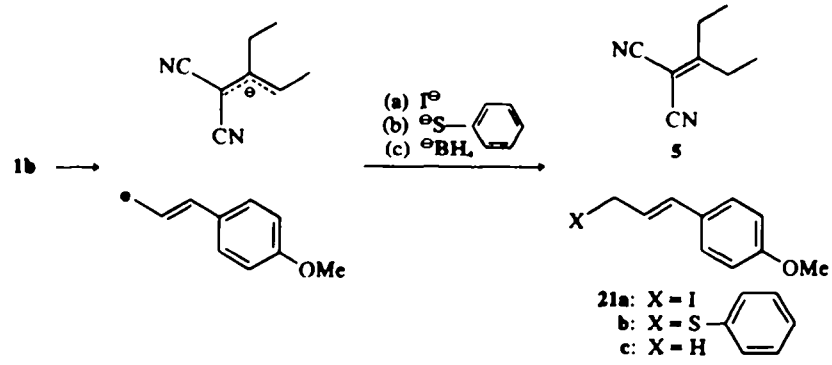


alkylate preferentially on C-2 of the malononitrile system rather than on the ring. Examination of models indicates that because of the ring rigidity and the planarity demanded by the delocalized system, there are interactions with ring hydrogens for ring alkylation that are not present for alkylation at C-2 of the malononitrile. Further support of this idea comes from the actual synthesis of compound **11**; in contrast to the syntheses of **1b** and **12**, where considerable by-products of compounds **4** and **14** respectively were obtained on alkylation of the corresponding anion with chloride **6**, none of the corresponding compound **18** was isolated in the preparation of **11**. It would appear, therefore, that the alkylation of the anion from **11** may be considerably more regioselective than those from **1b** or **12**. Experimental confirmation that compound **11** does, in fact, like compound **1b**, ionize, is presented later in this paper. Regarding the sluggish rearrangement of compound **12**, it is pertinent to note that whereas the conversion of **1b** to **4** involves the conversion of a trisubstituted double bond to a tetrasubstituted double bond, the conversion of **12** to **14** involves a change in the nature but not the degree of substitution around the corresponding double bond. Thus it is possible that the driving force for rearrangement of **1b** may be more connected with this aspect rather than the drive for conjugation that we had previously considered. Clearly these rationalizations concerning the reactivity differences between compounds **1b**, **11** and **12** are merely *post facto* suggestions, and further experimentation is required to test them.

For the reasons outlined above, we next approached the question of testing the idea of ionic intermediates in the conversion of **1b** to **4**. Of the two alternatives of ion trapping and of rate dependence as a function of solvent we selected the former, mainly because we still lacked a substrate

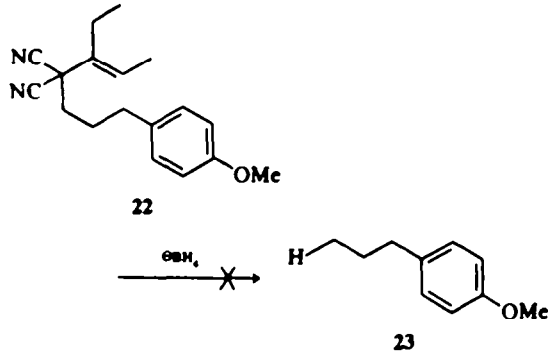
which both rearranged readily and was stereochemically secure, and partly for other reasons.*

The ion trapping experiments conducted were those indicated in Scheme 6. The rearrangement of **1b** to **4** was firstly conducted in the presence of nucleophile[29]) were not pursued, and the rearrangement was conducted in the presence of sodium borohydride.[30] Under these conditions, a small amount of anethole, compound **21c**, (identified by identical retention time on GLC and superimposa-



SCHEME 6. Ion trapping experiments.

iodide ion in the hope of trapping the carbonium ion as the iodide **21a**, with the anion presumably becoming protonated eventually and emerging as dinitrile **5**. An unstable compound was indeed isolated from the reaction, possessing an NMR spectrum very similar to that of chloride **6**, but with the 2-proton doublet (CH_2 adjacent to halogen) appearing at δ3·7 ppm instead of the chloride position of δ4·2 ppm. This compound was presumed to be the iodide **21a**, but in view of its instability (confirmed by a separate preparation from chloride **6** and sodium iodide), a new trapping agent that would give a stable product was sought, and thiophenoxide was next tried. Although an independent preparation of thioether **21b** confirmed its stability, experiments using thiophenoxide as the trapping agent were not successful in obtaining this compound from the isomerization of **1b** to **4**. Positive evidence (glc-mass spectrometry) for the formation of dinitrile **5**, however, was obtained. In order to guard against the remote possibility that compounds **21** could arise by direct nucleophilic attack on **1b**, rather than by interception of the intermediate ions, it was considered desirable to use a trapping agent of low nucleophilicity, but with a good ability to trap carbonium ions. For this reason the experiments with thiophenoxide (a powerful ble mass spectrum with those of an authentic sample) and of dinitrile **5** were formed, showing that the ions could be trapped by a relatively non-nucleophilic reagent. Although it seemed highly improbable that anethole could have arisen by the direct nucleophilic attack route, we felt that we could establish this point more rigidly by repeating the experiment on the dihydro derivative **22**. In view of the loss of conjugation with the aromatic



