Acyl Rearrangements in Radical Reactions

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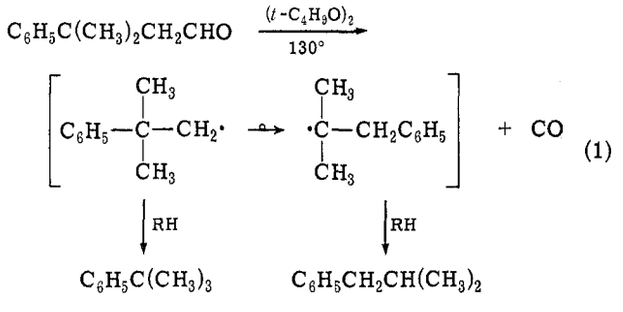
Solutions of the *tert*-butyl perlevulinate esters Ia,b,c undergo thermal decomposition (131°) *via* radical intermediates. The latter two peresters give some unrearranged *tert*-butyl ethers, but the remaining products are exclusively derived from acyl rearranged radicals (*e.g.*, methyl isobutyl ketone from Ib and 4-phenyl-2-pentanone, 4-phenyl-3-penten-2-one, and 4-phenyl-4-penten-2-one from Ic). No phenyl rearranged products (<1%) are found among the decomposition products from Ic, which also include rearranged dimeric diketones. Rearrangement during the decomposition of deuterium-labeled Ia was assessed at *ca.* 10%; thus substituents at the migration origin seem to provide a driving force for the 1,2-acyl shift. Reaction of 4-bromo-3,3-dimethyl-2-butanone (VIII) with triphenyltin hydride gave chiefly the unrearranged ketone pinacolone along with 3–5% of methyl isobutyl ketone. Slightly more rearrangement was observed with the corresponding chloride. The merits of a cyclopropoxy radical intermediate or transition state for these rearrangements are discussed.

Although examples of intramolecular 1,2 shifts of adjacent substituents to cationic sites are well documented,[1a-f] corresponding rearrangements to radical sites[2] are less common.[1g] In particular, no unambiguous cases of concerted hydrogen or alkyl shifts in 1,2-radical rearrangements have been observed,[3] in contrast with the facile rearrangement of these groups in carbonium ions.

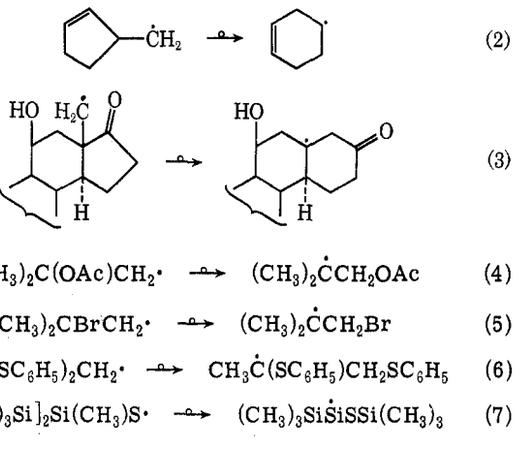
On the other hand, numerous examples of 1,2 shifts of aryl groups to radical sites have been reported,[4] beginning with Winstein and Seubold's study of the neophyl radical (eq 1).



(1)

Similar results were obtained when different methods of generating a given radical were employed. For example, the 2,2,2-triphenylethyl radical generated by aldehyde decarbonylation, thermal decomposition of azo compounds, the Hunsdiecker reaction, peroxide decomposition, or Kolbe electrolysis normally undergoes extensive rearrangement to the 1,1,2-triphenylethyl radical, but can be intercepted before rearrangement by hydrogen abstraction from triphenyl tin hydride.[5] These studies[4,5] suggest that the major factors influencing aryl rearrangements are the nature and number of substituents at the β-carbon atom (the migration origin) and the relative ease of competitive hydrogen abstraction from solvent or solute molecules.

Rearrangements involving 1,2 shifts of olefin substitutents[6] (eq 2), acyl groups[7] (eq 3), acetate[8] (eq 4), halogen[9] (eq 5), sulfur substituents[10] (eq 6), and silicon substituents[11] (eq 7) have also been reported. The



mechanisms of most of these rearrangements have not been rigorously studied, and in some cases cleavage–recombination pathways have been shown to operate.[9c]

In this paper we report the results of our study of 1,2-acyl shifts to free-radical sites,[12] an area in which our interest was initially aroused by certain radical-initiated transformations of epoxy ketones.[7b]

(1) Chapters by (a) Y. Pocker, (b) J. Berson, (c) P. A. S. Smith, (d) J. King and P. de Mayo, (e) E. W. Warnhoff, (f) N. L. Wendler, and (g) C. Walling in "Molecular Rearrangements," P. de Mayo, Ed., Interscience, New York, N. Y., 1963.

(2) In this paper we restrict our attention to monoradicals. The exceptional behavior of diradicals is well illustrated by the work of F. D. Greene, W. Adam, and G. Knudsen, Jr., *J. Org. Chem.*, **31**, 2087 (1966).

(3) The exceptional rearrangement occurring to a small extent during thermal decomposition of 2,2'-bisazocamphane appears to proceed by a cleavage–recombination mechanism: J. A. Berson, C. J. Olsen, and J. S. Walia, *J. Amer. Chem. Soc.*, **84**, 3337 (1962).

(4) (a) S. Winstein and F. Seubold, *J. Amer. Chem. Soc.*, **69**, 2916 (1947); (b) D. Curtin and M. Hurwitz, *ibid.*, **74**, 5381 (1952); (c) F. Seubold, *ibid.*, **75**, 2532 (1953); (d) C. Overberger and H. Gainer, *ibid.*, **80**, 4561 (1958); (e) M. Kharasch, A. Poshkus, A. Fono, and W. Nudenberg, *J. Org. Chem.*, **16**, 1458 (1951); (f) J. Wilt and H. Philip, *ibid.*, **25**, 891 (1960); (g) C. Rüchardt, *Chem. Ber.*, **94**, 2609 (1961); (h) C. Rüchardt and R. Hecht, *ibid.*, **98**, 2460, 2471 (1965); (i) P. Cote and B. Vittimberga, *J. Amer. Chem. Soc.*, **93**, 276 (1971).

