Alkyl Shifts in Thermolyses. VII.[1] Stereochemistry and Kinetics of the Carbethoxyspiropentane to Carbethoxymethylenecyclobutane Rearrangement. Evidence for Concertion and an Intermediate[2]

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Abstract: Pyrolysis of carbethoxyspiropentane gave a 9:1 mixture of 1-carbethoxymethylenecyclobutane and 2-carbethoxymethylenecyclobutane, respectively, under kinetic control. Using a flow reactor log k was found to be equal to $14.7-48{,}700/2.3RT$. Pyrolysis of the four 4-methylcarbethoxyspiropentanes revealed that rearrangement occurred faster than epimerization at C_1 in every case and that the major rearrangement product was 3-methylcarbethoxymethylenecyclobutane. Thus, the more highly substituted carbon migrated much faster than the unsubstituted one by factors from 3 to 16. Significantly, the rates of rearrangement of the 4-methyl esters were very similar to that of the parent ester. Rearrangement of three of the 4,5-dimethylcarbethoxyspiropentanes also occurred at the same rate as the parent giving mostly the 2,3-dimethylcarbethoxymethylenecyclobutanes with predominant (~90%) retention of configuration of the migrating carbon. Pyrolysis of three of the 2,4-dimethylcarbethoxyspiropentanes gave mostly the 2,3-dimethylcarbethoxymethylenecyclobutanes, but in each case the major isomer (63–83%) was that predicted by conservation of orbital symmetry with retention at both the migrating group, C_4, and the migration terminus, C_2, or with inversion at both C_2 and C_4. Since retention at C_4 was demonstrated previously, the retention–retention pathway must be the preferred one, which is also consistent with least motion control. Since the rate of the rearrangement was independent of a methyl substituent at C_4 but the product distribution reflected that substitution, a two-step reaction is proposed in which the first step is rate-determining and leads to an intermediate which has the C_1–C_2 bond only stretched. This intermediate could have sufficient overlap to still allow a cyclic array of interacting orbitals in the subsequent product determining transition state to permit orbital symmetry control.

The spiropentane (**1**) to methylenecyclobutane (**2**) thermal rearrangement, which was first studied quantitatively by Flowers and Frey[4] and by Burkhardt,[5] is in many respects like the cyclopropane to propylene thermal isomerization[6] which is the focus of current controversy. Approximate kinetic–thermodynamic considerations suggest the presence of an intermediate

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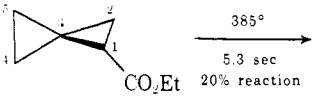
trimethylene biradical which is responsible for the structural isomerization as well as geometric and optical isomerization of cyclopropane prior to the structural rearrangement[7] while relatively rigorous quantum chemistry indicates no secondary minimum in the potential energy surface for the geometric and optical isomerization of cyclopropane.[8]

Because of the similarity between the cyclopropane and spiropentane isomerizations,[9] we have examined the kinetics and overall stereochemistry of the latter reaction in a case where prior geometric isomerization is slow compared with structural rearrangement. Thus, carbethoxyspiropentane as well as a number of mono- and dimethylcarbethoxyspiropentanes were subjected to pyrolysis.[1,10] As will be demonstrated, the reaction is partially concerted in an orbital-symmetry conservation–least motion controlled sense but also appears to proceed *via* an intermediate because of the response of the rate and product distribution to methyl substitution.

Results

Pyrolysis of Carbethoxyspiropentane. In a preliminary examination, the parent compound carbethoxyspiropentane (**3**) was pyrolyzed in a flow system.



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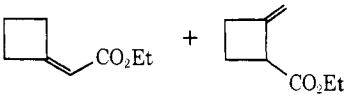

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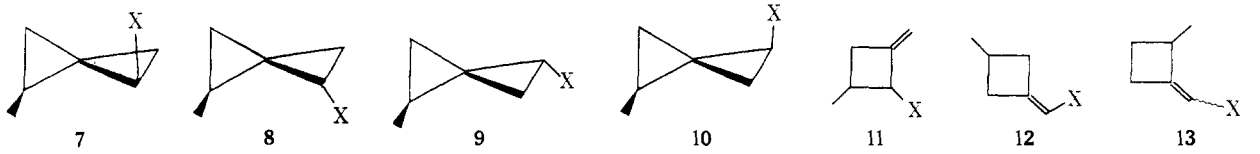
Under conditions where 20% of the starting material disappeared, two products, **4** and **5**, in a ratio of 9:1 were formed. Carbethoxymethylenecyclobutane (**4**) was isolated from a preparative scale, sealed-tube pyrolysis and identified by its spectral characteristics. 2-Methylenecarbethoxycyclobutane (**5**) was synthesized independently; its retention time on UCON and

(1) For part VI, see J. J. Gajewski and L. T. Burka, *J. Amer. Chem. Soc.*, **94**, 8860 (1972).
(2) Taken in part from the thesis of L. T. B., submitted in partial fulfillment of the requirements for the Ph.D. degree at Indiana University, Jan 1972.
(3) Fellow of the Alfred P. Sloan Foundation, 1971–1973.
(4) M. C. Flowers and H. M. Frey, *J. Amer. Chem. Soc.*, **83**, 5550 (1961).
(5) P. J. Burkhardt, *Diss. Abstr.*, **23**, 1524 (1962).
(6) For a review see W. L. Carter and R. G. Bergman, *J. Amer. Chem. Soc.*, **91**, 7411 (1969).
(7) (a) S. W. Benson, *J. Chem. Phys.*, **34**, 521 (1961); (b) H. E. O'Neal and S. W. Benson, *J. Phys. Chem.*, **72**, 1866 (1968).
(8) J. A. Horsley, Y. Jean, C. Moser, L. Salem, R. M. Stevens, and J. S. Wright, *J. Amer. Chem. Soc.*, **94**, 279 (1972); P. J. Hay, W. J. Hunt, and W. A. Goddard III, *ibid.*, **94**, 638 (1972).
(9) J. J. Gajewski and L. T. Burka, *ibid.*, **94**, 8857 (1972), and references contained therein, particularly J. C. Gilbert, *Tetrahedron*, **25**, 1459 (1969).
(10) J. J. Gajewski and L. T. Burka, *J. Org. Chem.*, **35**, 2190 (1970).

Table I. Products from Pyrolysis[a] of 4-Methylcarbethoxyspiropentanes **7**, **8**, **9**, and **10** at 385° for 5.3 sec[e]



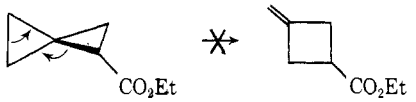
7 **8** **9** **10** **11** **12** **13**

X = CO_2Et

Compd	% reaction[b]	% of total products **7**	**8**	**9**	**10**	**11**	**12**	**13**[d]
7	33 ± 2		4.5 ± 0.7		3.5 ± 0.6	8.4 ± 0.4[c]	78.4 ± 1.5	5.1 ± 0.9[f]
8	27 ± 1	7.2 ± 0.5		3.6 ± 0.4		8.6 ± 0.3	77.2 ± 0.7	4.7 ± 0.9[f]
9	17 ± 1		9.1 ± 0.2		33.2 ± 1.0	6.2 ± 2.0	40.5 ± 0.7	13.2 ± 1.5[g]
10	27 ± 2	6.6 ± 0.5	5.2 ± 0.5	28.8 ± 0.6		7.8 ± 0.2[c]	37.2 ± 0.9[c]	14.5 ± 1.0[h]

[a] Results reported are averages of three to five runs. [b] Based on integration with respect to an internal standard, *n*-octane; includes both epimerization and rearrangement. [c] Isolated from a preparative sealed tube pyrolysis and identified by its spectral properties. [d] Independently synthesized, retention times identical with synthesized material on UCON and TCEP capillary columns. [e] Under the same conditions the parent compound **3** rearranged to the extent of 20%. [f] Anti isomer predominated. [g] Anti:syn = 1:2. [h] Anti:syn = 3:2.

TCEP capillary columns was identical with that from pyrolysis of **3**. Under conditions where nearly 80% of **3** reacted, the ratio of **4**:**5** had dropped to 81:19 indicating that **5** was probably being formed from **4**, possibly *via* a methylenecyclobutane degenerate rearrangement.[11] Thus, there is a kinetic preference for formation of the α,β-unsaturated ester in the pyrolysis of carbethoxyspiropentane. Furthermore, the carbethoxy group evidently strongly directs the initial cleavage of the C_1–C_2 bond which is adjacent to it, since no product with retention time similar to that of 3-methylenecarbethoxycyclobutane (**6**) was found. This material could be formed only by a combination of C_1–C_3 and C_4–C_5 bond fission.



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The kinetics of rearrangement of carbethoxyspiropentane (**3**) were determined in a commercial gold flow reactor and found to be reasonably first order giving acceptable but not highly accurate activation parameters.[12] Thus, $\log k = 14.7\text{-}48{,}700/2.3RT$. It is interesting to compare this with the rate constant for rearrangement of methylspiropentane where $\log k = 14.85\text{–}53{,}800/2.3RT$.[13] Thus, the carbethoxy group appears to stabilize the transition state for rearrangement about 5 kcal/mol over a methyl group.

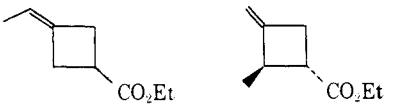
Pyrolysis of 4-Methylcarbethoxyspiropentanes. The question of epimerization was next investigated. The results of pyrolysis of the four 4-methylcarbethoxyspiropentanes (medial,anti (**7**); proximal (**8**); medial-syn (**9**); and distal (**10**))[10] indicated that rearrangement to the α,β-unsaturated esters **12** and **13** was at least competitive with epimerization (Table I) in contrast to the parent hydrocarbon.[9] Thus two of the compounds, **9** and **10**, rearranged at about the same rate as they epimerized, but the other two, **7** and **8**, rearranged about nine times as fast as they epimerized.