ring, it would be anticipated that formation of the carbonium ion would be essentially completely inhibited, and thus no dihydroanethole would be formed if the formation of anethole from **1b** had occurred via the carbonium ion intermediate. If, on the other hand, anethole had been formed by direct nucleophilic attack on **1b**, then dihydroanethole should be able to be formed from nucleophilic attack on **22**, although at a slower rate. This rate difference can be estimated to be a factor of approximately 270 on the basis of the rate ratio of 40 arising from the change of the allyl group to an Et group,[31] and the additional effect of 6·8 of the γ, *trans* aromatic ring.[32] The reaction of **22**, (prepared by the

*The rate dependence on solvent polarity rests on the assumption that the transition state resembles product (in this case the ionic intermediate). This is a reasonable assumption if the ions are relatively unstable and the process is highly endothermic (28). In this reaction, however, the substrates have been chosen deliberately to yield highly stabilized ions and thus the assumption that the transition state possesses a great deal of charge development may no longer be valid. In the extreme of such a case, it might be possible to envisage an ionic reaction with little or no solvent effect on the rate.

reaction of the brosylate of 3-*p*-methoxyphenyl-1-propanol with the anion of dinitrile **5**) with borohydride was therefore conducted at 167° for 46 h, which, assuming an activation energy of 19·0 kcals. mole^{-1},[9] would more than compensate for the rate retardation of **22** relative to **1b**. Under these conditions, no trace of dihydroanethole **23** could be detected, thus adding further evidence that the formation of anethole **21c** from **1b** had not been due to direct nucleophilic attack of borohydride.

With the method for ion trapping at hand, the hypothesis advanced for the non-rearrangement of the cyclohexane derivative **11** to **18** could be returned to and tested. If, as suggested, the molecule did, in fact, ionize, but then recombined to regenerate **11** rather than proceed to **18**, then it should still be possible to trap the intermediate carbonium ion with borohydride, as done on the rearrangement of **1b**, and again to isolate anethole. The trapping experiment on this "non-reaction" was therefore performed and anethole (identified again by GLC-mass spectrometry) was indeed found to be formed, thus providing evidence that diene **11** does ionize and does not have peculiar behaviour in this regard.

From the results described above, we believe that the conversion of **1b** to **4**, which is at least closely related to the Cope rearrangement, proceeds *via* carbanion–carbonium ion intermediates in a fragmentation–recombination type of mechanism similar to that proposed for certain cyclopropene racemizations.[14] Further work on the search for better substrates, and for substrates which might demonstrate an ionic [3,3]-sigmatropic shift are in progress.

EXPERIMENTAL

M.ps were determined on a Fisher–Johns block. IR spectra were obtained on a Perkin–Elmer 257 spectrophotometer, UV spectra on a Perkin–Elmer 202 spectrophotometer, and PMR spectra in $CDCl_3$, with TMS as internal standard, on a Varian T-60 instrument. Microanalyses were performed by the Spang Microanalytical Laboratory, Ann Arbor, Michigan. Thin-layer and preparative-layer chromatography were performed on pre-coated plates supplied by E. Merckag, Darmstadt, Germany. All solvents for chromatography were redistilled before use. GLC, where appropriate, was performed on a Hewlett–Packard F and M Model 402 gas chromatograph.

2-(1-Ethylpropylidene)malononitrile **5** was prepared as previously described.[8,10]

p-Methoxy-α-vinylbenzyl alcohol **7**

Method 1. Anisaldehyde (6·8 g, 0·05 mole) was dissolved in dried, freshly distilled THF (50 ml). N_2 was bubbled through the system for 30 min. The reaction flask was then placed in a CCl_4-liquid N_2 bath, and vinyllithium reagent added dropwise at −15° with constant stirring, the stirring being continued for 30 min after completion of addition. The mixture was poured on to crushed ice, extracted with ether (3 × 50 ml), and the combined extract dried ($MgSO_4$) and evaporated. The residue was made into a paste with silica gel (170 gm), washed with n-hexane (700 ml) to remove the mineral oils, and then with a soln of $CHCl_3$ (665 ml) and MeOH (35 ml) to recover the product. The soln was evaporated, and then distilled (120–130°, 12 mm) over K_2CO_3 (5·0 gm) to yield the product (6·0 gm, 73%); ν_{max}^{neat} 3400 (broad) (OH), and 1620 cm^{-1} (C=C); λ_{max}^{EtOH} 227 (ε 7600) and 277 nm (ε 11,000); δ2·87 (1H, broad singlet, OH), 3·78 (3H, s, OCH_3), 4·8–6·4 (4H, m, olefinic and benzylic H), and 6·6–7·4 ppm (4H, q, aromatic H); (Lit.[11] b.p. 129–130°, 12 mm).