(5) L. Kaplan, *J. Amer. Chem. Soc.*, **88**, 4531 (1966).

(6) (a) L. H. Slaugh, *J. Amer. Chem. Soc.*, **87**, 1522 (1965); (b) L. K. Montgomery and J. Matt, *ibid.*, **89**, 6556 (1967); (c) T. Halgren, M. Howden, M. Medof, and J. D. Roberts, *ibid.*, **89**, 3051 (1967).

(7) (a) H. Reimann, A. Capomaggi, T. Strauss, E. Oliveto, and D. H. R. Barton, *ibid.*, **88**, 4481 (1961); (b) W. Reusch, C. Johnson, and J. Manner, *ibid.*, **88**, 2803 (1966).

(8) D. Tanner and F. Law, *ibid.*, **91**, 7535 (1969).

(9) (a) A. Nesmeyanov, R. Kh. Freidlina, and A. Belyavsky, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1028 (1959); (b) P. S. Skell, R. Allen, and N. Gilmore, *J. Amer. Chem. Soc.*, **83**, 504 (1961); (c) W. Haag and E. Heiba, *Tetrahedron Lett.*, 3683 (1965).

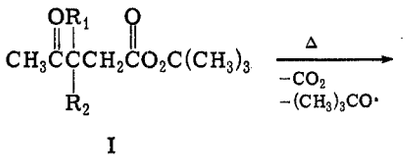
(10) R. Kh. Freidlina, A. Terentiev, and R. Petrova, *Dokl. Akad. Nauk SSSR*, **149**, 860 (1963); **151**, 866 (1963).

(11) (a) H. Sukurai, R. Koh, A. Hasomi, and M. Kumada, *Bull. Chem. Soc. Jap.*, **39**, 2050 (1966); (b) C. Pitt and M. Fowler, *J. Amer. Chem. Soc.*, **90**, 1928 (1968); *cf.* J. Wilt, O. Kolewe, and J. Kraemer, *ibid.*, **91**, 2624 (1969).

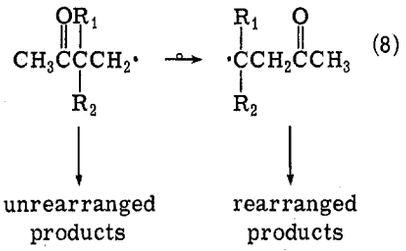
(12) A preliminary report of this work was presented at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968, Abstracts P-79.

Results

The radical intermediates necessary for this study were generated by thermal decomposition of appropriately substituted *tert*-butyl perlevulinate esters (eq 8). Substituents R_1 and R_2 provide a means for distinguishing rearranged from unrearranged products, and in most cases introduce a "driving force" for the rearrangement.

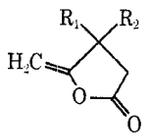


I

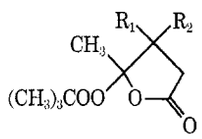


(8)

Efforts to prepare pure samples of *tert*-butyl perlevulinate esters were at first frustrated by the formation of enol lactones (II) or pseudoesters (III). Indeed,



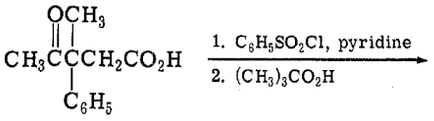
II



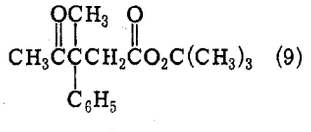
III

interconversion of I and III often occurs in the presence of acid or base catalysts. The presence of unreactive pseudoester contaminants was easily detected by a characteristic strong band at 901 cm^{-1} in the infrared spectrum, as well as by thin layer chromatography.

These difficulties in perester synthesis were circumvented by the mixed sulfonic anhydride method of Brewster and Ciotti[13] and the *N*,*N*′-carbonyldiimidazole method of Hecht and Rüchardt,[14] as shown in eq 9 and 10.



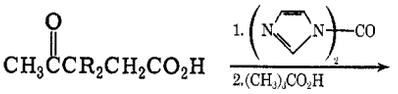
IV



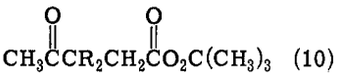
(9)

Ic

The thermal decomposition of peresters Ia–c was studied at 130–132° using 0.25 *M* solutions in diphenyl ether, triglyme, or *p*-cymene. These thermolyses were effected in such a way (Experimental Section) that the progress of the reactions could be followed by observing either the carbon dioxide evolution or the disappearance of perester. Although we did not attempt a careful kinetic analysis of the reactions, four facts did emerge from our initial examination.



Va, R = H
b, R = CH_3



(10)

Ia, R = H
b, R = CH_3

(1) The rate of carbon dioxide evolution tended to be uneven, and the total recovery in ascarite traps ranged from 65 to 90%.

(2) The rate of decomposition of all the peresters was essentially independent of the solvent being used.

(3) With the exception of Ia, the rate of decomposition during the first 40–60 min exceeded the roughly first-order rate observed for the later states of reaction. Induced decomposition is possible at the concentrations employed in these studies.

(4) The apparent first-order rate constants calculated from measurements made during the second and third hours of reaction (peresters Ia–c had essentially disappeared after 4–5 hr at 130°) are close to that reported for *tert*-butyl-3-phenylperpropanoate[15] under similar conditions.

Volatile reaction products were continuously swept from the reaction flask into a cold trap by a slow nitrogen stream. This trap contained most of the *tert*-butyl alcohol and acetone formed during the reaction, and the effect of a change in solvent on the ratio of these compounds confirmed the radical nature of these perester decompositions.[16] Thus, the alcohol to acetone ratio was large (10–200) in those solvents (triglyme and *p*-cymene) which offered the *tert*-butoxy radical a source of readily abstractable hydrogen atoms, and low (0.5–1.0) in diphenyl ether.

Abstraction of solvent hydrogen by the concurrently generated carboxy radical ($CH_3COCR_1R_2CH_2CO_2\cdot$) would produce the corresponding levulinic acids; however, the yield of such acids after complete perester decomposition seldom exceeded 1% in any of the solvents used.

