Mechanism of Decarboxylation of Bicyclic Acids by Lead Tetra-acetate

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Oxidative decarboxylation of bicyclo[3.2.1]octane-2-carboxylic acids and bicyclo[2.2.2]octane-2-carboxylic acid by lead tetra-acetate gives mainly acetates by both a carbonium ion and a non-carbonium ion pathway. Analysis of products in the decarboxylation of these and other acids indicates the intermediacy of organolead intermediates, which in the non-carbonium ion route give acetates with retention of stereochemistry. This duality of mechanism is used to explain product distributions reported in earlier studies of related carboxylic acids.

By variation of experimental conditions, decarboxylation of carboxylic acids by lead tetra-acetate has been used[1] to give a wide variety of products. Oxidative decarboxylation in acetic acid affords acetates.[2] The mechanism of this and related reactions has been extensively investigated and it is established that reaction proceeds *via* a series of pre-equilibria[3] [equations (1)—(4)], subsequent formation of alkyl radicals by homolytic decomposition of a lead(IV) carboxylate[4] [equation (5)], and finally formation of ester by oxidative substitution[2,5,6] [equation (6)].

$$\mathrm{RCO_2H + Pb(OAc)_4 \rightleftharpoons RCO_2Pb(OAc)_3 + AcOH} \qquad (1)$$

$$\mathrm{RCO_2H + RCO_2Pb(OAc)_3 \rightleftharpoons (RCO_2)_2Pb(OAc)_2 + AcOH} \qquad (2)$$

$$\mathrm{RCO_2H + (RCO_2)_2Pb(OAc)_2 \rightleftharpoons (RCO_2)_3Pb(OAc) + AcOH} \qquad (3)$$

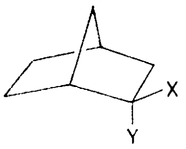
$$\mathrm{RCO_2H + (RCO_2)_3Pb(OAc) \rightleftharpoons (RCO_2)_4Pb + AcOH} \qquad (4)$$

$$\mathrm{RCO_2Pb(OAc)_3 \longrightarrow R\cdot + CO_2 + Pb^{III}(OAc)_3} \qquad (5)$$

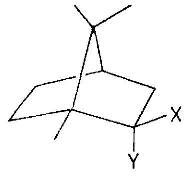
$$\mathrm{R\cdot + Pb(OAc)_4\ [or\ Pb^{III}(OAc)_3] \longrightarrow ROAc + Pb^{III}(OAc)_3\ [or\ Pb^{II}(OAc)_2]} \qquad (6)$$

The mechanism of the final oxidative substitution is not clearly understood. Electron transfer from the alkyl radical could lead to carbonium ion intermediates. Alternatively formation of an organolead intermediate could precede ester formation. Evidence shows that in certain cases carbonium ions are intermediates. Isotopic labelling studies[2] show scrambling of the α- and β-carbon atoms in formation of acetates of 2-phenylethanol, only consistent with a bridged carbonium ion intermediate. Decarboxylation of cyclobutanecarboxylic acid[7,8] gives rearranged acetates consistent with ionic intermediates.

With a number of bridged bicyclic acids the intermediacy of carbonium ions is less clear and the experimental observations are still 'open to several interpretations.'[1] In particular oxidative decarboxylation of either optically active *exo*-(1) or *endo*-norbornane-2-carboxylic acid (2) gives mainly *exo*-norborn-2-yl acetate with partial retention of optical activity.[9] If reaction proceeded *via* the bridged norbornyl cation only racemic ester could be expected. Decarboxylation of *exo*-(3) or



(1) $X = CO_2H; Y = H$
(2) $X = H; Y = CO_2H$
(49) $X = OAc; Y = Me$



(3) $X = CO_2H; Y = H$
(4) $X = H; Y = CO_2H$
(5) $X = OSO_2C_6H_4Me$-*p*; $Y = H$
(48) $X = H; Y = OAc$

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[1] R. A. Sheldon and J. K. Kochi, *Org. Reactions*, 1972, **19**, 279.

[2] J. K. Kochi, A. Bemis, and C. L. Jenkins, *J. Amer. Chem. Soc.*, 1968, **90**, 4616.

[3] J. K. Kochi, *J. Amer. Chem. Soc.*, 1965, **87**, 3609.

[4] J. K. Kochi, J. D. Bacha, and T. W. Bethea, *J. Amer. Chem. Soc.*, 1967, **89**, 6538.

[5] J. K. Kochi, R. A. Sheldon, and S. S. Lande, *Tetrahedron*, 1969, **25**, 1197.