Method 2. *p*-Bromoanisole (23 g; 0·12 mole) was reacted with Mg (0·3 g; 0·12 mole) in ether, and resulting Grignard reagent reacted with acrolein (6·9 g; 0·12 mole) under the conditions of White and Fife.[11] Vacuum distillation yielded the product (6·5 g; 32% yield) with physical and spectral properties as above.

p-(3-Chloropropenyl)anisole **6** (*p*-methoxycinnamyl chloride).

Compound **7** (1·64 g, 0·01 mole) was reacted with $SOCl_2$ (1·19 g; 0·01 mole) in anhyd ether as described[11] with the minor modification that the $SOCl_2$ was added dropwise to a soln of the alcohol in ether that had been cooled in an ice bath in order to control the vigorously exothermic reaction. The product was recrystallized from light petroleum (bp 30–60°) yielding 1·68 g (92%), λ_{max}^{EtOH} 270 nm (ε 5700), δ3·80 (3H, s, OCH_3), 4·22 (2H, d, J = 6Hz, CH_2-Cl), 5·8–6·6 (2H, m, olefinic), and 6·7–7·6 ppm (4H, q, aromatic), mp 71–72° (Lit.[11] mp 71·5–73°). Irradiation at 250 Hz (CH_2Cl), to decouple the coupling with the olefinic protons, permitted determination of the olefinic coupling constant as 15·5 Hz.

2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile **1b**

A soln of i-PrONa was prepared by dissolving Na (0·38 g; 0·0167 mole) in i-PrOH (10 ml) at 50°. When the Na had dissolved the soln was cooled in an ice-water bath and 1-ethylpropylidene malononitrile (0·0167 mole, 2·24 g) added dropwise to give a clear orange soln of the malononitrile anion. *p*-Methoxycinnamyl chloride (3·0 g; 0·0165 mole) was then added as a solid in one portion and the mixture stirred at room temp for 2 h. Water (100 ml) was added, and the soln extracted with benzene (3 × 25 ml). The combined extracts were washed with water (2 × 25 ml), dried (Na_2SO_4) and evaporated giving a yellow-brown liquid (4·6 g). Chromatography on alumina (Woelm neutral, Activity III) yielded the product (1·4 g, 30%), eluted with 10% benzene in light petroleum (bp 30–60°), $\nu_{max}^{CHCl_3}$ 2240 cm^{-1} (weak, CN); λ_{max}^{EtOH} 263 nm (ε 28,000); δ1·10 (3H, t, J = 8 Hz, CH_3-CH_2), 1·65 (3H, d, J = 6 Hz, allylic CH_3), 2·27 (2H, q, J = 8 Hz, CH_2-CH_3), 2·77 (2H, d, J = 8 Hz, $=CH-CH_2$), 3·70 (3H, s, OCH_3), 5·7–6·6 (3H, m, olefinic H) and 6·7–7·5 ppm (4H, q, aromatic H). (Found: C, 77·17; H, 7·24; N, 9·78. Calc'd for $C_{18}H_{20}N_2O$: C, 77·11; H, 7·19; N, 9·99%).

Cyclohexylidenemalononitrile

Malononitrile (3·3 g; 0·05 mole) and cyclohexanone (5·45 g; 0·05 mole) were reacted in benzene (12 ml) in the presence of ammonium acetate (0·38 g) and AcOH (0·61 g) under the conditions described[10] to give cyclohexylidenemalononitrile which was distilled under vacuum yielding 6·3 g (86%), b.p. 76–84° (0·11 mm), n_D^{25} 1·5116 (Lit.[10] n_D^{25} 1·5110;) ν_{max}^{neat} 2220 (CN), 1590 cm^{-1} (C=C); λ_{max}^{EtOH}

237 nm (ε 15,000); δ 1·4 – 2·0 (6H, m, nonallylic ring H) 2·4 – 2·8 (4H, m, allylic H).