(11) W. von E. Doering and J. C. Gilbert, *Tetrahedron, Suppl.*, 7, 397 (1966).

(12) The instrument was a Chemical Data Systems Pyrochrome model. Literature values for the activation parameters for rearrangement of cycloheptatriene and vinylcyclopropane were reproduced if the conversion was near 50% at all temperatures.

(13) M. C. Flowers and A. R. Gibbons, *J. Chem. Soc. B*, 612 (1971).

The β,γ-unsaturated ester **11** probably arises from a methylenecyclobutane degenerate rearrangement of **12** in the same way that **5** is produced from **4**. Compounds **14** and **15**, which could be produced by some



14 **15**

combination of C_1–C_3, C_4–C_5 fission, were not observed in the pyrolyses of **7**–**10**.

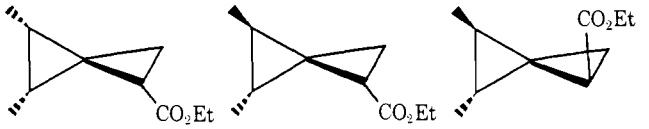
Of considerable interest in these pyrolyses is the fact that the major products were the α,β-unsaturated esters **12** and **13** just as in the parent system, **3**. Furthermore, there was from **7** and **8** a 16-fold preference for migration of C_4, the methyl-bearing carbon, over C_5, the methylene group, to C_2, reflected in the **12**:**13** ratio of 16 to 1 in each case. This preference was also exhibited with the spiropentane esters, **9** and **10**, where the **12**:**13** ratio was 2.5–3:1 at relatively low conversions. In all of these reactions the material balance was high as measured against an internal standard.

Finally, also of interest in these pyrolyses are the rates with which the 4-methyl derivatives rearrange compared with the parent, carbethoxyspiropentane (**3**). Under conditions in the flow system where **3** rearranged to the extent of 20%, the per cent rearrangements (epimerization excluded) of **7**–**10** were 31, 24, 11, and 16%, respectively (Table I). Thus, all of the rate constants are within a factor of 2 of that of the parent indicating a minimal effect of the 4-methyl group on the rate-determining step of the pyrolysis.

Preparation and Characterization of 2,3-Dimethyl-1-carbethoxymethylenecyclobutanes. The results of the 4-methylcarbethoxyspiropentane pyrolyses indicated that there might be a possibility of observing the stereochemical consequences of the rearrangement. This offered encouragement for investigation of the more heavily substituted systems, 4,5-dimethylcarbethoxyspiropentane and 2,4-dimethylcarbethoxyspiropentane. The expected methylenecyclobutane products from these systems, **16**, **17**, **18**, and **19**, were prepared from *cis*- and *trans*-2,3-dimethylcyclobutanone[14]

(14) N. J. Turro and R. B. Gagonian, *J. Amer. Chem. Soc.*, **92**, 2036 (1970).

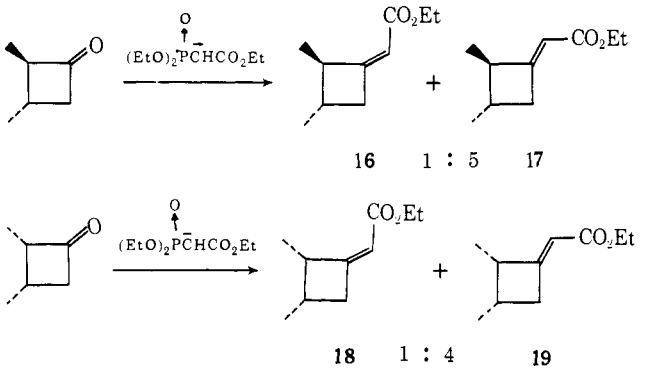
Table II. Pyrolysis[a] of 4,5-Dimethylcarbethoxyspiropentanes **20**, **21**, and **22** at 385° for 5.3 sec



20 **21** **22**

Compd	% reaction[b]	% of total products[d] 16[c]	17[c]	18[c]	19[c]	20	21	22
20	20 ± 3	9.0 ± 1.1	8.3 ± 1.0	17.6 ± 1.2	21.8 ± 2.6		10.5 ± 0.5	11.4 ± 0.6
21	20 ± 1	57.6 ± 2.8	16.0 ± 2.5	8.8 ± 0.2	0.6 ± 0.3	5.0 ± 0.9		7.0 ± 0.1
22	24 ± 3		69.9 ± 1.1		7.7 ± 1.2	4.2 ± 0.7	10.9 ± 0.9	

[a] Results reported are averages of three to four runs. [b] Based on integration with respect to an internal standard, *n*-octane; includes both epimerization and rearrangement. [c] Independently synthesized; retention times identical with synthesized material on UCON and TCEP capillary columns. [d] Each pyrolysis produced several minor unidentified products.



and the sodium salt of triethyl phosphonoacetate.[15] Reaction with the trans ketone produced two esters in a 1:5 ratio; the cis ketone gave two different esters in a 1:4 ratio. Assuming that no epimerization occurred in the reactions, the major product from each ketone was expected to be an anti compound **17** or **19**, due to steric interaction of the carbethoxy group and the 2-methyl group. The major product from each ylide reaction showed an upfield shift of the pmr signal of the 2-methyl protons relative to the minor products (see Experimental Section) and a corresponding downfield shift of the signal assigned to the protons on the 4 carbon. These shifts are consistent with the prediction that the anti compounds are the major products from the reaction.

Pyrolysis of 4,5-Dimethylcarbethoxyspiropentanes. Short-term pyrolyses of the 4,5-dimethylcarbethoxyspiropentanes **20**, **21**, and **22**[1] revealed that the α,β-unsaturated esters **16–19** were the major products analogous to the major product from the pyrolysis of carbethoxyspiropentane (Table II). Other, less abundant, products included epimerized starting material in each case: **21** and **22** from **20**, the result of reversible C_4–C_5 fission; **20** and **22** from **21**, the result of both reversible C_4–C_5 and C_1–C_2 bond fission; and **20** and **21** from both modes of fission.

However, the distribution of the α,β-unsaturated esters **16–19** clearly indicates partial retention at the migrating carbon. Thus, at roughly 20% conversion *cis-anti*-4,5-dimethylcarbethoxyspiropentane (**20**) gave twice as much *cis*-2,3-dimethylcarbethoxymethylenecyclobutanes (**18** and **19**) as the trans compounds **16** and **17**, while the *trans*-4,5-dimethylcarbethoxyspiropentanes (**21** and **22**) gave more than nine times as much of the *trans*-2,3-dimethyl-substituted cyclobutane esters **16** and **17** than the cis ones, **18** and **19**. Since the epimerization of starting material was at most only half as fast as rearrangement in these pyrolyses, the ratio of cis and trans products should not be greatly affected by this geometric isomerization at such low conversions.

However, as will be described later, at 20% conversion a substantial amount of the trans products from **20** are derived by subsequent reaction of the cis products and the actual ratio of **18** and **19** to **16** and **17** is more like 10, kinetically. Finally, though the kinetics of the rearrangement of **20–22** were not determined, the data of Table II indicate that under the same conditions **3** rearranged to the extent of 20% and **20–22** rearranged to the extent of 16, 18, and 21%, respectively. Thus, methyl substitution at both C_4 and C_5 had little effect on the rate-determining step of the carbethoxyspiropentane to carbethoxymethylenecyclobutane rearrangement.

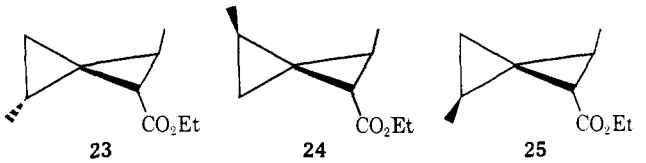
Pyrolysis of the 2,4-Dimethylcarbethoxyspiropentanes. In an effort to determine the stereochemical outcome at the migration terminus and the direction of the rotation of C_1, various 2,4-dimethylcarbethoxyspiropentanes[1] were pyrolyzed for short reaction times. The major products from the reactions of three of these, namely **23**, **24**, and **25**, were the 2,3-dimethylcarbethoxymethylenecyclobutanes (**16–19**), which constituted at least 62% of the total product at the lowest conversions (Table III). These major products, which must arise by preferential migration of C_4 to C_2 after C_1–C_2 fission to form the α,β-unsaturated system, again resemble those from the parent carbethoxy compound. Further, the preferential migration of the methyl-bearing carbon, C_4, over C_5 is consistent with the pyrolyses of the 4-methylcarbethoxyspiropentanes (**7–10**) where the major α,β-unsaturated ester product was derived by C_4 not C_5 migration. Finally, it is clear that there is stereospecificity in the overall rearrangement since the major product from **23** is **16** (83% of **16–19**) while that from **24** is **17** (62% of **16–19**), and that from **25** is **18** (71% of **16–19**). The specificity can be rationalized by a combination of conservation of orbital symmetry[16] and least motion control (see Discussion).

Two other 2,4-dimethylcarbethoxyspiropentanes were also investigated which gave results considerably dif-

(15) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

(16) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970.