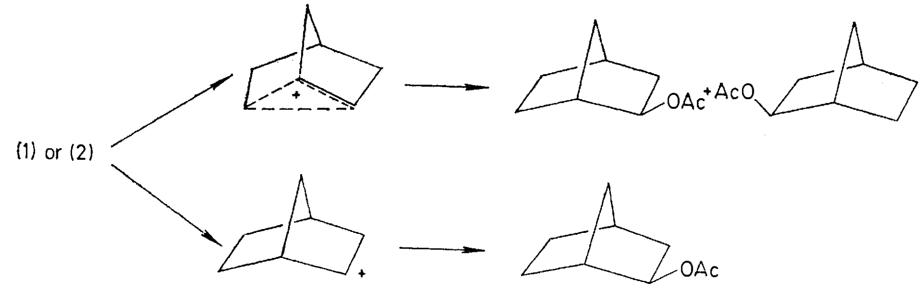
[6] J. K. Kochi and R. V. Subramanian, *J. Amer. Chem. Soc.*, 1965, **87**, 4855.

[7] J. K. Kochi and J. D. Bacha, *J. Org. Chem.*, 1968, **33**, 2746.

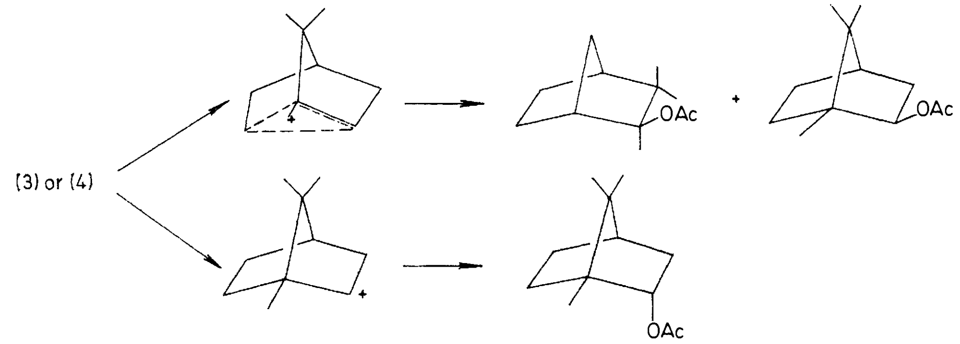
[8] J. K. Kochi and A. Bemis, *J. Amer. Chem. Soc.*, 1968, **90**, 4038.

[9] E. J. Corey and J. Casanova, *J. Amer. Chem. Soc.*, 1963, **85**, 165.

endo-bornane-2-carboxylic acid (4) gives[10] the same mixture of esters, markedly different from that obtained[11] by acetolysis of (5). The product distributions in both series have been explained[9,10] by competitive formation of classical and non-classical ions. Decarboxylation of (1) or (2) was considered to give racemic *exo*-acetate *via* the bridged ion and the classical norbornyl carbonium ion was considered[9] to be the precursor of the chiral *exo*-acetate (Scheme 1). Similarly the formation of *endo*-acetate from (3) or (4) was explained[10] by preferential *endo*-attack upon a non-bridged carbonium ion, whilst other products originated from a bridged carbonium ion (Scheme 2). The implied significant energy barrier between the respective bridged and non-bridged ions is most unlikely in the light of more recent studies.[12]



Scheme 1



Scheme 2

In order to explain these results and to understand the importance of the possible mechanisms of ester formation we have studied the decarboxylation of other bicyclic acids. Our results establish the importance of a carbonium ion pathway and a further route in which carbonium ions are not intermediates.

EXPERIMENTAL

Materials.—Established routes were used for the synthesis of *exo*-bicyclo[3.2.1]octane-2-carboxylic acid[13] (6), *endo*-bicyclo[3.2.1]octane-2-carboxylic acid[13] (7), bicyclo[2.2.2]octane-2-carboxylic acid[14] (8), 3-*exo*-methylbicyclo[2.2.1]heptane-2-*endo*-carboxylic acid[15] (9), and 3-*endo*-methylbicyclo[2.2.1]heptane-2-*exo*-carboxylic acid[16] (10).

Reaction Conditions.—(*a*) Thermal decarboxylation was typically achieved by reaction of an acid (100 mg) with lead tetra-acetate (300 mg) in dry acetic acid (20 ml) containing potassium acetate (65 mg) at 90° for 4 *h* under nitrogen. The cooled solution was poured into water, the excess of acetic acid neutralised by careful addition of solid potassium carbonate, and the aqueous solution extracted with light petroleum (b.p. <40°; 3 × 20 ml). The organic extract was dried ($MgSO_4$) and then analysed. In a similar manner decarboxylation was affected in benzene and benzene containing 5% pyridine.

(*b*) Photodecarboxylation at 20° was achieved by irradiation through Pyrex, using a 125 W medium pressure mercury lamp, of a solution of an acid (50 mg) in dry acetic acid (8 ml) containing lead tetra-acetate (175 mg) and potassium acetate (34 mg). Work up was as in (*a*).