The majority of the volatile perester decomposition products were divided between the cold traps and the final reaction solution. After unreacted perester was reduced and the resulting carboxylic acids were extracted, the crude rection mixture was distilled at reduced pressure (spinning band column), thereby concentrating the volatile components in the first few fractions. Analysis of these fractions and the cold trap condensates by gas–liquid chromatography (with the aid of internal standards) yielded the results outlined in Table I. Product identification was accomplished by chromatographic and spectroscopic comparison of glc-trapped samples with authentic compounds (see the Experimental Section for the sources of these materials).

Dimeric reaction products were also observed in the pyrolysis of Ic. We presume that the initially ob-

(13) J. H. Brewster and C. J. Ciotti, *J. Amer. Chem. Soc.*, **77**, 6214 (1955).
(14) R. Hecht and C. Rüchardt, *Chem. Ber.*, **96**, 1281 (1963).
(15) M. M. Martin, *J. Amer. Chem. Soc.*, **84**, 1986 (1962).
(16) J. H. Raley, F. F. Rust, and W. E. Vaughan, *ibid.*, **70**, 1337 (1948).

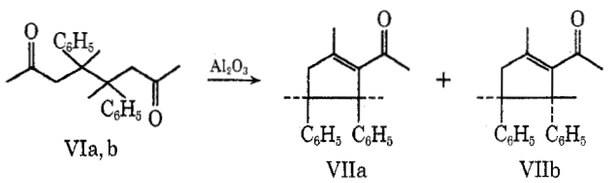
TABLE I

MONOMERIC VOLATILE PRODUCTS FROM β-ACETYL PERESTER DECOMPOSITION

Perester	Solvents	Volatile products[a]	Average yields,[b] %[c]
Ia	Diphenyl ether or triglyme	$CH_3COC_2H_5$	44
Ib	Diphenyl ether or triglyme	$CH_3COC(CH_3)_2CH_2OC(CH_3)_3$ (XI)	11
		$CH_3COCH_2CH(CH_3)_2$	12[d]
		$CH_3COC(CH_3)_3$	0.6[d]
Ic	Diphenyl ether or *p*-cymene	$CH_3COC(CH_3)C_6H_5CH_2OC(CH_3)_3$ (X)	26
		$CH_3COCH_2CH(CH_3)C_6H_5$	15
		$CH_3COCH{=}C(CH_3)C_6H_5$	9
		$CH_3COCH_2C(C_6H_5){=}CH_2$	9

[a] Excluding *tert*-butyl alcohol and acetone. [b] With one exception (see following note) these yields did not vary by more than 1 or 2% on changing the solvent. [c] Corrected for unreacted perester. [d] These yields are from runs made in diphenyl ether. In triglyme the yields were doubled.

tained pyrolysate contains the stereoisomeric diketones VIa and b; however, these compounds were not



VIa, b VIIa VIIb

detected by our glc analysis procedure. Chromatography of the distillation pot residue on neutral alumina apparently transformed VIa and b into the isomeric acetylcyclopentenes VIIa and b, which were easily detected and purified (the configurational assignments are described in the Experimental Section). No corresponding dimeric products were found in the pyrolysates from Ia or Ib.

The distillation pot residue also contained a number of other compounds which we believe result from a combination of substrate radicals with solvent molecules. Aside from noting that these were high molecular weight substances having carbonyl absorption at *ca.* 1710 cm^{-1}, we made no effort to identify them. All the reactions in diphenyl ether yielded methylated phenyl ethers, and the *p*-cymene reaction produced up to 16% cymene dimers.

In order to determine the extent of acetyl rearrangement in the decomposition of *tert*-butyl perlevulinate, we attempted to introduce an isotopic label onto the perester. Since efforts to exchange the C-2 protons in the ethylene ketal of levulinic acid or its ethyl ester failed under moderate conditions and resulted in ketal cleavage when more vigorous methods were employed, we chose to effect direct exchange of the C-3 and C-5 protons of levulinic acid itself by saponification of the ethyl ester in heavy water (eq 11).

$$CH_3COCH_2CH_2CO_2C_2H_5 + D_2O \xrightarrow{NaOD} CD_3COCD_2CH_2CO_2Na \quad (11)$$

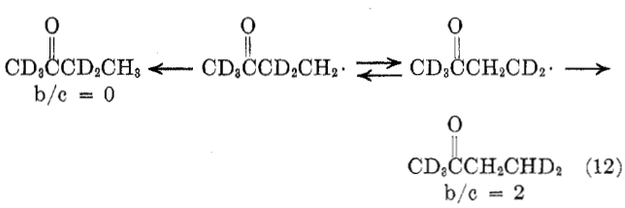
The acid obtained by careful neutralization of this saponification mixture was converted to the corresponding *tert*-butyl perester (eq 10), which was analyzed as a 2,4-dinitrophenylhydrazone (DNP) derivative. Unfortunately, the usefulness of this labeled perester was limited by the broad range of deuterium incorporation revealed by mass spectrometric analysis of the DNP: d_0 0.7%, d_1 1.3%, d_2 2.8%, d_3 7.5%, d_4 26.5%, d_5 44.5%, d_6 12.8%, d_7 3.9%. The isotopic composition of the 2-butanone obtained by pyrolysis of the deuterium-labeled perester in triglyme was also determined by mass spectrometry (d_0 and d_1 <1%, d_2 1.6%, d_3 7.4%, d_4 24.3%, d_5 46.3%, d_6 16.7%, d_7 3.4%) and the distribution of deuterium in this ketone was deduced from its nmr spectrum (Table II).

TABLE II

PROTON DISTRIBUTION IN DEUTERIUM-LABELED 2-BUTANONE

Source of 2-butanone	Area of proton resonance signals (relative to c = 3.0) CH_3——CO——CH_2——CH_3 a b c
Perester pyrolysis in triglyme	0.60 ± 0.08 0.22 ± 0.02 3.0
Perester pyrolysis in diphenyl ether	0.69 ± 0.06 0.25 ± 0.02 3.0

The relative areas of the three distinct proton resonance signals characterizing the labeled 2-butanone (a δ 2.06, b δ 2.39, c δ 1.02) will clearly change as rearrangement takes place (eq 12). If the perester could



(12)

have been cleanly and specifically labeled, the resulting 2-butanone would consist entirely of d_5 molecules with hydrogen located only at positions b and c. The ratio b/c would be zero in the absence of any rearrangement, and would rise to 2 in the event of a complete and directionally specific shift of the acetyl group. However, since it is likely that rearrangement proceeds through a symmetrical intermediate or at least is reversible, the greatest experimentally observed b/c ratio would in fact be 0.5. The expression relating this ratio to the mole fraction of rearrangement (x) is $b/c = 2x/(3 - 2x)$ for the hypothetical case of complete rearrangement and $b/c = 2x/(3 + x)$ for the expected methylene scrambling. Applying the latter expression to the experiments recorded in Table II fixes the per cent rearrangement at 13% in diphenyl ether and 11.5% in triglyme.