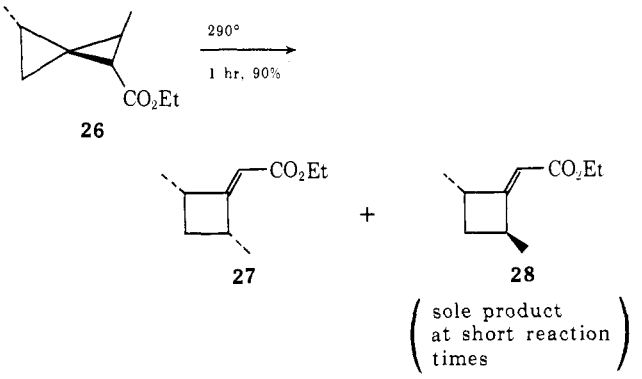
Table III. Pyrolysis[a] of 2,4-Dimethylcarbethoxyspiropentanes **23**, **24**, and **25**

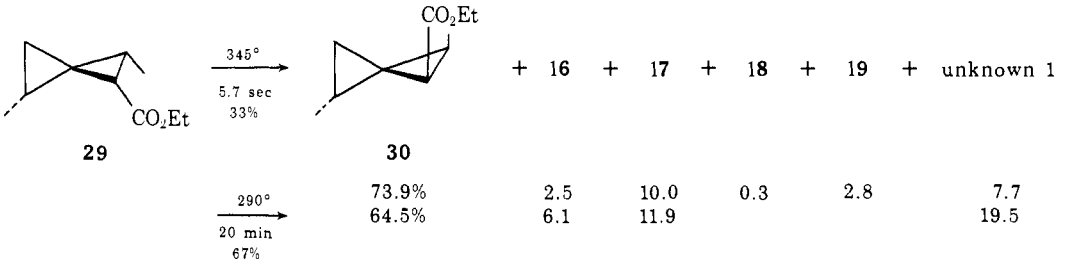


23 **24** **25**

Compd	Temp, °C (sec)	% reaction[b]	% of total products[d] 16[c]	17[c]	18[c]	19[c]
23	385 (5.3)	23 ± 2	38.9 ± 0.7	6.6 ± 0.5	12.1 ± 0.7	7.5 ± 0.7
	355 (5.6)	7 ± 3	71.7 ± 7	2.3 ± 0.5	10.2 ± 2	2.5 ± 0.5
24	385 (5.3)	36 ± 2	13.1 ± 0.3	28.4 ± 0.2	12.4 ± 0.7	9.5 ± 2.2
	345 (5.7)	9 ± 2	8.0 ± 0.5	40.0 ± 4	12.2 ± 3	2.6 ± 2
25	385 (5.3)	48 ± 4	34.4 ± 0.9	Trace	50.4 ± 1.1	Trace
	345 (5.7)	3 ± 2	25.3 ± 3	Trace	60.8 ± 6	Trace

[a] Results reported are averages of 2–4 runs. [b] Based on integration with respect to an internal standard, *n*-octane. [c] Independently synthesized, retention times were compared to synthesized material on TCEP and UCON capillary columns. [d] Each pyrolysis gave about 2% of material resulting from epimerization at both C-1 and C-2. In addition to the products reported each pyrolysis gave several unidentified minor products.



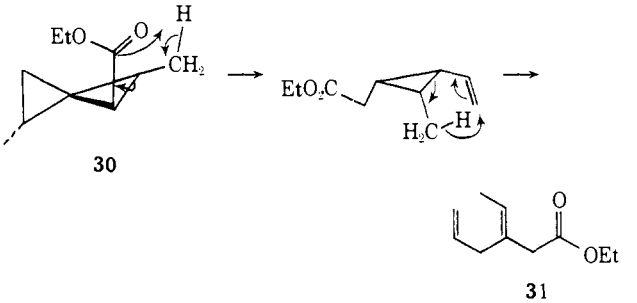


ferent from **23**, **24**, and **25**. When *trans*-2-methyl-*distal*-4-methylcarbethoxyspiropentane (**26**)[1] was pyrolyzed at 345° for 5.7 sec, only one major product was observed. The retention time of this compound did not correspond to that of any of the 2,3-dimethylcyclobutane compounds from the other spiropentane pyrolyses. A preparative, long-term, sealed-tube pyrolysis of **26** gave two products in a 56:44 ratio whose spectral properties were consistent with *cis*- and *trans*-2,4-dimethylcarbethoxymethylenecyclobutane (**27** and **28**).

Assignment of the cis–trans relationship of the methyl groups was based on their shielding of the ring protons on C_3 of the cyclobutane ring. In **28**, both protons are shielded by one methyl group and should have about the same chemical shift (δ 1.81); in **27**, however, one proton (δ 1.78) is shielded by both methyl groups while the other (δ 2.46) is normal (see compound **4**). The isomer produced by pyrolysis of **26** in the flow system for short reaction times was **28**.

The retention times of compounds **27** and **28** were checked against those of unidentified products from pyrolysis of **23**, **24**, and **25**. One peak, amounting to 4.4 ± 0.6% of the total product from pyrolysis of **23** at 385°, had the same retention time as **28** on the UCON capillary. The pyrolysis of **24** and **25** at 385° produced a peak with retention time corresponding to that of **27**: 10.4 ± 1.5% from **24** and a trace (*ca.* 0.5%) from **25**.

The other 2,4-dimethyl compound investigated was *cis*-2-methyl-*medial*,*syn*-4-methylcarbethoxyspiropentane (**29**).[1] Double epimerization at C_1–C_2 to give **30** occurred much faster than rearrangement. From pmr, unknown 1 appeared to be the trienic ester, **31**, which could be derived from **30** by a series of hydrogen shifts.[17]

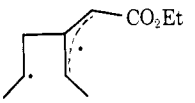


The fact that the *cis*-2-methyl ester derivatives like **29** rearrange faster than the corresponding trans isomers like **23**–**25** allows the possibility that the cis materials could be intermediates in the pyrolyses of the trans isomers as a result of epimerization (at C_1 and/or C_2 in **23**–**25**) and give **16**–**19**. That this is not the case is suggested by the fact that **29** and/or **30** give predominantly **17**, the *trans-anti*-cyclobutane ester. However,

(17) D. E. McGreer and N. W. K. Chiu, *Can. J. Chem.*, **46**, 2217 (1968).

17 is but a minor product from **23**; thus, the cis compounds like **29** or **30** are probably not involved to any substantial extent in the pyrolyses of **23–25** (Table III). Further, unknown 1, the presumed trienic ester, which appears to be formed *via* **30** from **29** is not a product in the pyrolyses of **23–25**.

Stability of 16–19 under the Pyrolysis Conditions. In order to determine the stability of the products from pyrolysis of the dimethylcarbethoxyspiropentanes, the four 2,3-dimethylcarbethoxymethylenecyclobutanes were pyrolyzed under the same conditions as the spiropentanes. Cis–trans isomerization was observed in the absence of much syn–anti isomerization, presumably *via* a diradical species such as **32**,[11] resulting from C_2–C_3



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cleavage. Restricted rotation within the allyl radical system would prevent carbethoxy group syn–anti isomerization.

Important for consideration is the rate with which the cyclobutane products interconvert relative to the rate at which they are produced. In the flow system at 385°, the conditions under which the 4,5-dimethyl compounds **20–22** rearranged to the extent of *ca.* 20%, the trans cyclobutane products **16** and **17** each gave approximately 10% of the cis materials **18** and **19**, respectively. The usual calculation of the relative amounts of primary and subsequent product in sequential first-order reactions[18] reveals that a negligible amount of cis compounds **18** and **19** could be formed from the trans products **16** and **17** in the pyrolysis of **21** and **22** at 20% conversion (Table III). However, in the pyrolysis of **20** a rather substantial portion of the trans product at 20% conversion derived from the cis product, since the cis products **18** and **19** rearrange to **16** and **17**, respectively, at least 5 and 3.5 times as fast, respectively, as **18** and **19** are produced from **20**. An exact calculation is difficult because of the number of pathways and reversibility, particularly in the case of the **18** → **16** and the **19** → **17** conversions, but a rough estimate is that the initial ratio of cis products (**18** and **19**) to trans products (**16** and **17**) from *cis,anti*-4,5-dimethylcarbethoxyspiropentane (**20**) is about 5:1.

This also implies that the trans:cis ratio from **21** and **22** is not as high kinetically as the product ratio would indicate.

There should be little concern about complications due to product interconversion in the pyrolyses of the 2,4-dimethylcarbethoxyspiropentanes (**23–25**), since these pyrolyses were conducted not only at lower temperatures but also for less than 10% conversion where product interconversion should be minimal. At any rate, the distribution of the 2,3-dimethylcyclobutane esters **16–19** from **23–25** at low conversions (Table III) represents a minimum value for the stereospecificity of the carbethoxyspiropentane to carbethoxymethylenecyclobutane thermal isomerization.

Pyrolyses of 20 and 21 in Benzene and Acetonitrile Solutions. Finally, in an attempt to investigate the effect of a polar medium on the carbethoxyspiropentane rearrangement, 4,5-dimethyl compounds **20** and **21** were pyrolyzed in benzene and acetonitrile solutions at 290° for 1 hr. The trans compound **21** rearranged at about the same rate in benzene and acetonitrile; the cis compound **20** rearranged only about 20% faster in acetonitrile. The products were the same as those observed in flow pyrolyses. Thus, there appears to be little polar character in the rate-determining transition state.

(18) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1953, pp 153–155.