2 - (1 - *Cyclohexenyl*) - 2 - (3 - p - *methoxyphenylallyl*)*malononitrile* **11**

Cyclohexylidenemalononitrile (1·75 g, 0·012 mole) was added dropwise at ice-bath temp to a soln of i-PrONa (0·012 mole) in i-PrOH (10 ml). The soln was warmed to room temp and *p*-methoxycinnamyl chloride (2·21 g, 0·012 mole) added in one portion. The soln was stirred for 15 min, three volumes of sat $NaHCO_3$ aq added, and extracted with benzene (4 × 20 ml). The combined benzene extracts were washed with water (4 × 10 ml), dried ($MgSO_4$), and evaporated. The residue (3·41 g) was chromatographed on alumina (Woelm, Activity III; 150 g), the product was eluted with benzene, and recrystallized from light petroleum (b.p. 30–60°) giving the product (1·53 g, 44%), mp 69–70°; $\nu_{max}^{CHCl_3}$ 2240 (weak, CN) and 1600 cm^{-1} (strong C=C); λ_{max}^{EtOH} 266 nm (ε 24,000); δ 1·72 (4H, m, non-allylic ring H), 2·2 (4H, m, allylic ring H), 2·86 (2H, d, J = 7 Hz, allylic CH_2), 3·77 (3H, s, OCH_3), 5·7 – 6·6 (3H, m, olefinic H) and 6·7 – 7·3 ppm (4H, q, aromatic H). Found: C, 78·12; H, 6·78; N, 9·48. Calc'd for $C_{18}H_{20}N_2O$: C, 78·05; H, 6·90; N, 9·58%).

(1 - *Isopropyl* - 2 - *methylpropylidene*)*malononitrile* **13**

Malononitrile (19·0 g, 0·29 mole) and diisopropyl ketone (32·54 g, 0·29 mole) were condensed as described,[35] to give the product (40·3 g, 87%), b.p. 84–92° (0·5 mm); n_D^{25} 1·4708; ν_{max}^{film} 2220 (strong, CN), 1580 cm^{-1} (C=C); λ_{max}^{EtOH} 238, ε 14,000); δ 1·22 (12H, d, J = 7Hz, CH_3) and 3·10 ppm (2H, m, methine). (Lit. n_D^{20} 1·4714, b.p. 97–98° (4 mm), λ_{max}^{EtOH} 237·5 (log ε 4·15).[35]

Reaction of chloride **6** *with dinitrile* **13**

Preparation of 2 - (1 - *isopropyl* - 2 - *methyl* - 1 - *propenyl*) - 2 - (3 - p - *methoxyphenylallyl*)*malononitrile* (**12**); (1 - *isopropyl* - 5 - p - *methoxyphenyl* - 2,2 - *dimethyl* - 4 - *pentenylidene*)*malononitrile* (**14**); 2 - *cyano* - 3 - *isopropyl* - 2 - (3 - p - *methoxyphenylallyl*) - 4 - *methyl* - 3 - *pentenamide* (**15**); 7 - p - *methoxyphenyl* - 2,4,4 - *trimethylhept* - 6 - *en* - 3 - *one* (**16**); *and* p - (1 - *isopropoxyallyl*)*anisole* (**17**). A soln of i-PrONa was prepared by dissolving Na (0·575 g; 0·025 mole) in i-PrOH (75 ml) at 50°. When the Na had dissolved, the dinitrile **13** (4·05 g; 0·025 mole) was added, followed by the addition of *p*-methoxycinnamyl chloride (4·55 g; 0·025 mole). The mixture was stirred at room temp for 1 h. Water (150 ml) was added, and the soln extracted with benzene (3 × 100 ml). The combined extracts were washed with water (3 × 300 ml), dried ($MgSO_4$) and evaporated to give a residue (7·9 g) which was chromatographed on alumina (Woelm, Activity III, 250 g), 50 ml fractions being taken. Fractions 1–46 (light petroleum b.p. 30–60°) gave 980 mg of **17**. Fractions 47–52 (2% benzene in light petroleum) and 53–57 (5% benzene) gave a further 670 and 390 mg respectively of **17** contaminated by dinitrile and chloride starting reagents. Fractions 58–64 (10% benzene in light petroleum) gave 745 mg of desired **12** with some impurity of **14**. Fractions 65–69 (10% benzene) yielded 240 mg of **14** with some impurity of **12**. Fractions 70–83 (25% benzene) gave 450 mg of **16** again with some impurity of **12**. Fractions 84–90 (50% benzene) and 91–107 (100% benzene) gave 15 and 105 mg respectively of unidentified materials. Stripping the column with MeOH gave 420 mg of a mixture containing amide **15**. Further purification was achieved by preparative layer chromatography on silica gel using 10% ether in light petroleum (b.p. 30–60°) as the developing solvent. In this way pure samples of compound **17** (980 mg; R_f 0·83), compound **12** (825 mg; R_f 0·50), **16** (85 mg; R_f 0·76) and **14** (165 mg; R_f 0·42) were obtained. Compound **15** was purified by preparative layer chromatography on alumina using ether as solvent (R_f 0·65) giving 100 mg.