The assumption that all the labeled 2-butanone is d_5 is of course not correct and the major error in the previous argument is that hydrogen atoms remaining at b due to incomplete exchange are counted as hydrogen atoms from rearrangement. This leads to an exaggerated estimate for the extent of rearrangement, the true value probably being less than 11%.[17a]

Radical intermediates similar to those generated by perester decomposition presumably form during the reduction of β-halo ketones by trialkyltin hydrides.[17b] Reduction of roughly 1 *M* benzene solutions of 4-

(17) (a) A check of the internal consistency of this conclusion with the isotopic composition revealed by the mass spectrometric analysis is described in an Appendix following the Experimental Section. (b) H. G. Kuivila, *Accounts Chem. Res.*, **1**, 299 (1968).

bromo-3,3-dimethyl-2-butanone (VIII), containing from 1.1 to 2.4 molar equiv of triphenyltin hydride, at 130° proceeded with very little rearrangement (eq 13). Under similar conditions, the corresponding

$$\underset{\text{VIII}}{CH_3COC(CH_3)_2CH_2Br} + (C_6H_5)_3SnH \xrightarrow[130°]{(C_4H_9O)_2} \underset{96\text{–}97\%}{CH_3COC(CH_3)_3} + \underset{4\text{–}3\%}{CH_3COCH_2CH(CH_3)_2} \quad (13)$$

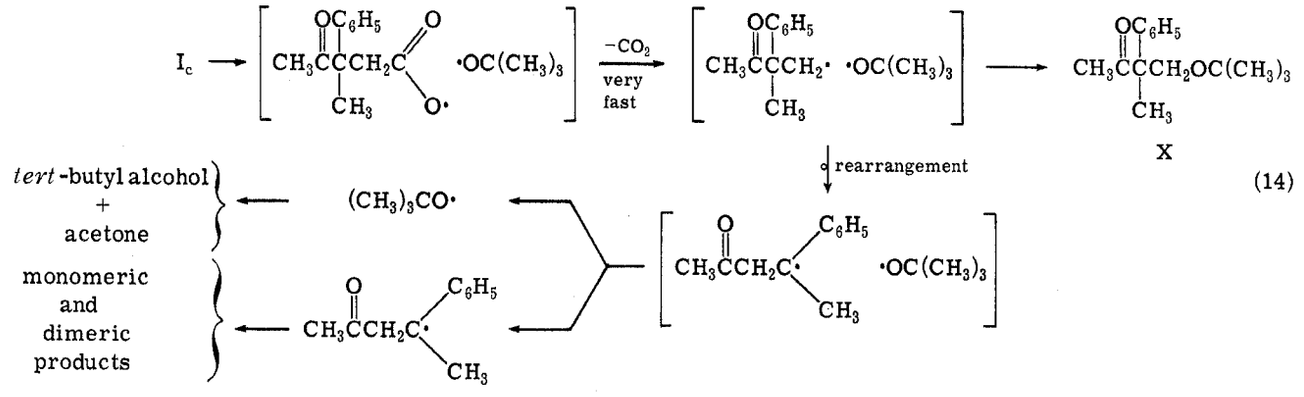
chloride (IX) gave slightly larger amounts of rearranged ketone (*ca.* 13%), and in one experiment using tri-*n*-butyltin hydride rearrangement accounted for 15% of the ketonic products.

Discussion

The herein reported examples of intramolecular 1,2-acyl shifts to conventionally generated free radicals should remove any doubts regarding the possibility or plausibility[7] of these transformations. Indeed, a surprising similarity between these rearrangements and the well-established 1,2-aryl shifts[4] exists. In both cases rearrangement to a more stable radical dominates solvent hydrogen abstraction, but can be prevented by interception of the unrearranged radical by trialkyltin hydrides. However, in the absence of a driving force for the 1,2 shift, very little rearrangement (*ca.* 13%) is observed.

The initial peroxide bond homolysis of the perlevulinate esters must be closely followed by (or possibly concerted with[18]) carbon dioxide release, as witnessed by the very low yields of the corresponding levulinic acids in all solvents. Acyl rearrangement of the resulting primary radicals from Ib and Ic must also be rapid, since only traces of the products from direct hydrogen abstraction are found, even in *p*-cymene and triglyme solvents.

Substantial amounts of unrearranged *tert*-butyl ethers are found among the decomposition products of peresters Ib and Ic (eq 14), and these set an upper limit for the "cage effect" or any alternative intramolecular decomposition mechanism. The absence of 6,6-dimethyl-5-oxa-2-heptanone (XII) among the products of *tert*-butyl perlevulinate (Ia) decomposition was confirmed by the addition of authentic XII to the product mixture, and may be due to a facile β elimination of *tert*-butyl alcohol followed by polymerization of the resulting methyl vinyl ketone. A similar argument could be used to rationalize the absence of any rearranged *tert*-butyl ethers from Ib and Ic; however, it is more likely that the stability of the rearranged radicals enables them to escape the "cage," and subsequent recombination of the radicals would be improbable. In fact, the very stable tertiary benzylic radical (rearranged) from Ic survives long enough to produce significant amounts of dimers (15–40%).



(14)

The facility with which trialkyltin hydrides deliver a hydrogen atom to labile radical intermediates was noted earlier.[5,17] Recent work by Wenkert, *et al.*,[19] suggested that β-halo ketones could be reduced by these reagents without rearrangement, and our study of 4-bromo-3,3-dimethyl-2-butanone (and the corresponding chloride) confirmed this for a substrate known to rearrange in the absence of tin hydrides.

Further studies should be conducted to determine whether the increased rearrangement observed for reduction of the corresponding chloro ketone (IX) is a reflection of acyl participation in the radical-forming step. A similar halogen effect in the 1,4 and 1,5 rearrangement of phenyl from silicon to carbon was recently noted by Wilt and Dockus[20] in tin hydride reductions of $C_6H_5(CH_3)_2Si(CH_2)_nX$.