Discussion

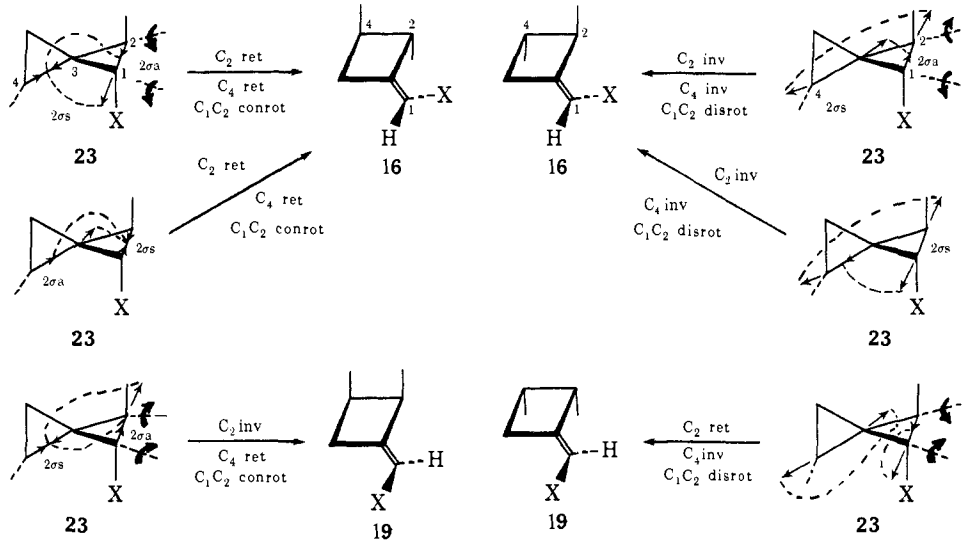
Concertion in the Rearrangement–Orbital Symmetry and Least Motion Control. The distribution of products observed in the pyrolysis of the dimethylcarbethoxyspiropentanes in which each compound gave one or more products in preference to the others is an indication that the reaction is at least partially concerted. There are eight possible orbital symmetry allowed σ 2s + σ 2a pathways[16] for this rearrangement, four of which give prediction of experimentally discernible possibilities at each center; thus only two different products as enantiomeric pairs can result *via* a concerted process for each compound, **23**, **24**, and **25**. Inversion at C_2 and inversion at C_4 (I–I) in the case of **23** gives the opposite enantiomer of **16** that should be produced by retention at C_2 and C_4 (R–R). Similarly, retention at C_2 with inversion at C_4 (R–I) and inversion at C_2 with retention at C_4 (I–R) gives the two enantiomers of **19** (Scheme I).

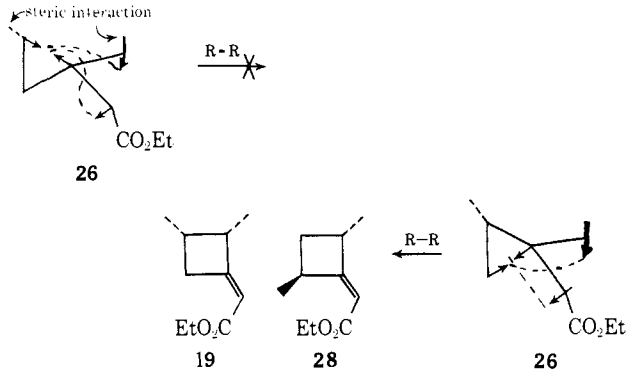
Inspection of the pyrolysis data shows that compound **16** derived by the R–R and I–I pathways was the major product in the rearrangement of **23** and that compound **19** was formed only to a small extent. A similar analysis of orbital symmetry allowed pathways for **24** and **25** results in the prediction of **17** and **18**, respectively, as the products from R–R and I–I pathways, and **18** and **17**, respectively, as products from R–I and I–R pathways. The major products from the pyrolysis of **24** and **25** are those predicted by the R–R and I–I processes. The I–I pathway is probably not important in the reaction, in view of the predominance of retention of configuration in the migrating carbon in the pyrolysis of 4,5-dimethylspiropentanes (Table II).

The experimental results from the pyrolysis of **26** can also be rationalized in terms of orbital symmetry conservation in which rearrangement to **19** is not observed but instead the C_5 methylene group migrated to give **28**. The reason for this change in migrating carbons is undoubtedly the steric interaction between the two methyl groups in the C_3–C_4 bond-breaking pathway leading to **19**. In **25**, the other compound in the series which gives a cis cyclobutane ester, the methyl–methyl interaction is probably not felt until after the C_2–C_4 bond begins to form, assuming that C_1–C_2 bond fission begins before C_3–C_4 bond fission. Even with **25**, the methyl–methyl interaction is strong enough to give more trans product than could be explained by the cis cyclobutane compound, **18**, subsequently rearranging to **16**. The methyl–methyl interaction apparently is more immediate in **26** causing the unsubstituted methylene group to migrate.

Thus, of the various orbital symmetry controlled processes only one is traversed to a major extent, and

Scheme I

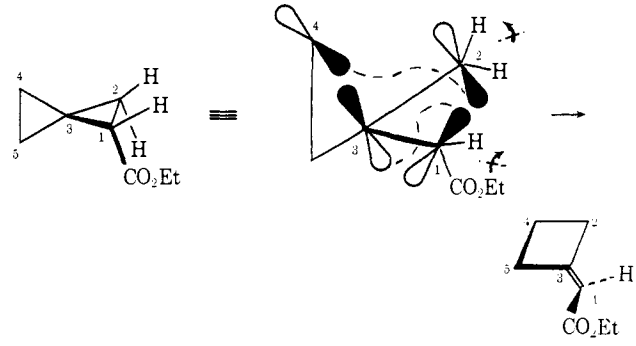




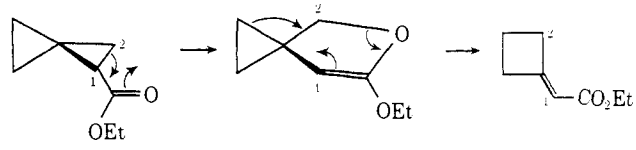
it is the one possibly involving the least motion of reacting centers. Indeed, in the starting material, the C_3–C_4 bond can easily interact with the C_1–C_2 bond with a minimum amount of molecular distortion resulting in the R–R pathway. It is essential to note that the direction of rotation of the carbethoxy group is an important component of the reaction and, in the absence of orbital symmetry control, it could end up either syn or anti to what was originally C_2. The fact that in the pyrolysis of **23**, **16**, a syn cyclobutane ester, is produced while in the pyrolysis of **24**, **17**, a anticyclobutane ester, is the major product, indicates that a random or least motion swing of the carbethoxy group does not occur. In every case, the carbethoxy group swings predominantly in the direction predicted by conservation orbital symmetry.

The observed results summarized in Table III clearly indicate that the reactions are not highly concerted. Even at very low conversions, the ratio of the orbital-symmetry-least-motion controlled product to the rest of the cyclobutane product varied between only 1.7 and 4.8. Thus, the reaction appears to have an appreciable nonconcerted component.

Finally, it should be noted that the Möbius–Hückel formulation of Zimmerman[19] can likewise be used to predict the results of the spiropentane pyrolyses. Since the ground-state rearrangement involves four electrons it must proceed through a Möbius transition state, *i.e.*, one with an odd number of negative overlaps of basis set orbitals. The basis set orbital array depicted below shows conrotatory breaking of the C_1–C_2 bond and retention of configuration at C_2 and C_4 which corresponds to the major stereochemical pathway.



Alternatives to Explain the Stereospecificity. Other mechanistic possibilities could be considered for the rearrangement of carbethoxyspiropentanes. One possible alternative is an analog of the vinylcyclopropane rearrangement with subsequent isomerization of the intermediate oxaspiroheptene.[20] This mechanism predicts that the carbethoxy group should always be syn to C_2 of the original spiropentane system. This was not the experimental result with **24** which gave predominantly **17**, an anti ester.



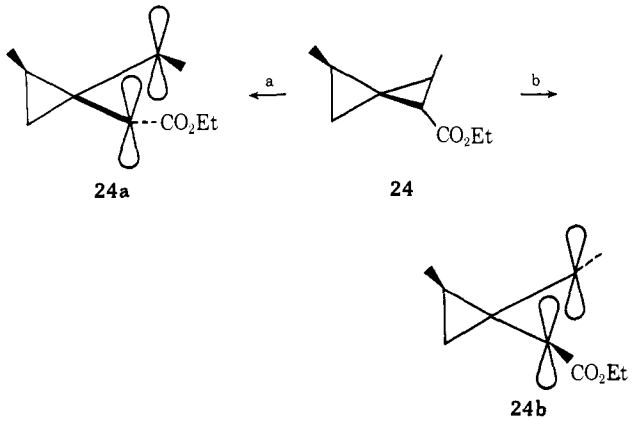
One other possible alternative mechanism is the opening of the carbethoxy-substituted cyclopropane to a π-cyclopropane[21] followed by rapid alkyl migration to give cyclobutane products. Opening of cyclopropane to π-cyclopropane was suggested from E–H calculations of Hoffmann and was predicted to be formed

(19) H. E. Zimmerman, *Accounts Chem. Res.*, **4**, 272 (1971).

(20) Rearrangements of this sort are known. Cyclopropanecarboxaldehyde isomerizes to dihydrofuran: C. L. Wilson, *J. Amer. Chem. Soc.*, **69**, 3002 (1947).