Spectral and analytical details

Compound **17**. $\nu_{max}^{CHCl_3}$ 1600 cm^{-1} (C=C); λ_{max}^{EtOH} 228 (ε 17,500); δ 1·20 (6H, 2 doublets, J = 7 Hz, $(C\underline{H}_3)_2CH$), 3·65 (1H, m, $(CH_3)_2\underline{C}H$-O), 4·7–6·6 (4H, m, olefinic H and Ar-$C\underline{H}$-O), and 6·7–7·4 ppm (4H, q, aromatic H); *m/e* 206 (M^+), 164, 163 (base), 148, 147, 137, 135, 121. (Found: C, 75·59; H, 8·72. Calc'd for $C_{13}H_{16}O_2$: C, 75·67; H, 8·79%).

Compound **12**. $\nu_{max}^{CHCl_3}$ 2240 (weak, CN); λ_{max}^{EtOH} 265 nm (ε 23,500); δ 1·28 (6H, d, J = 6 Hz, $CH(C\underline{H}_3)_2$), 1·83 and 1·97 (3H, s, each, allylic CH_3), 2·93 (2H, d, J = 7 Hz, allylic CH_2), 2·8 – 3·2 (1H, m, allylic CH), 3·78 (3H, s, OCH_3), 5·9 – 6·7 (2H, m, olefinic H), and 7·1 ppm (4H, q, aromatic H); *m/e* 308 (M^+), 260, 147 (base), 121, 85, 83. (Found: C, 77·78; H, 7·93; N, 8·85. Calc'd for $C_{20}H_{24}N_2O$: C, 77·87; H, 7·82; N, 9·08%).

Compound **16**. $\nu_{max}^{CHCl_3}$ 1695 cm^{-1} (strong, C=O); λ_{max}^{EtOH} 263 nm (ε 21,000); δ 1·03 (6H, d, J = 6 Hz, $(C\underline{H}_3)_2CH$), 1·20 (6H, s, $(CH_3)_2C$<), 2·40 (2H, d, J = 6 Hz, allylic CH_2), 3·20 (1H, m, allylic CH), 3·80 (3H, s, OCH_3), 5·7 – 6·6 (2H, m, olefinic H) and 7·1 ppm (4H, q, aromatic H); *m/e* 260 (M^+), 147 (base), 136, 135, 121, 77. (Found: C, 78·23; H, 8·95. Calc'd for $C_{17}H_{24}O_2$: C, 78·45; H, 9·23%).

Compound **14**. $\nu_{max}^{CHCl_3}$ 2210 (strong, CN); ν_{max}^{EtOH} 258 nm (ε 20,000); δ 1·38 (6H, s, and 6H, d, J = 7 Hz, methyls), 2·56 (2H, d, J = 6 Hz, allylic CH_2), 3·40 (1H, m, allylic CH), 3·82 (3H, s, OCH_3), 5·4 – 6·6 (2H, m, olefinic H) and 7·1 ppm (4H, q, aromatic H); *m/e* 308 (M^+), 148, 147 (base), 115, 91. (Found: C, 77·73; H, 7·67; N, 8·82. Calc'd for $C_{20}H_{24}N_2O$; C, 77·87; H, 7·82; N, 9·08%).

Compound **15**. $\nu_{max}^{CHCl_3}$ 3450 (NH_2) and 1700 cm^{-1} (C=O); ν_{max}^{EtOH} 263 nm ε 20,500); δ 1·24 (6H, d, J = 7 Hz, $(C\underline{H}_3)_2CH$), 1·77 and 1·83 (3H, s, each, allylic CH_3), 3·0 (3H, m, allylic CH_2 and CH), 3·80 (3H, s, OCH_3), 5·8 – 6·6 (4H, m, olefinic H and NH_2), 7·1 ppm (4H, q, aromatic H); *m/e* 147, 118, 87, 85, 83 (base), 82. No molecular ion (326) visible. (Found: C, 73·41; H, 8·14; N, 8·60. Calc'd. for $C_{20}H_{26}N_2O_2$: C, 73·60; H, 8·03; N, 8·58%).

2 - (1 - *Ethyl* - 1 - *propenyl*) - 2 - (3 - p - *methoxyphenylpropyl*)*malononitrile* **22**

A soln of i-PrONa was prepared by dissolving Na (0·058 g, $0·25 \times 10^{-2}$ mole) in i-PrOH (10 ml) at 50°. The soln was cooled in an ice-bath and **5** (0·34 g, $0·25 \times 10^{-2}$ mole) added dropwise to give the clear orange soln of the malononitrile anion. 3 - *p* - Methoxyphenyl - 1 - propanyl brosylate (m.p. 57°, 0·787 g, $0·25 \times 10^{-2}$ mole, prepared by brosylation[36] of the corresponding alcohol)[37] was added as a solid in one portion and the mixture heated under reflux overnight. Water (50 ml) was added and the soln extracted with benzene (3 × 25 ml). The combined extracts were washed with water (2 × 25 ml), dried (Na_2SO_4), and evaporated giving a yellow-brown liquid (0·71 g) which was purified by silica gel preparative layer chromatography (developing solvent light petroleum (b.p. 30–60°)-ether (1 : 1); R_f 0·69), $\nu_{max}^{CHCl_3}$ 2220 (weak, CN), 1610 (C=C), 1030 and 825 cm^{-1}; δ 1·2 (3H, t, J = 6 Hz, CH_2–$C\underline{H}_3$), 1·5 – 3·0 (11H, m, other aliphatic H), 3·86 (3H, s, OCH_3), 6·1 (1H, q, J = 7 Hz, olefinic H), and 6·7 to 7·3 ppm (4H, q, aromatic