The preferential rearrangement of an acetyl group rather than a phenyl group[21a] in the primary radical derived from Ic (eq 4) is certainly one of the most interesting and unexpected results to emerge from our investigations. It seems unlikely that this specificity represents an inherent superiority in the migratory applitude of acyl groups, but probably reflects instead a tendency to form the most stable radical. This cannot be accomplished by an equilibrium, however, since the reverse of either rearrangement would be prohibitively endothermic.

In their review of intramolecular free-radical reactions Heusler and Kalvoda[21b] suggest that a 1,2-acyl shift proceeds *via* a cyclopropoxy radical intermediate (eq 15), a view which we accepted and adopted in an earlier paper.[7b] This attractive mechanism parallels currently accepted mechanisms for aryl[4] and vinyl[6] rearrangement, and is consistent with what is known about cyclopropoxy radical intermediates.[22] On the

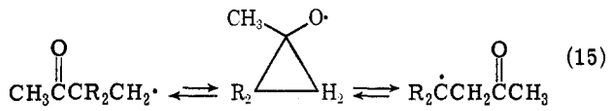
(18) P. D. Bartlett and R. Hiatt, *J. Amer. Chem. Soc.*, **80**, 1398 (1958).

(19) E. Wenkert, P. Bakuzis, J. Baumgarten, D. Doddrell, P. Jeffs, C. Leicht, R. Mueller, and A. Yoshikoshi, *ibid.*, **92**, 1617 (1970).

(20) J. Wilt and C. Dockus, Abstracts, 161st National Meeting of the American Chemical Society, Los Angeles, Calif., 1971, ORGN 163.

(21) (a) As little as 1% of the saturated and unsaturated ketones resulting from a phenyl shift (*i.e.*, 3-methyl-4-phenyl-2-butanone and 3-methyl-4-phenyl-3-buten-2-one) could have been detected by our glc and nmr analysis procedure. (b) K. Heusler and J. Kalvoda, *Angew. Chem., Int. Ed. Engl.*, **3**, 525 (1964).

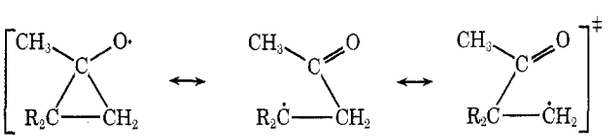
(22) C. H. DePuy, *Accounts Chem. Res.*, **1**, 33 (1968).



(15)

other hand, the influence of substituents (R) at the α-methylene group is difficult to reconcile with the intermediacy of a discrete cyclopropoxy radical, since the relative stability of the rearranged radical should have a negligible effect on the rate-determining initial step (see eq 15). The driving force introduced by the α substituents may, of course, have nothing to do with the stability of the rearranged radical. Thus, a combination of nonbonded interactions in the initial radical, the "Thorpe–Ingold effect," and other undefined aspects of the "*gem*-dialkyl effect"[23] would be expected to increase the rate of cyclopropane formation, as bulky R groups are introduced. This interpretation of the substituent driving force does not, however, help to explain the selective acetyl shift in Ic.

An alternative rationalization of these facts is suggested by the extraordinary facility with which cyclopropoxy radicals rearrange on formation. For example, cyclopropanol nitrite esters undergo thermal homolysis and rearrangement at temperatures as low as $-80°$, the rates of these reactions being extremely sensitive to the nature of substituents at C-2.[24] The authors propose that O–NO bond homolysis and cyclopropane ring opening are concerted, and that relief of ring strain and radical delocalization in the transition state account for the accelerating effect. In a similar way, hydroxyl hydrogen abstraction by molecular oxygen is facilitated in cyclopropanols by concerted opening of the adjacent three-membered ring,[25] and is even further enhanced by the second hydroxyl substituent in vicinal cyclopropanediols.[26] We suggest, therefore, that a discrete cyclopropoxy radical (localized) is not an intermediate in the rearrangements discussed in this paper, but that a cyclic transition state having radical character at both the migration origin and terminus must be invoked. In this way the substituent driving force and the preferential acetyl migration in Ic can be explained.



Rüchardt[4h] and Vittimberga[4i] have drawn similar conclusions regarding aryl rearrangements. In both cases the ability of the migrating group (*i.e.*, acyl or aryl) to engage in a bonding interaction with the nearby unpaired electron must significantly lower the activation energy for its rearrangement relative to that for an alkyl group.[27]

An alternative fragmentation–recombination mechanism for these acyl shifts has not been ruled out, but we regard this as an unlikely possibility for the following reasons.

(1) The rearrangements described here take place under much milder conditions than those employed by Berson, *et al.*,[3] to effect the only documented example of alkyl rearrangement by this mechanism.

(2) The acyl radical fragments formed in this mechanism should suffer a facile decarbonylation, and yet no substantial products derived from such a process were observed (*e.g.*, α-methylstyrene from Ic).

Experimental Section

Melting points were obtained using a Hoover "Uni-Melt" apparatus or a Reichert hot-stage microscope and are uncorrected. A Perkin-Elmer 237B grating spectrophotometer was used to obtain infrared spectra; Varian A-60 and HA-100 high-resolution spectrometers were used to record nmr spectra; and mass spectra were obtained using a Hitachi RMU-6 spectrometer. Vapor phase chromatographic analyses and separations were performed with Varian Aerograph A-90P3 and 1200 instruments. All elemental analyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Preparation of Substituted Levulinic Acids. A. Levulinic Acid-d_5.—A mixture of ethyl levulinate (28.8 g) and anhydrous potassium carbonate (30 g) in 100 ml of D_2O was refluxed under a dry nitrogen atmosphere for 48 hr, concentrated under vacuum, and refluxed for an additional 12 hr with a fresh portion of D_2O. Careful neutralization of the chilled reaction mixture with concentrated hydrochloric acid followed immediately by several methylene chloride extractions gave, after drying and evaporating the combined extracts, 24.3 g of deuterium-labeled levulinic acid. Mass spectrometric analysis was conducted with the *tert*-butyl perester.