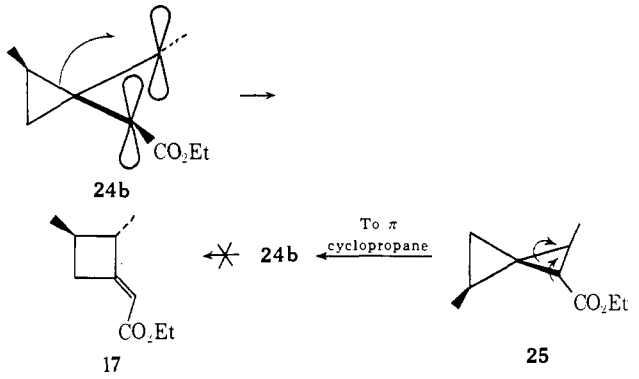
(21) R. Hoffmann, *ibid.*, **90**, 1475 (1968).

via a conrotatory opening.[21] Thus, from **24**, for example, two possible π-cyclopropanes can result from conrotatory openings. Path a is unlikely due to the



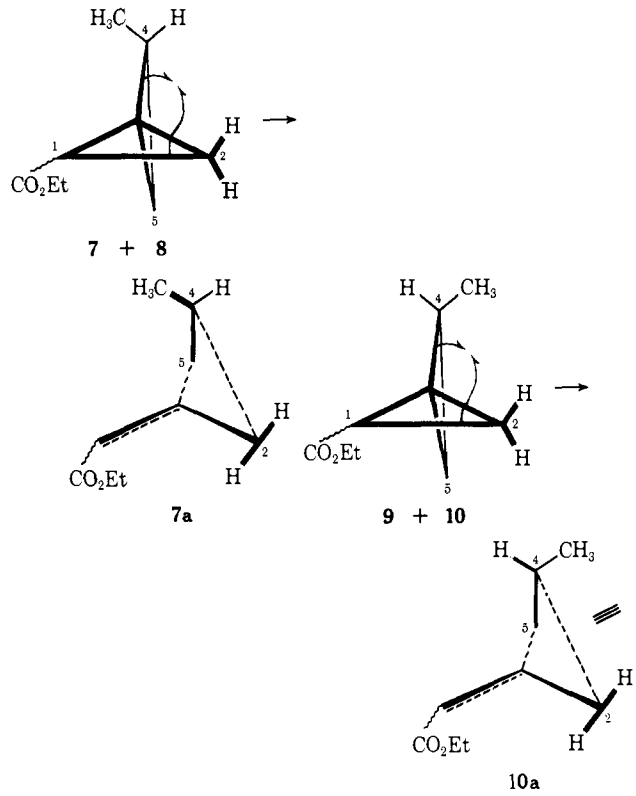
24a **24** **24b**

steric interaction of the carbethoxy group and the methyl group; only path b would be expected to be followed to any great extent. Product formation from **24b** (assuming retention in the migration and attack at the nearest lobe of C_2) would produce **17**, which is indeed the major product. Unfortunately, this mechanism also predicts **17** to be the major product from **25** which is not the case, and predicts that an *anti*-carbethoxymethylene compound should be the major product from all three compounds, **23**, **24**, and **25**. This is not the observed fact. Thus, it would appear that the π-cyclopropane is not an intermediate on the reaction pathway unless the methylcarbethoxy steric interaction is not as great as molecular models would suggest.



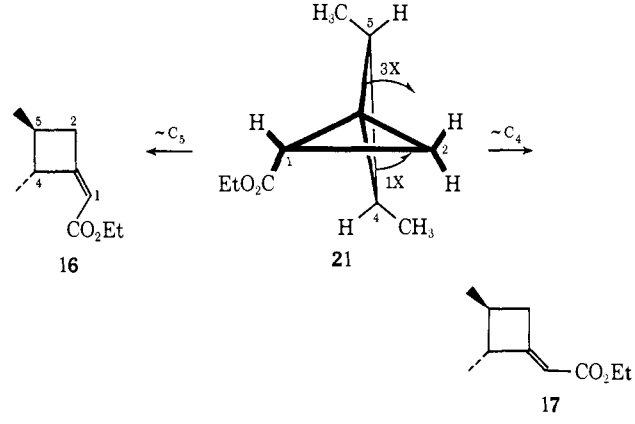
17 **25**

Steric Effects in the Migration. Examination of the results from pyrolysis of the 4-methylcarbethoxyspiropentanes in relation to the orbital symmetry-allowed R–R pathway allows an explanation of the facts that compounds **9** and **10** give substantial amounts of **13** (20% of product) which is the result of C_5 migration instead of C_4, whereas **7** and **8** give little **13** (6% of product, Table I). Examination of models reveals that isomerization of **7** and **8** to **12** should be relatively smooth (*via* **7a**) *via* the R–R pathway but that a bad steric interaction develops between the hydrogen on C_2 and the methyl group as the rearrangement proceeds in **9** and **10** (*via* **10a**). This interaction is increased to the extent that C_1–C_2 bond fission leads to C_3–C_4 bond fission, thus forcing the C_2 methylene group further into the methyl group at C_4 in **10a**. Thus, the less favorable migration of an unsubstituted methylene group becomes competitive with the migration of a

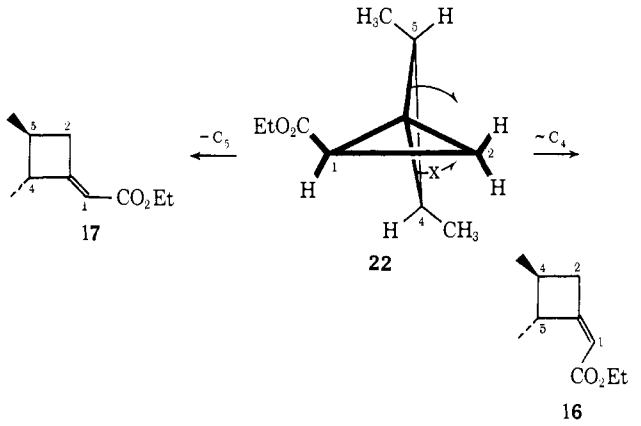


substituted one. Since the overall pathway for rearrangement of **9** and **10** is of higher energy than for **7** and **8**, it is not surprising that **9** and **10** undergo more epimerization than **7** and **8**.

This same steric effect must play a role in the distribution of products from the *trans*-4,5-dimethylcarbethoxyspiropentanes (**21** and **22**). The R–R pathway predicts that both *trans*-dimethylcyclobutane compounds (**16** and **17**) should be produced from both **21** and **22** depending upon which carbon group migrates. However, examination of the pyrolysis data reveals that **21** and **22** do not behave similarly. Migration of C_4 in **21** with retention to form **17** should result in the same sort of bad steric interaction as found in the **10** → **10a** reaction. Thus, **17** is but a minor product from pyrolysis of **21**.



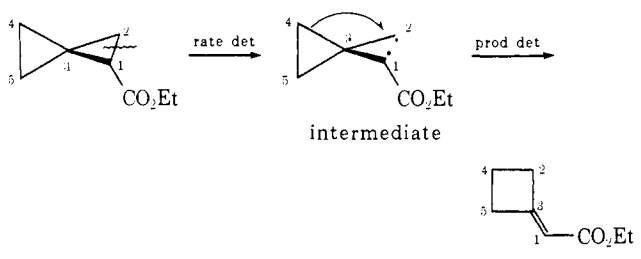
Finally, pyrolysis of the *trans*-4,5-dimethyl compound **22** gives almost exclusively the *trans*-dimethyl-*syn*-cyclobutane ester **17**, a result also consistent with steric effects. By migration of C_5 to C_2, **17** should be and is produced but by C_4 migration the carbethoxy group on C_1 must pass by the methyl on C_5 to give **16**, which is barely detectable as a product.



Different Rate- and Product-Controlling Steps. Methyl substitution on the 2 carbon influences the rate of isomerization in a positive sense; *i.e.*, 2-methyl substitution appears to cause faster reaction if analogous compounds are compared. It is not clear what effect the methyl groups on C_4 or C_5 should have on the rate of reaction. But, in fact, the rate of rearrangement of the 4-substituted compounds varies from only 0.5 to twice the rate for carbethoxyspiropentane (**3**). Part of this difference can be explained in terms of a rate retardation for **9** and **10** due to steric hindrance as discussed previously. It is crucial, however, to explain the fact that the methyl-substituted carbon in **7** and **8** migrates 16 times faster than the unsubstituted methylene. If the product-determining step and the rate-determining step are the same, it would seem that **7** and **8** should rearrange 16 times as fast as **3**, since migration of an unsubstituted methylene group in **7**–**10** should be as fast as migration of a methylene group in **3**. Even though compounds **9** and **10** rearrange about as fast as or slower than **3**, there is still a 3:1 preference for migration of the methyl-substituted methylene.

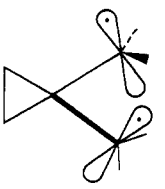
This same rate and product behavior appear with the dimethylcarbethoxyspiropentanes. The rates of rearrangement of the 4,5-dimethyl compounds **20**–**22** are practically identical with the parent compound, and while the 2,4-dimethyl compounds **23**–**26** rearrange faster than the parent owing to the 2-methyl substituent, migration of the more highly substituted carbon (C_4) is dramatically favored over C_5 migration except when overwhelming steric effects prevent it as with **26**.

The rate and product data can be interpreted as resulting from a two-step reaction in which the first step (C_1–C_2 bond fission) is rate determining and the second step (C_3–C_4 fission) is product determining.[22,23]



Unless very subtle or unknown factors are operating in this rearrangement, a single-step pathway would have to reflect the preference for substituted methylene migration in an increased rate of the reaction for **7**–**10** and **20**–**22** compared with that of the parent compound, **3**. Lastly, if the rearrangement is a two-step one, then the origin of the stereospecificity must be rationalized if not explained in terms of likely intermediates.