H); (Found: 282·1726. Calc'd for $C_{18}H_{22}N_2O$, 282·1731).

3-p-Methoxyphenylallyl phenyl sulfide **21b**

Compound **6** (4·0 g) in acetone (2 ml) was added to a mixture of THAM buffer soln,[39] pH 9·0 (20 ml), thiophenol (2·0 g), and sufficient i-PrOH to cause soln. The soln was stirred at room temp for 30 min, during which time the product precipitated from soln, and was then extracted with ether (2 × 50 ml). The combined extracts were washed with water (2 × 25 ml), dried ($MgSO_4$), and evaporated. The residue was recrystallized from ether–benzene giving white plates (1·4 g), mp 114–115°; $\nu_{max}^{CHCl_3}$ 1610 cm^{-1} (C=C), λ_{max}^{EtOH} 271 nm (ε 25,000); δ3·65 (2H, d, J = 6 Hz, CH_2–S), 3·77 (3H, s, OCH_3), 5·7–6·5 (2H, m, olefinic H), and 6·7–7·5 ppm (9H, m, aromatic H. (Found: C, 75·00; H, 6·25; S, 12·46. Calc'd for $C_{16}H_{16}OS$: C, 74·96; H, 6·29; S, 12·50%).

Acryloyl chloride (b.p. 74–76°; δ6·0–6·8 ppm (m)) was prepared in 70% yield from acrylic acid by the method of Stempel *et al.*[39] (Lit. b.p. 72–74° (740 mm)).[39]

Allyl-1,1-d₂ alcohol. (b.p. 100–108°) was prepared in 40% yield by reduction of acryloyl chloride by $LiAlD_4$ as reported[40] (Lit. b.p. 98°). The NMR spectrum showed signals at δ 5·3–5·9 (2H, m) and 6·40 ppm (1H, m), and the absence of the finely split doublet (2H) at δ4·1 ppm present in the spectra of nondeuterated samples. It was found that distillation of the product[40] was essential in order for the final condensation step of the synthetic sequence to proceed.

Allyl-1,1-d₂ chloride. (b.p. 36–50°) was prepared in quantitative yield by the reaction of allyl-1,1-d_2 alcohol with thionyl chloride in the presence of di-*n*-butyl ether and tri-*n*-butylamine according to the method of Young *et al.*[41] for preparing allyl-1-^{14}C chloride. The NMR spectrum showed signals at δ5·2–5·7 (2H, m) and 6·37 ppm (1H, m), and the absence of the finely split doublet at δ4·1 (2H) present in the spectra of nondeuterated samples. Samples prepared for the next step of the sequence were distilled directly into a small quantity of isopropanol to minimize difficulties associated with the high volatility of allyl chloride.

2 - (1,1 - Dideuterioallyl) - 2 - (1 - ethyl - 1 - propenyl)malononitrile **1c**

Allyl-1,1-d_2 chloride was reacted with the Na anion of **5**, as described by Cope *et al.* for the preparation of the undeuterated analogue.[6,27] The NMR spectrum showed signals at δ1·17 (3H, t, J = 7·5 Hz, CH_2–$\underline{CH}_3$), 1·77 (3H, d, J = 7 Hz, allylic CH_3), 2·28, (2H, q, J = 7·5 Hz, $C\underline{H}_2$–CH_3), and 5·1–6·2 ppm (4H, m, olefinic H), and the absence of the 2 proton doublet (J = 6 Hz) at δ2·65 ppm present in spectra of nondeuterated samples.

Pyrolysis of compound **1b**

Dinitrile **1b** was distilled at 110° (0·7 mm) to give a quantitative yield of **4**, ν_{max} 2220 cm^{-1} (strong, CN); λ_{max}^{EtOH} 263 nm (ε 26,000); δ1·22 (3H, d, J = 7 Hz, CH–$\underline{CH}_3$), 1·23 (3H, t, J = 7·5 Hz, CH_2–$\underline{CH}_3$) 2·2–3·6 (5H, m, allylic H), 3·78 (3H, s, OCH_3), 5·5–6·6 (2H, m, olefinic H), and 6·7–7·5 ppm (4H, q, aromatic H). (Found: C, 77·02; H, 7·25; N, 10·04. M.W. 280·1588. Calc'd for $C_{18}H_{20}N_2O$: C, 77·11; H, 7·19; N, 9·99% M.W. 280·1575).