B. 3,3-Dimethyllevulinic acid was prepared by the method of Baumgarten and Gleason.[28]

C. 3-Methyl-3-phenyllevulinic Acid.—A solution of the conjugate base of 3-phenyl-2-butanone,[29] prepared by heating 4.45 g (0.03 mol) of the ketone in 100 ml of dry DMSO with 0.80 g of sodium hydride, was added dropwise (1 hr) under nitrogen to a rapidly stirred solution of ethyl bromoacetate in 100 ml of dry DMSO, the temperature being maintained at *ca.* 25°. After the pale yellow reaction mixture was stirred for an additional 30 min, it was poured into ice water and extracted with ether. The dried ether extracts yielded a yellow oil, which after fractional distillation at 0.5 Torr resulted in a 70% yield of ethyl 3-methyl-3-phenyllevulinate, nmr absorptions at δ 1.07 (3 H, triplet, $J \cong 7$ Hz), 1.70 (3 H, singlet), 1.90 (3 H, singlet), 2.90 (2 H, AB quartet center, $J \cong 16$ Hz), 3.98 (2 H, quartet, $J \cong 7$ Hz), 7.28 (5 H, singlet). Saponification of this ester by refluxing ethanolic KOH solution (24 hr) gave, after acidification with hydrochloric acid and extraction with ether, crude 3-methyl-3-phenyllevulinic acid, which on crystallization from hot water gave white needles, mp 96.5–97°, in 80% yield. Broad infrared absorptions at 3400 and 1710 cm^{-1} and nmr absorptions ($CDCl_3$) at δ 1.72 (3 H, singlet), 1.88 (3 H, singlet), 2.93 (2 H, AB quartet center, $J \cong 16$ Hz), 7.28 (5 H, singlet), and 9.46 (1 H, singlet) support the structural sssignment.

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.48; H, 6.80.

Preparation of *tert*-Butyl Perlevulinate Esters. A. The Acylimidazole Method.[14]—A solution of the levulinic acid in dry THF was added dropwise to a stirred solution of an equimolar quantity of 1,1′-carbonyldiimidazole in THF. An hour after the initial gas evolution had ceased (*ca.* 30 min) an equimolar amount of freshly distilled *tert*-butyl hydroperoxide was added dropwise, and the reaction mixture was stirred for 2 days at room temperature. Solvent evaporation under vacuum (temperature <50°) left a residue which was dissolved in ether and washed successively with cold 10% sulfuric acid, cold sodium carbonate, and water. The crude perester obtained from the dried ether extracts could be freed from traces of hydroperoxide by drying under vacuum. Yields ranged from 40 to 60%.

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The perester from deuterium-labeled levulinic acid (Ia) was distilled, bp 84–85° (0.001 Torr), and characterized by infrared absorptions at 2985, 1775, 1705, 1370, 1105, and 850 cm^{-1} and nmr absorptions at δ 1.24 (9 H, singlet) and 2.44 (1.95 H, multiplet). The 2,4-dinitrophenylhydrazone derivative of this perester, mp 134°, exhibited the following ions in the parent ion region of the mass spectrum: *m/e* (rel intensity) 368 (0.6), 369 (1.2), 370 (2.6), 371 (6.7), 372 (23.5), 373 (41.6), 374 (17.9), and 375 (5.9).

The perester from 3,3-dimethyllevulinic acid (Ib) was distilled, bp 93–94° (2×10^{-4} Torr), and characterized by infrared absorptions at 2980, 1770, 1700, 1355, 1080, and 850 cm^{-1} and nmr absorptions at δ 1.21 (6 H, singlet), 1.27 (9 H, singlet), 2.12 (3 H, singlet), and 2.57 (2 H, singlet). A 2,4-dinitrophenylhydrazone derivative, mp 121–122°, was prepared.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10; N, 14.13. Found: C, 51.64; H, 6.13; N, 14.20.

B. The Sulfonyl Anhydride Method.[13]—To a solution of 3-methyl-3-phenyllevulinic acid (1.03 g, 5 mmol) in 45 ml of dry pyridine was added 19.91 g (10 mmol) of *p*-toluenesulfonyl chloride, and this mixture was stirred for 1 hr at room temperature before being cooled in an ice bath. Freshly distilled *tert*-butyl hydroperoxide (0.42 g, 4.8 mmol) was added to the cold reaction mixture, stirring was maintained for 2.5 hr at 0°, and the resulting solution was poured into ice water and extracted with ether. After being washed with cold aqueous acid, sodium carbonate solution, and water, the ether extracts were dried and evaporated under vacuum. Chromatography of the crude perester on a Florisil column removed traces of unreacted hydroperoxide. The resulting perester (Ic) was a viscous, colorless oil, giving a singlet spot on silica gel tlc, and characterized by infrared absorptions at 2930, 1775, 1710, 1377, 1361, and 850 cm^{-1} and nmr absorptions at δ 1.10 (9 H, singlet), 1.77 (3 H, singlet), 1.90 (3 H, singlet), 2.84 (2 H, AB quartet center, $J \cong 15$ Hz), and 7.26 (5 H, singlet).

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.78; H, 7.94.

Perester Thermolysis. A. Solvent Purification. 1. Diphenyl ether (>99% pure) was washed with a 10% potassium hydroxide solution, dried over anhydrous sodium sulfate, and distilled, bp 257–258°. When the purified ether was heated to 200° for 5 hr under a stream of dry nitrogen, no volatile substances were observed in a Dry Ice trap.

2. *p*-Cymene (reagent grade, "terpene-free") proved to be contaminated with sufficient volatile impurities to complicate our product analysis. Purification was effected by refluxing for 2 days over sulfur, extraction of the distilled *p*-cymene with concentrated sulfuric acid, subsequent washing with dilute sodium hydroxide followed by brine, and final fractionation on a spinning band column. The purified solvent showed no impurities on glc analysis.

3. Triethylene glycol dimethyl ether (triglyme) was refluxed over lithium aluminum hydride for 24 hr and then distilled, bp 220–221°. Earlier fractions contained glyme and diglyme. When the purified triglyme was heated to 150° in a nitrogen stream only a trace (*ca.* 2 mg) of volatile substances collected in a Dry Ice cooled trap after 4 hr.