Intermediate in the Spiropentane Isomerization. The stereochemical course of spiropentane isomerization can be explained as a stereospecific rearrangement to an intermediate followed by stereospecific rearrangement to product. Two such intermediates, π-cyclopropane and oxaspiroheptene, have been considered previously and ruled out. Another possible intermediate is an orthogonal biscyclopropylcarbinyl diradical such as **32**, analogous to the orthogonal trimethylenemethane diradical postulated to occur in methylenecyclopropane isomerizations.[24] However,



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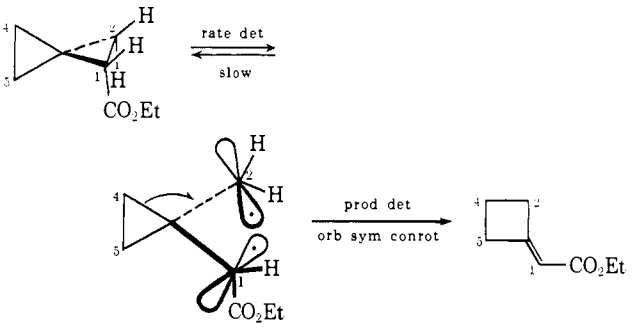
there appears to be no consistent set of motions for formation and rearrangement of **32** to give the products observed from the 2,4-dimethylcarbethoxyspiropentane pyrolyses.

Finally, a possible intermediate is **33** in which the C_1–C_2 bond is broken without rotation. This species



33

can explain the observed results if (1) rotation about bonds in the diradical is relatively slow with respect to rearrangement (at least in the case of the mono- and dimethylcarbethoxyspiropentanes which is borne out in fact); (2) ring closure back to starting material has an activation energy due to ring strain, eclipsing of substituents, or other sources; and (3) there is enough interaction between the orbitals to provide the necessary cyclic array of orbitals interacting in the rearrangement step to give rise to the orbital symmetry controlled stereospecificity. Bergman has indicated that a stretched cyclopropane may be an energy minimum on the pathway responsible for the racemization of optically active 1-methyl-2-ethylcyclopropane,[6] where the rate of rotation was found to be three or four times the rate of cyclization. The rotation of C_1 and C_2 of the spiropentanes in the present investigation may

(22) M. C. Flowers and A. R. Gibbons, *J. Chem. Soc., Perkin Trans. 2*, 545, 555 (1972), have apparently arrived at the same conclusion as a result of application of RRKM calculations on the spiropentane thermolysis at low pressures.

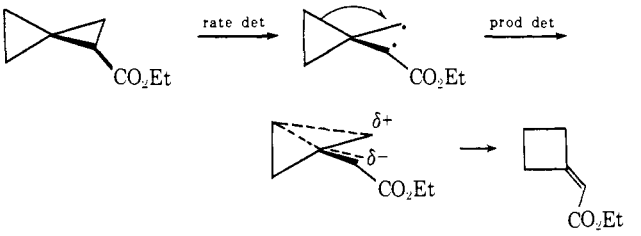
(23) For a similar analysis in allene dimerizations, see W. R. Dolbier, Jr., and S.-H. Dai, *J. Amer. Chem. Soc.*, **92**, 1774 (1970).

(24) J. J. Gajewski, *ibid.*, **93**, 4450 (1971).

be hindered by substituents on C_4 and C_5 allowing rearrangement to take place without much epimerization; examination of models indicates this may be so. The experimental results then can be explained by rate determining formation of **33** which undergoes a concerted rearrangement to methylenecyclobutane products. This second step may be concerted since the p orbitals in the bis-orthogonal biradical **33** may still interact sufficiently to allow electron interaction and subsequent atomic motions appropriate to an orbital symmetry controlled pathway.

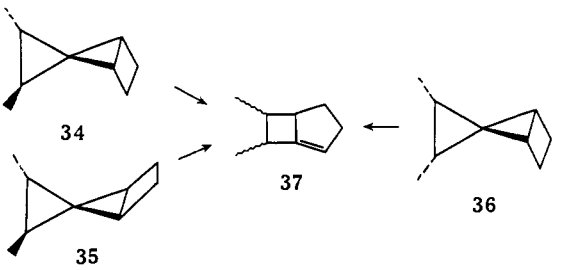
Energy Surface for the Spiropentane Isomerization. The kinetic and stereochemical results for the isomerization of carbethoxyspiropentane require a two-step pathway with partial stereospecificity. Further, the discussion above focuses on an intermediate with a stretched bond. If this formulation is correct, then strongly implied is the suggestion that stretching of a spiropentane bond (or perhaps even a cyclopropane bond) is described by a potential function with secondary minimum at *ca.* 2.2 Å. This suggestion is consistent with Benson's approximate thermodynamic kinetic estimates for the potential surface.[7] Thus, in a simple way, Benson would calculate $\Delta\Delta H_f$ between spiropentane and the biradical as being 54.8 kcal/mol (the enthalpy difference between cyclopropane and the trimethylene biradical) minus 8 kcal/mol (the extra strain in spiropentane over two cyclopropanes which is relieved upon opening[11]) equals 46.8 kcal/mol. The activation energy for ring opening of the spiropentane as measured by geometric isomerization is 51.5 kcal/mol.[9] Therefore, there is calculated a 4.7-kcal/mol barrier for reclosure of the 1,1-cyclopropyl biscarbinyl biradical back to spiropentane and an 8.7-kcal/mol barrier for subsequent rearrangement of the biradical to methylenecyclobutane since the activation energy for the structural rearrangement of spiropentane is 55.5 kcal/mol.[13] Placement of a carbethoxy group on the spiropentane system obviously alters these relationships by lowering the activation energy for ring opening by the value of the keto radical resonance energy and by lowering to an even greater extent the activation energy for rearrangement since carbethoxyspiropentane structural rearrangement is more facile than geometric isomerization. However, the carbethoxy group should not much alter the activation energy for reclosure of the biradical back to carbethoxyspiropentane, as all of Benson's calculations would suggest.[7] Thus, a potential energy minimum in the rearrangement studied here was predicted by Benson.

Comparison of Carbethoxyspiropentane to the Parent System. Polar Effects. Why do carbethoxy-substituted spiropentanes undergo rearrangement faster than epimerization whereas methyl and deuterium substituted systems undergo epimerization much faster than rearrangement? The suggestion is made that the second step of the reaction may be partly dipolar in nature so as to resemble the ring expansion of the cyclopropylcarbinyl cation to form the cyclobutyl system,[25] a rearrangement well known for its facility and one which occurs with retention at the migrating carbon.[26] The electron-withdrawing ester function

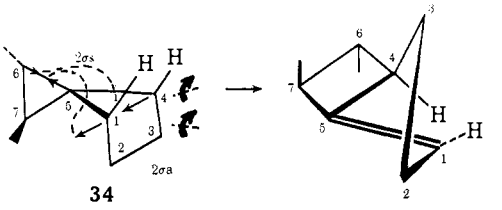


facilitates charge polarization and possible rearrangement. It is not without interest that highly polar solvents do not enhance the rate of the rearrangement, a result also consistent with a two-step process with the first being relatively nonpolar and rate determining and the second being a dipolar, product-determining step.

Finally, it should be noted that Roth[27] examined the stereochemical outcome of the migrating carbon in a spiropentane rearrangement confined to a bicyclic system and found little stereospecificity. Thus, pyrolysis of **34**, **35**, and **36** gave all possible isomers of **37**



in comparable amounts. These results are not inconsistent with those reported here since Roth's compounds are sterically prohibited from rearranging in the stereochemical sense found with carbethoxyspiropentane. Thus, by the $2\sigma s$ and $2\sigma a$ (R–R) pathway, compound **34** must give the bicyclic olefin with a "trans" double bond, and the same is true of **35**–**36**. It is no wonder then that a nonconcerted reaction was observed here.



Conclusion

Placing a carbethoxy group on the spiropentane system alters the usual geometric/structural isomerization rate ratio in the hydrocarbon case to favor structural isomerization. The lack of rate effect by C_4 methyl substitution but dramatic preference for methyl-substituted carbon migration is consistent with a two-step reaction *via* a potential energy minimum as predicted by Bensonian thermodynamic estimates.[7] Partial stereospecificity in the reaction is consistent with overall orbital symmetry control, *via* a biradical intermediate that has a stretched C_1–C_2 bond with no rotation of the groups comprising the bond relative to starting material.

To the extent that the spiropentane system resembles

(25) For review see R. Breslow in "Molecular Rearrangements," Vol. I, P. DeMayo, Ed., Interscience, New York, N. Y., 1962.

(26) Z. Majerski and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **93**, 665 (1971).

(27) W. R. Roth and K. Enderer, *Justus Liebigs Ann. Chem.*, 733, 44 (1970).

the cyclopropane one, similar conclusions are at odds with recent quantum chemical calculations.[8] Therefore an appropriate study of the latter system is in order.

Experimental Section

General. Nuclear magnetic resonance spectra were recorded on Varian A-60, HA-100, and HR-220 spectrometers. Carbon tetrachloride was used as solvent with TMS as internal standard; chemical shifts are reported as δ values in ppm relative to TMS. Infrared spectra were obtained with a Perkin-Elmer Model 621 spectrophotometer using 0.5 to 5% solutions in carbon tetrachloride. Vapor phase chromatography was performed on Varian Aerograph A90P-3 and Series 1220-2 (capillary) instruments using the following columns: 20 ft × 0.38 in. 25% UCON, 50 HB 2000 Polar on 60–80 Chromosorb W (UCON); 12 ft × 0.25 in. 20% tris(cyanoethoxy)-propane on 60–80 Chromosorb W (TCEP); 5 ft × 0.25 in. 30% SE-30 on 60–80 Chromosorb W (SE-30); 250 ft × 0.01 in. i.d. UCON 50 HB 2000 Polar (UCON capillary); and 200 ft × 0.10 in. i.d. TCEP (TCEP capillary). Operating temperature and helium flow rate or pressure are given in parentheses after the column. High resolution mass spectra were recorded on an A.E.I. Model MS-9.