Pyrolysis of compound **11**

Dinitrile **11** (726 mg) was heated at 140° for 36 h under N_2. The brown residue was chromatographed on silica gel and recrystallized from light petroleum (b.p. 30–60°) to give **19** as white crystals (105 mg), m.p. 71–72°; $\nu_{max}^{CHCl_3}$ 2225 (strong, CN), 1600 cm^{-1} (C=C); λ_{max}^{EtOH} 231 nm (ε 13,800); δ1·0–1·9 (6H, m, non-allylic ring H), 1·9–3·2 (3H, m, allylic H), 3·2–3·7 (1H, m, benzylic H), 3·80 (3H, s, OCH_3), 4·8–5·4 (2H, m, CH_2 =), 5·4–6·6 (1H, m, CH =), and 6·7 to 7·5 ppm (4H, q, aromatic H). (Found: C, 77·97; H, 6·99; N, 9·48. Calc'd for $C_{19}H_{20}N_2O$: C, 78·03; H, 6·90; N, 9·58%).

Pyrolysis of compound **12**

Dinitrile **12** was heated under reflux in BuOH (b.p. 118°) for 7 days. The resulting mixture, purified as described above in the preparation of **12**, was shown to consist of 64% compound **14** and 36% unchanged **12**, identical in all respects with samples encountered in the preparation of **12**.

Pyrolysis of compound **1c**

Deuterated dinitrile **1c** (90 mg) was heated under reflux in i-PrOH (15 ml) for 7 h. Water (50 ml) was added and the soln extracted with ether (2 × 20 ml) and $CHCl_3$ (1 × 20 ml). The combined extracts were washed with water (2 × 20 ml), dried ($MgSO_4$), and evaporated giving a residue (61 mg) which was chromatographed on alumina (Woelm, Activity III, 12 g), the product being eluted with 15% benzene in light petroleum (b.p. 30–60°). The NMR spectrum of the product was identical with that of non-deuterated samples of **8**[6] with the exception of the olefinic region which integrated for only 1·0 proton (δ5·68 ppm, t, J = 8 Hz).

Pyrolysis of compound **1b** *in presence of sodium borohydride*

A soln of **1b** (56 mg, 2×10^{-4} mole), $NaBH_4$ (58·4 mg, 16×10^{-4} mole), and NaOH (16 mg, 4×10^{-4} mole) in diglyme (0·5 ml) and water (0·2 ml)[30] was heated at 88° for 16 h. Water (1 ml) was added and the mixture extracted with light petroleum (b.p. 30–60°) (3 × 5 ml). The combined extracts were washed with water (2 × 5 ml), dried ($CaCl_2$), and evaporated to give a residue which was subjected to GLC-mass spectrometric analysis on Hewlett-Packard Model 700 gas chromatograph equipped with an 8-foot SE30 on chromosorb B column (130°) attached to an Atlas CH-4 mass spectrometer. Anethole (**21c**), retention time 6·08 min; *m/e* 148 (M^+, base), 147, 133, 117, 105, 77) and **5** (retention time 1·7 min: *m/e* 134 (M^+), 106, 93, 78, 58, 44, 43 (base)) were identified by identity of retention time and fragmentation pattern with those of authentic samples.

Pyrolysis of compound **22** *in presence of sodium borohydride*

A soln of dinitrile **22** (0·97 g, $3·4 \times 10^{-3}$ mole), $NaBH_4$ (1·05 g, $27·5 \times 10^{-3}$ mole) and NaOH (285 mg, $6·9 \times 10^{-3}$ mole) in diglyme (5 ml) and water (1 ml) was heated at 167° for 46 h. Work-up and analysis as described above in the pyrolysis of **1b** showed no detectable trace of **23**.

Pyrolysis of compound **11** *in presence of sodium borohydride*

A soln of **11** (58·4 mg, 2×10^{-4} mole), $NaBH_4$ (58·4 mg, 16×10^{-4} mole) and NaOH (16 mg, 4×10^{-4} mole) in diglyme (0·5 ml) and water (0·2 ml) was heated at 88° for 16 h. Water (1 ml) was added and the mixture extracted with light petroleum (b.p. 30–60°) (3 × 5 ml). The combined extracts were washed with water (2 × 5 ml), dried ($CaCl_2$), and evaporated. GLC-mass spectrometric analysis of the

residue as described above demonstrated the presence of anethole.