B. General Reaction Procedure.—A three-necked reaction flask was equipped with a magnetic stirring bar, a rubber serum cap, and gas inlet and exit tubes. The inlet tube was connected to a source of dry, carbon dioxide free nitrogen. The exit tube was connected to two Dry Ice–isopropyl alcohol traps in series, and these in turn were connected to a pair of parallel, tared, ascarite-filled tubes equipped with stopcocks, and finally to a bubble counter.

All but 1–2 ml of the solvent to be used was added to the reaction flask, which was then lowered into a preheated oil bath (130°), purged with nitrogen, and connected to the traps and ascarite tubes, one of which was open to the exit gas stream. The perester was dissolved in the remaining solvent and rapidly introduced into the hot solvent by injection through the serum cap. The rate of carbon dioxide evolution was determined by weighing alternate ascarite traps at various time intervals, one trap remaining connected to the system at all times. Alternatively, aliquots were withdrawn from the reaction solution for analysis of unreacted perester.[30]

After 3 hr at 130°, the oil bath was removed and the reaction vessel was cooled by a Dry Ice bath for a brief period in order to quench the pyrolysis. Unreacted perester (negligible amounts remain) was decomposed by a little sodium iodide, ice water was added, and the pH was adjusted to *ca.* 6. After the phases were separated and the water layer was extracted with ether, the combined organic phases were washed with aqueous sodium hydroxide to remove acids, dried over anhydrous sodium sulfate, and carefully distilled through a spinning band column. The volatile products not found in the Dry Ice traps were in this manner concentrated in the first 3–4 ml of distillate. The distillation residue was examined by tlc and glc prior to chromatography on silica gel. Quantitative results were obtained by glc analysis of residue solutions containing *trans*-stilbene as an internal standard.

Reaction Product Identification. A.—A comparison of glc retention times, infrared spectra, and nmr spectra of products believed to be 2-butanone, 3,3-dimethyl-2-butanone, and 4-methyl-2-pentanone with the authentic compounds (Aldrich Chemical Co.) confirmed these assignments.

B. 4-Phenyl-2-pentanone was prepared by the reaction of methylmagnesium bromide with ethyl cinnamate, according to the procedure of Munch-Peterson,[31] semicarbazone mp 135–136°.

C. 4-Phenyl-3-penten-2-one was identified from its infrared spectrum ($\bar{\nu}_{max}$ 1680 and 1600 cm^{-1}) and nmr spectrum: δ 2.18 (3 H, singlet), 2.48 (3 H, singlet), 6.43 (1 H, singlet), and 7.34 (5 H, singlet).

D. 4-Phenyl-4-penten-2-one was identified from its infrared spectrum ($\bar{\nu}_{max}$ 1715 and 1600 cm^{-1}) and nmr spectrum: δ 2.03 (3 H, singlet), 3.47 (2 H, singlet), 5.20 and 5.50 (singlets in a poorly defined 2 H AB quartet), and 7.31 (5 H, singlet).

E. 3-Methyl-4-phenyl-2-butanone was prepared by catalytic hydrogenation of 3-methyl-4-phenyl-3-buten-2-one, synthesized by acid-catalyzed condensation of benzaldehyde with 2-butanone.[32]

F. 3-Phenyl-2-pentanone was prepared by alkylation of the enolate base from methyl benzyl ketone with ethyl iodide,[29] semicarbazone mp 187–190°.

G. 3-Methyl-3-phenyl-2-butanone was prepared by methylation of 3-phenyl-2-butanone, 2,4-dinitrophenylhydrazone derivative mp 151°.

H. 6,6-Dimethyl-5-oxa-2-heptanone (XII) was prepared from methyl vinyl ketone and *tert*-butyl alcohol according to the method of Milas, *et al.*[33] Nmr absorptions at δ 1.13 (9 H, singlet), 2.05 (3 H, singlet), 2.50 (2 H, triplet, $J = 7$ Hz), and 3.55 (2 H, triplet, $J = 7$ Hz) support the structural assignment.

I. 3,3,6,6-Tetramethyl-5-oxa-2-heptanone (**XI**) was isolated from the first spinning band distillation fraction during the work-up of perester Ib decomposition. This volatile keto ether was purified by preparative glc (20% SE-30 column), and exhibited infrared absorptions ($\bar{\nu}_{max}$ 2960, 1710, 1365, 1195, 1080, and 980 cm^{-1}) and nmr absorptions [δ 1.09 (6 H, singlet), 1.16 (9 H, singlet), 2.05 (3 H, singlet), and 3.25 (2 H, singlet)] consistent with its structure. A 2,4-dinitrophenylhydrazone derivative, mp 115–116°, was prepared.

Anal. Calcd for $C_{16}H_{24}N_4O_5$: C, 54.54; H, 6.90; N, 15.90. Found: C, 54.74; H, 6.97; N, 16.06.

J. 3,6,6-Trimethyl-3-phenyl-5-oxa-2-heptanone (**X**) was isolated from the decomposition products of perester Ic by chromatography on alumina. Final purification by glc gave a clear liquid with an nmr spectrum: δ 1.13 (9 H, singlet), 1.47 (3 H, singlet), 1.90 (3 H, singlet), 3.75 (2 H, AB quartet, $J \cong 9$ Hz), and 7.23 (5 H, singlet).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.87; H, 9.42. Found: C, 77.14; H, 9.33.

K. *cis*- and *trans*-1-Acetyl-2,4,5-trimethyl-4,5-diphenylcyclopentene (**VIIa and b**).—Pure samples of these isomers were obtained by preparative glc of the distillation residue from perester Ic decomposition, after an initial chromatography on neutral alumina. Both isomers exhibited strong infrared absorption at 1670 and 1615 cm^{-1} and a parent ion at *m/e* 304 in the mass spectrum. The nmr spectrum of the cis isomer consisted of signals at δ 1.48 (3 H, singlet), 1.67 (3 H, singlet), 1.78 (3 H, singlet), 2.16 (3 H, singlet), 2.74 (2 H, AB quartet, $J \cong 16$ Hz), and 6.84 (sharp multiplet, 10 H).

The trans isomer (VIIb) showed a relative upfield shift of the methyl resonances and a downfield shift of the aromatic protons: δ 1.02 (3 H, singlet), 1.18 (3 H, singlet), 1.70 (3 H, singlet), 2.10

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(3 H, singlet), 2.84 (2 H, AB quartet, $J \cong 18$ Hz), and 7.18 (10 H, multiplet).