Flow pyrolyses were carried out in a Chemical Data Systems Model 1100 Pyrochrom used in conjunction with capillary glpc. Integration of the glpc signal was performed by a Vidar Model 6210 digital integrator. Materials used in the pyrolyses were at least 98% homogeneous by capillary glpc, and were passed through a 5 ft × 0.25 in. 20% SE-30 column immediately prior to use. The results of the pyrolyses are reported in Tables I–III.

Preparative Pyrolysis of Carbethoxyspiropentane (3). Carbethoxyspiropentane[10] (40 μl) was sealed in a carefully neutralized 100-ml Pyrex tube and heated at 310° for 10 hr. After this time 98% of the starting material had disappeared giving one major product (83%) and two minor products (13 and 1%). The major component of the mixture, carbethoxymethylenecyclobutane (**4**), was isolated using the SE-30 column (120°, 100 ml/min): ir 2975, etc., 1715, 1675, 1442, 1388, 1365, 1332, 1260, 1235, 1218, 1170, 1082, 1034, 960, 930, and 845 cm^{-1}; nmr (220 MHz) δ 1.22 (t, J = 7 Hz, 3 H), 2.09 (p, J = 7 Hz, 2 H), 2.75 (triplet with fine structure, 2 H), 3.08 (triplet with fine structure, 2 H), 4.03 (q, J = 7 Hz, 2 H), and 5.43 (m, 1 H); m/e 140.0839 (calcd for $C_8H_{12}O_2$, 140.0837).

2-Methylenecarbethoxycyclobutane (5). 2-Methylenecyclobutanecarboxylic acid was prepared as described previously[28] and esterified using ethanol and p-toluenesulfonic acid: ir 3078, 2980, etc., 1735, 1670, 1440, 1365, 1315, 1248, 1186, 1160, 1042, and 885 cm^{-1}; nmr (220 MHz) δ 1.26 (t, J = 7 Hz, 3 H), 1.98–2.16 (m centered at 2.08, 1 H), 2.26–2.43 (m centered at 2.34 similar to multiplet at 2.08, 1 H), 2.66 (m, 2 H), 3.65 (m, 1 H), 4.11 (m, 2 H), 4.77 (q, J = 3 Hz, 1 H), and 4.93 (q, J = 3 Hz, 1 H); m/e 140.0847 (calcd for $C_8H_{12}O_2$, 140.0837).

3-Methylenecarbethoxycyclobutane (6). Several alkylidenecarbethoxycyclobutanes were prepared from the corresponding nitriles;[29] a typical procedure is given for the preparation of **6**. 3-Methylenecyclobutanecarbonitrile (300 mg) was heated at 100° with 5 ml of 7% potassium hydroxide for 2.5 hr. After this time the aqueous solution was washed with ether, acidified, and again extracted with ether. The crude acid obtained by removal of solvent was esterified using ethanol with boron trifluoride etherate as a catalyst. The crude ester was purified using the SE-30 column (110°, 100 ml/min); 150 mg of ester was obtained: ir 3075, 2977, 2925, 1730, 1675, 1472, 1460, 1440, 1405, 1385, 1365, 1430, 1260, 1220, 1178, 1090, 1050, and 875 cm^{-1}; nmr (220 MHz) δ 1.25 (t, J = 7 Hz, 3 H), 2.70–3.10 (m, 5 H), 4.06 (q, J = 7 Hz, 2 H), and 5.19 (m, 2 H); m/e 140,0833 (calcd for $C_8H_{12}O_2$, 140.00837).

3-Ethylidenecarbethoxycyclobutane (14). From 300 mg of 3-ethylidenecyclobutanecarbonitrile[29] there was obtained 230 mg of 3-ethylidenecarbethoxycyclobutane (**14**): ir 2972, etc., 1730, 1447, 1365, 1335, 1255, 1215, 1127, 1090, 1042, 950, and 845 cm^{-1}; nmr (60 MHz) δ 1.10–1.65 (t, J = 7 Hz, at 1.25 partially superimposed on a multiplet centered at 1.50, 6 H), 2.90 (m, 5 H), 4.15 (q, J = 7 Hz, 2 H), and 5.20 (m, 1 H); m/e 154.1001 (calcd for $C_9H_{14}O_2$, 154.0994).

***trans*-2-Methyl-3-methylenecarbethoxycyclobutane (15).** *trans*-2-Methyl-3-methylenecyclobutanecarbonitrile[29] (80 mg) was treated as described above to yield about 50 mg of ester: ir 3070, 2955, etc., 1728, 1672, 1440, 1365, 1340, 1307, 1250, 1227, 1158, 1090, 1035, and 870 cm^{-1}; nmr (100 MHz) δ 1.16 (d, J = 7 Hz) superimposed on a triplet, J = 7 Hz, at 1.22, total of 6 H, 2.40–3.30 (m, 4 H), 4.07 (q, J = 7 Hz, 2 H), and 4.71 (m, 2 H); m/e 154.1001 (calcd for $C_9H_{14}O_2$, 154.0994).

Preparative Pyrolysis of *distal*-4-Methylcarbethoxyspiropentane (10). The ester[10] (100 μl) was sealed in a neutralized, evacuated 100-ml Pyrex tube and heated at 325° for 90 min. After this time the starting material had completely disappeared giving one major component (*ca.* 30%) and numerous lesser components. The major component was isolated using the UCON column (150°, 200 ml/min) and was identified by its spectral characteristics as 3-methylcarbethoxymethylenecyclobutane (**12**): ir 2950, etc., 1712, 1675, 1445, 1365, 1332, 1260, 1217, 1183, 1081, 1031, and 850 cm^{-1}; nmr (220 MHz) δ 1.19 (d, J = 7 Hz), 1.28 (t, J = 7 Hz), total of 6 H, 2.25–2.70 (m, 3 H), 2.85–3.00 (multiplet centered at 2.92, 1 H), 3.15–3.35 (multiplet centered at 3.27, 1 H), 4.05 (q, J = 7 Hz, 2 H), and 5.48 (p, J = 2 Hz, 1 H); m/e 154.1000 (calcd for $C_9H_{14}O_2$, 154.0994).

One of the minor components (*ca.* 10%) could be isolated cleanly using the UCON column and was identified as 2-methyl-4-methylenecarbethoxycyclobutane (**11**): ir 3075, 2958, etc., 1735, 1672, 1448, 1365, 1300, 1237, 1170, 1155, 1032, and 880 cm^{-1}; nmr (220 MHz) δ 1.20 (d, J = 6 Hz), 1.26 (t, J = 7 Hz), total of 6 H, 2.20 (m, 1 H), 2.72 (m, 2 H), 3.16 (m, 1 H), 4.10 (m, 2 H), 4.76 (q, J = 3 Hz, 1 H), and 4.93 (q, J = 3 Hz, 1 H); m/e 154.1000 (calcd for $C_9H_{14}O_2$, 154.0994).

2-Methylcarbethoxymethylenecyclobutane (13). 2-Methylcyclobutanone was prepared as described by Hanack and Herterich.[30] The ketone (120 mg, 1.43 mmol) was added to the sodium salt of triethyl phosphonoacetate [31 mg (1.29 mmol) of sodium hydride and 270 mg (120 mmol) of triethylphosphonium acetate] in 3 ml of freshly distilled dimethoxyethane.[15] The mixture was stirred at 50° for 1 hr, poured into 10 ml of water, and extracted with ether. The residue obtained after drying and removing the ether contained two components in the ratio 1:6 which could be separated using the UCON column (175°, 150 ml/min).

The major component was identified as 2-methyl-*anti*-carbethoxymethylenecyclobutane: ir 2970, etc., 1712, 1665, 1442, 1363, 1330, 1255, 1232, 1220, 1170, 1090, 1035, 940, and 845 cm^{-1}; nmr (220 MHz) δ 1.17 (d, J = 7 Hz), 1.24 (t, J = 7 Hz), total of 6 H, 1.64 (m, 1 H), 2.24 (m, 1 H), 2.80–3.20 (m, 3 H), 4.05 (q, J = 7 Hz, 2 H), and 5.44 (q, J = 2 Hz, 1 H); m/e 154.1001 (calcd for $C_9H_{14}O_2$, 154.0994).

The minor component was identified as 2-methyl-*syn*-carbethoxymethylenecyclobutane: ir 2975, etc., 1712, 1666, 1450, 1363, 1330, 1285, 1255, 1235, 1185, 1193, 1090, 1033, and 840 cm^{-1}; nmr (220 MHz) δ 1.24 (t, J = 7 Hz), 1.31 (d, J = 7 Hz), total of 6 H, 1.62 (7-line multiplet, 1 H), 2.27 (m, 1 H), 2.55–2.74 (m, 1 H), 2.78–3.00 (m, 1 H), 3.30–3.55 (m, 1 H), 4.06 (q, J = 7 Hz, 2 H), and 5.42 (q, J = 7 Hz, 1 H); m/e 154.1001 (calcd for $C_9H_{14}O_2$, 154.0994).