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REFERENCES

[1]A. C. Cope and E. M. Hardy, *J. Am. Chem. Soc.* **62**, 441 (1940)
[2]R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*. Academic Press, (1970)
[3]See for example [a]J. A. Berson and P. B. Dervan, *J. Am. Chem. Soc.* **95**, 267 (1973); [b]J. A. Berson and P. B. Dervan, *Ibid.* **94**, 7597 (1972); [c]J. A. Berson, P. B. Dervan, and J. A. Jenkins, *Ibid.*, **94**, 7598 (1972); [d]J. A. Berson and L. Salem, *Ibid.* **94**, 8917 (1972); [e]M. J. Goldstein and M. S. Benzon, *Ibid.*, **94**, 7147 (1972), and refs therein
[4]H. P. Koch, *J. Chem. Soc.* 1111 (1948)
[5]W. von E. Doering and W. R. Roth, *Angew. Chem.* Int. Ed. **2**, 115 (1963)
[6]G. S. Hammond and C. D. DeBoer, *J. Am. Chem. Soc.* **86**, 899 (1964)
[7]R. W. Thies, *Ibid.* **94**, 7074 (1972)
[8]D. C. Wigfield and S. Feiner, *Canad. J. Chem.* **48**, 855 (1970)
[9]M. J. S. Dewar and L. E. Wade, *J. Am. Chem. Soc.* **95**, 290 (1973)
[10]A. C. Cope and K. E. Hoyle, *Ibid.* **63**, 733 (1941)
[11]W. N. White and W. K. Fife, *Ibid.* **83**, 3846 (1961)
[12]J. A. Berson and G. L. Nelson, *Ibid.* **89**, 5503 (1967)
[13]K. Humski, T. Strelkov, S. Borcic, and D. E. Sunko, *Chem. Commun.* 693 (1969)
[14]K. Humski, R. Malojcic, S. Borčić, and D. E. Sunko, *J. Am. Chem. Soc.* **92**, 6534 (1970)
[15]R. Malojcic, K. Humski, S. Borčić, D. E. Sunko and R. Bošković, *Tetrahedron Letters* 2003 (1969)
[16]L. M. Jackman and S. Sternhell, *Applications of Nuclear Mangetic Resonance in Organic Chemistry* (2nd Edition) Pergamon Press (1969)
[17]F. F. Caserio, G. E. Dennis, R. H. DeWolfe, and W. G. Young, *J. Am. Chem. Soc.* **77**, 4182 (1955)
[18]W. S. Johnson, T. Li, C. A. Harbert, W. R. Bartlett, T. R. Herrin, B. Staskun, and D. H. Rich, *Ibid.* **92**, 4461 (1970)
[19]R. B. Bates and D. M. Gale, *Ibid.* **82**, 5749 (1960)
[20]K. H. Dahm, B. M. Trost, and H. Roller, *Ibid.* **89**, 5292 (1967)
[21]S. F. Brady, M. A. Ilton, and W. S. Johnson, *Ibid.* **90**, 2882 (1968)
[22]A. F. Thomas, *Chem. Commun.* 1657 (1968)
[23]W. S. Johnson, T. Li, D. J. Faulkner, and S. F. Campbell, *J. Am. Chem. Soc.* **90**, 6225 (1968)
[24]R. Zurfluh, E. N. Wall, J. B. Siddall, and J. A. Edwards, *Ibid.*, **90**, 6224 (1968)
[25]E. J. Corey, J. A. Katzenellenbogen, *Ibid.*, **91**, 1851 (1969)
[26]W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Petersen, *Ibid.*, **92**, 741 (1970)
[27]A. C. Cope, K. E. Hoyle, and D. Heyl, *Ibid.*, **63**, 1843 (1941)
[28]G. S. Hammond, *Ibid.*, **77**, 334 (1955)
[29]P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.* 3331 (1952)
[30]H. C. Brown and H. M. Bell, *J. Org. Chem.* **27**, 1928 (1962)
[31]A. Streitweiser, Jr., *Chem. Revs.* **56**, 571 (1956)
[32]R. H. DeWolfe and W. G. Young, *Ibid.*, **56**, 765 (1956)
[33]J. Hine, *Physical Organic Chemistry* (2nd Edition) p. 175. McGraw-Hill, New York (1962)
[34]E. W. Yankee and D. J. Cram, *J. Am. Chem. Soc.* **92**, 6328 (1970)
[35]H. Hart and Y. C. Kim, *J. Org. Chem.* **31**, 2784 (1966)
[36]S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.* **70**, 821 (1948)
[37]J. C. Bardhan and D. N. Mukherji, *J. Chem. Soc.* 4629 (1956)
[38]G. Gomori, *Methods in Enzymology* Vol. 1, pp. 138–144. Academic Press, New York (1955)
[39]G. H. Stempel Jr., R. P. Cross, and R. P. Mariella, *J. Am. Chem. Soc.* **72**, 2299 (1950)
[40]R. D. Schuetz and F. W. Millard, *J. Org. Chem.* **24**, 297 (1959)
[41]S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, *J. Am. Chem. Soc.* **80**, 5965 (1958)