Preparation of 4-Halo-3,3-dimethyl-2-butanones (VIII and IX).

A.—Reduction of ethyl 3,3-ethylenedioxy-2,2-dimethylbutanoate (62.5 g), prepared from ethyl 3-keto-2,2-dimethylbutanoate[34] by reaction with ethylene glycol, by a solution of lithium aluminum hydride (6.5 g) in tetrahydrofuran (150 ml) gave, after the customary work-up and acid-catalyzed hydrolysis in aqueous acetone, 3,3-dimethyl-4-hydroxy-2-butanone, bp 78–79° (14 Torr), in 88% yield after distillation. The infrared spectrum of this ketol ($\bar{\nu}_{max}$ 3400, 2950, 1710, 1475, 1120, and 1035 cm^{-1}) and its nmr spectrum [δ 1.08 (6 H, singlet), 2.09 (3 H, singlet), 3.47 (2 H, singlet), and 4.18 (1 H, singlet)] support this structural assignment.

The tosylate prepared from this ketol by reaction with *p*-toluenesulfonyl chloride in pyridine, mp 56°, was converted to 4-bromo-3,3-dimethyl-2-butanone (VIII) by treatment with a sixfold excess of lithium bromide in refluxing 2-butanone for 48 hr. Distillation of crude VIII, bp 79° (18 Torr), gave the pure keto bromide: $\bar{\nu}_{max}$ 2980, 1705, 1470, 1350, 1248, and 1150 cm^{-1}; nmr δ 1.24 (6 H, singlet), 2.16 (3 H, singlet), and 3.52 (2 H, singlet); parent ions at *m/e* 178 and 180 in the mass spectrum.

B.—4-Chloro-3,3-dimethyl-2-butanone (IX) was prepared by the reaction of 1,2,2-trimethylcyclopropanol[35] with *tert*-butyl hypochlorite. Distillation of crude IX, bp 25° (0.5 mm), gave pure chloro ketone: $\bar{\nu}_{max}$ 2980, 1710, 1470, 1355, 1105, and 765 cm^{-1}; nmr δ 1.22 (6 H, singlet), 2.16 (3 H, singlet), and 3.63 (2 H, singlet); parent ions at *m/e* 134 and 136 in the mass spectrum.

The bromide can also be prepared from this cyclopropanol intermediate.

Reaction of 4-Halo-2-butanones with Triphenyltin Hydride.—A benzene solution containing 1.5 equiv of triphenyltin hydride, 1.0 equiv of 4-halo-3,3-dimethyl-2-butanone, and 3–5 mol % di-*tert*-butyl peroxide was placed in an ampoule and degassed as follows. (1) The ampoule was slowly inserted into a liquid nitrogen bath. (2) The cooled ampoule was evacuated. (3) The ampoule was allowed to warm to ambient temperature. This process was repeated three times, following which the ampoule was sealed while under vacuum. The sealed ampoule was suspended in an oil bath (130°) for 36–48 hr. At the end of this time the ampoule was removed and cooled, and the contents were analyzed by glc.

Appendix

In order to check the internal consistency of our conclusions regarding acetyl rearrangement in the 3-ketobutyl radical, we have calculated the isotopic composition at each position in the labeled 2-butanone (Table III) from the mass spectral data and the following assumptions.

(1) If there is no rearrangement, all the deuterium in 2-butanone-d_5 is at positions a and b. The extra hydrogen in d_2-, d_3-, and d_4-labeled ketone is at positions a and b, while the extra deuterium in the d_6 and d_7 compounds must be at c.

(2) If 10% of the methylene units at c rearrange to b, a reasonable a/b hydrogen ratio (*ca.* 2.7 from Table II) is possible only if *all* the extra hydrogen in the sample (*i.e.*, the 0.44 fraction associated with the d_2-, d_3-, and d_4-labeled ketone) is located at a.

(3) The distribution of hydrogen and deuterium for a 5% rearrangement of methylene groups lies midway between the 0 and 10% values.

Since the total number of hydrogen and deuterium units remains unchanged for the cases in Table III, we can judge them by comparing the ratio of hydrogen atoms at positions a, b, and c with the experimental results given in Table II. In the absence of rearrangement the ratio is 0.35:0.13:3.0; at 5% rearrangement it is 0.43:0.15:3.0, changing to 0.51:0.21:3.0 for 10% methylene exchange. Although none of these examples fit the observed ratio (0.60:0.22:3.0) exactly, the best agreement is clearly for 10% exchange (20% rearrangement). The assumption that isotopic exchange in the levulinic ester precursor is complete at methylene group b but incomplete at the acetyl methyl group (a) is not entirely unreasonable, since the inductive effect of the carboxyl group should enhance the acidity of the methylene protons. We conclude, therefore, that a small but significant amount of rearrangement has occurred during decomposition of the perlevulinate ester.

TABLE III

CALCULATED HYDROGEN–DEUTERIUM DISTRIBUTIONS IN 2-BUTANONE

Extent of methylene rearrangement,[a] %	Hydrogen and deuterium distribution		
	a	b	c
0	0.32 H, 2.68 D	0.12 H, 1.88 D	2.77 H, 0.23 D
5	0.38 H, 2.62 D	0.15 H, 1.85 D	2.68 H, 0.32 D
10	0.44 H, 2.56 D	0.18 H, 1.82 D	2.59 H, 0.41 D

[a] The rearrangement values in this table must be multiplied by two before being compared with the per cent rearrangements discussed earlier.

Registry No.—Ia, 34965-32-7; Ia (DNP), 34965-33-8; Ib, 34965-34-9; Ib (DNP), 34965-35-0; Ic, 18854-62-1; VIIa, 34965-37-2; VIIb, 34965-38-3; VIII, 19961-40-1; IX, 13104-53-5; X, 34965-41-8; XI, 34965-42-9; XI (DNP), 34965-43-0; 2-butanone, 78-93-3; ethyl 3-methyl-3-phenyllevulinate, 34965-44-1; 3-methyl-3-phenyllevulinic acid, 34965-45-2; 3,3-dimethyl-4-hydroxy-2-butanone, 1823-90-1; 3,3-dimethyl-4-hydroxy-2-butanone (tosylate), 24706-89-6.

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