***cis*- and *trans*-2,3-Dimethylcyclobutanone.** The ketones were prepared by a method similar to that of Turro and McDaniels.[14,31] Triethylamine (28 g, 0.28 mol) was added over a 3-hr period to a stirred solution of 48 g (0.25 mol) of dichloroacetyl bromide and 24 g (0.43 mol) of *cis*- and *trans*-2-butene in 250 ml of hexane. After stirring overnight the mixture was filtered, washed with ether, and dried with magnesium sulfate. The residue obtained by removal of solvent was distilled under reduced pressure to give 14 g of material, bp 55–65° (1.5 Torr). Granular zinc (20 g) was added in small portions to a solution of the dichloro ketone (10 g) in 50 ml of acetic acid. After addition of the zinc the mixture was stirred for 2 hr, filtered, added to 100 ml of water, and extracted with pentane. The pentane solution was washed with sodium bicarbonate and dried, and the solvent was removed by distillation. The residue contained two compounds in the ratio 1:2 according to glpc. Treatment of a portion of this mixture with sodium methoxide in methanol reversed this ratio to 3:1. The mixture was separated preparatively using the TCEP column (135°, 120 ml/min). Nmr spectra of the pure compounds agree with those reported[14] for *trans*- and *cis*-2,3-dimethylcyclobutanone; the trans compound was the minor component in the original mixture.

***trans*-2,3-Dimethyl-*syn*- and -*anti*-carbethoxymethylenecyclobutane (16 and 17).** *trans*-2,3-Dimethylcyclobutanone (100 mg) was added to the sodium salt of triethylphosphonium acetate as described

(28) J. J. Gajewski, *J. Amer. Chem. Soc.*, **92**, 3688 (1970).

(29) Generous samples of these compounds were kindly supplied by Dr. Allan Cairncross at E. I. DuPont de Nemours and Co.

(30) M. Hanack and I. Herterich, *Tetrahedron Lett.*, 3847 (1969).

(31) N. J. Turro and D. M. McDaniels, private communication.

above to give two esters in the ratio 1:5. Those were separated using the UCON column (140°, 150 ml/min).

The minor product was identified as *trans*-2,3-dimethyl-*syn*-carbethoxymethylenecyclobutane (**16**): ir 2950, etc., 1715, 1673, 1453, 1365, 1335, 1326, 1260, 1235, 1217, 1181, 1115, 1093, 1032, 960, 860, and 830 cm^{-1}; nmr (220 MHz) δ 1.16 (d, J = 7 Hz, 3 H), 1.24, triplet (J = 7 Hz) superimposed on a doublet (J = 7 Hz) at 1.28, total of 6 H, 1.90–2.10 (m, 1 H), 2.12–2.25 (symmetrical multiplet centered at 2.18, 1 H), 2.80–3.05 (m, 2 H), 4.05 (q, J = 7 Hz, 2 H), and 5.48 (3-line multiplet with 2-Hz separation of lines, 1 H); *m/e* 168.1146 (calcd for $C_{10}H_{16}O_2$, 168.1150).

The major product was identified as *trans*-2,3-dimethyl-*anti*-carbethoxymethylenecyclobutane (**17**): ir 2950, etc., 1710, 1160, 1445, 1363, 1330, 1300, 1258, 1238, 1132, 1150, 1112, 1090, 1035, 950, and 847 cm^{-1}; nmr (220 MHz) δ 1.13 (d, J = 7 Hz), 1.24 (t, J = 7 Hz), total of 9 H, 1.94 (5-line multiplet with 7-Hz spacing of lines, 1 H), 2.35–2.60 (m, 2 H), 3.17–3.33 (symmetrical multiplet centered at 3.25, apparently a d of d of t with 17, 8.5, and 3-Hz spacing of lines, 1 H), 4.05 (q, J = 7 Hz, 2 H), and 5.45 (4-line multiplet with 2-Hz spacing of lines, 1 H); *m/e* 168.1146 (calcd for $C_{10}H_{16}O_2$, 168.1150).

***cis*-2,3-Dimethyl-*syn*- and -*anti*-carbethoxymethylenecyclobutane (18 and 19).** *cis*-2,3-Dimethylcyclobutanone (100 mg) was added to the sodium salt of triethylphosphonium acetate as described above to give two esters in the ratio 1:4 which were separated using the UCON column (140°, 150 ml/min).

The minor product was identified as *cis*-2,3-dimethyl-*syn*-carbethoxycyclobutane: ir 2963, etc., 1712, 1670, 1460, 1440, 1422, 1363, 1331, 1291, 1259, 1240, 1212, 1182, 1122, 1095, 1050, 1032, 1012, 960, 945, 878, and 831 cm^{-1}; nmr (220 MHz) δ 1.05 (d, J = 7 Hz, 3 H), 1.18 (d, J = 7 Hz), 1.25 (t, J = 7 Hz), total of 6 H, 2.35–2.65 (m, 2 H), 2.70–2.90 (m, 1 H), 3.40 (m, 1 H), 4.05 (q, J = 7 Hz, 2 H), and 5.44 (4-line multiplet with 2-Hz spacing, 1 H); *m/e* 168.1146 (calcd for $C_{10}H_{16}O_2$, 168.1150).

The major product was identified as *cis*-2,3-dimethyl-*anti*-carbethoxymethylenecyclobutane (**19**): ir 2955, etc., 1713, 1668, 1450, 1440, 1363, 1333, 1258, 1242, 1218, 1185, 1135, 1098, 1032, 945, and 848 cm^{-1}; nmr (220 MHz) δ 1.02, doublet, superimposed on a doublet at 1.03, total of 6 H; 1.24 (t, J = 7 Hz, 3 H), 2.40–2.70 (m, 2 H), 3.00–3.20 (multiplet which appears to be a q of d with 9- and 2.5-Hz spacing between lines, 2 H), 4.05 (q, J = 7 Hz, 2 H), and 5.48 (4-line multiplet with 2-Hz spacing, 1 H); *m/e* 168.1163 (calcd for $C_{10}H_{16}O_2$, 168.1150).

Preparative Pyrolysis of *trans*-2-Methyl-*distal*-4-methylcarbethoxyspiropentane (26). The ester (80 μl) was sealed in a neutralized 50-ml Pyrex tube and heated at 290° for 1 hr. After this time 90% of the starting material had disappeared; two major products were formed in the ratio 56:44. These were isolated by preparative glpc using the UCON column (160°, 150 ml/min).

The major component was identified from its spectral characteristics as *trans*-2,4-dimethylcarbethoxymethylenecyclobutane (**28**): ir 2960, etc., 1720, 1670, 1452, 1370, 1337, 1292, 1262, 1238, 1207, 1185, 1143, 1105, 1040, and 850 cm^{-1}; nmr (220 MHz) δ 1.13 (d, J = 7 Hz, 3 H), 1.24 (t, J = 7 Hz), and 1.30 (d, J = 7 Hz), total of 6 H, 1.82 (m, 2 H), 3.18 (broad multiplet, 1 H), 3.38 (broad multiplet, 1 H), 4.06 (q, J = 7 Hz, 2 H), and 5.44 (unsymmetrical triplet, J = 2 Hz, 1 H); *m/e* 168.1143 (calcd for $C_{10}H_{16}O_2$, 168.1150).

The minor component was identified as *cis*-2,4-dimethylcarbethoxymethylenecyclobutane (**27**): ir 2955, etc., 1717, 1667, 1440, 1363, 1332, 1278, 1260, 1222, 1178, 1095, 1030, and 847 cm^{-1}; nmr (220 MHz) δ 1.20 (d, J = 7 Hz), 1.25 (t, J = 7 Hz), and 1.31 (d, J = 7 Hz) total of 9 H, 1.78 (m, 1 H), 2.46 (q of m, J = 10 Hz, 1 H), 2.87 (broad multiplet, 1 H), 3.27 (broad multiplet, 1 H), 4.06 (q, J = 7 Hz, 2 H), and 5.48 (unsymmetrical triplet, J = 2 Hz, 1 H); *m/e* 168.1156 (calcd for $C_{10}H_{16}O_2$, 168.1150).

Pyrolysis of *cis*- and *trans*-4,5-Dimethylcarbethoxyspiropentane (29 and 21) in Solvent. Pyrolyses were carried out in sealed, neutralized 2-mm Pyrex capillary tubing; xylene was used as an internal standard (see Table IV).

Table IV. Solvent Pyrolysis of **20** and **21** at 290° for 1 hr

Compound	Solvent	% reaction
20	Benzene	58 ± 3
20	Acetonitrile	71 ± 3
21	Benzene	36 ± 3
21	Acetonitrile	40 ± 3

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Cycloamyloses as Enzyme Models. The Decarboxylation of Phenylcyanoacetate Anions

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Abstract: Decarboxylation rate constants in aqueous solution were determined for eight ortho-, meta-, and para-substituted phenylcyanoacetate anions and for the 2-phenyl-2-cyanopropionate and 6-nitrobenzisoxazole-3-carboxylate anions in the presence and in the absence of cycloheptaamylose. The decarboxylation rate constants of four para-substituted phenylcyanoacetate anions were determined in ethanol. In addition, 4-chlorophenylcyanoacetate decarboxylation was examined in methanol, 2-propanol, dioxane, and aqueous 2-propanol and the pH–rate profile was determined for the aqueous reaction in the presence and absence of cycloheptaamylose. Activation parameters were determined for the aqueous, cycloheptaamylose-accelerated, and aqueous 2-propanol decarboxylations of the 4-chlorophenylcyanoacetate anion. All data were consistent with cycloheptaamylose catalysis arising from the solvation change experienced by the carboxylate anion on transfer from an aqueous environment to the cycloheptaamylose complex. The interrelationships among structure, binding constant, and reactivity for the cycloheptaamylose-accelerated reactions were examined and implications for binding and reactivity in enzymatic systems were discussed.

Apolar interactions are considered a major driving force for the binding of small molecules to proteins.[2,3] Supporting evidence includes, for example, the correlation between binding free energy and surface

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