Table 1

Products of decarboxylation of bicyclo-octanecarboxylic acids in acetic acid at 90°

	Concentration of reactants (10^{-3}M)			Products (%)		
Acid	Acid	Lead tetra-acetate	Potassium acetate	(11)	(12)	(13)
(6)	0·34	0·34	0	36·2	48·2	15·6
(6)	0·34	0·34	0·34	37·3	47·5	15·2
(6)	0·35	1·12	0·34	37·9	47·1	15·0
(7)	0·65	0·65	0	36·6	47·6	15·8
(7)	0·65	0·65	0·65	37·1	47·5	15·4
(7)	0·34	1·03	0·35	33·7	52·0	14·3
(8)	0·62	0·82	6·3	25·7		74·3
(8)	1·08	3·25	2·17	28·4		71·6

[10] G. E. Gream and D. Wege, *Tetrahedron Letters*, 1967, 503.

[11] W. Huckel, C-M. Jennewein, H.-J. Kern, and O. Vogt, *Annalen*, 1968, **719**, 157.

[12] G. A. Olah, A. M. White, J. R. De Member, A. Commeyras, and C. Y. Lui, *J. Amer. Chem. Soc.*, 1970, **92**, 4627.

[13] B. C. C. Cantello, J. M. Mellor, and G. Scholes, *J. Chem. Soc.* (*C*), 1971, 2915.

[14] R. Seka and O. Trampasch, *Ber.*, 1942, **75**, 1379.

[15] J. A. Berson, A. W. McRowe, R. G. Bergman, and D. Houston, *J. Amer. Chem. Soc.*, 1967, **89**, 2563.

[16] S. Beckmann and R. Mezger, *Chem. Ber.*, 1957, **90**, 1564.

TABLE 2

Products of decarboxylation of bicyclo-octanecarboxylic acids at 85°

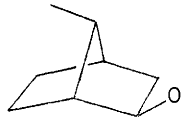
Acid	Solvent	Concentration of reactants (10^{-3}M) Acid	Lead tetra-acetate	Potassium acetate	Products (%) (11)	(12)	(13)
(6)	Benzene	0·34	1·03	0·35	34·9	51·8	13·3
(6)	95% Benzene–5% pyridine	0·34	1·03	0·35	35·7	50·2	14·1
(7)	Benzene	0·65	1·95	0·65	28·9	58·5	12·6
(7)	95% Benzene–5% pyridine	0·65	1·95	0·65	29·9	57·0	13·1
(8)	Benzene	3·25	9·75	3·25	26·4		73·6
(8)	95% Benzene–5% pyridine	1·08	3·25	2·17	26·8		73·2
(7)	Acetic acid [a]	0·34	0·38	0·34	31·4	55·7	12·9
(7)	Acetic acid [b]	0·34	0·47	0·34	29·7	58·9	11·4

[a] Photodecarboxylation at 20°. [b] Photodecarboxylation at 48°.

TABLE 3

Products of decarboxylation of acids (9) and (10) in acetic acid at 90°

Acid	Products (%) (21)	(22)	(23) + (24) + (25)	(26)	(27)	(28)
(9)	15·7	22·1	57·5		4·7	0
(10)	49·2	37·5	11·5	1·8		0



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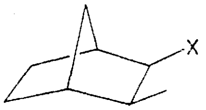
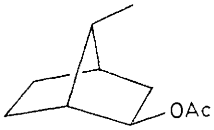


(23) X = OAc
(43) X = Pb(OAc)$_3$



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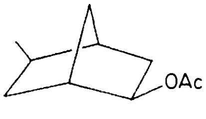

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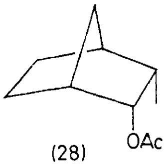

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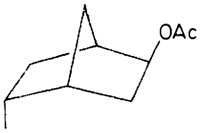

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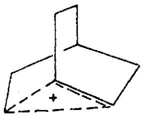

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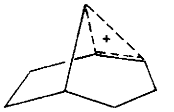

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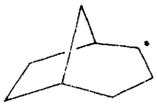

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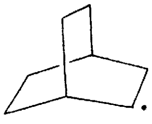

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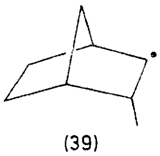

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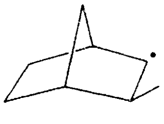

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Analysis.—G.l.c. analysis of acetates was carried out on a 50 ft × 0·02 in capillary column of 1,2,3-tris-(2-cyanoethoxy)propane at 90°. Where reaction mixtures were analysed as the alcohols, reduction was affected with lithium aluminium hydride and the alcohols were analysed by g.l.c. on a 9 ft column of 10% diglycerol on Chromosorb W at 70°. Products from the bicyclo-octanecarboxylic acids were analysed as alcohols and structures assigned to the products by comparison of retention times with those of authentic samples.[17] Acetates were isolated in *ca.* 55% yield, some acid (*ca.* 35%) was recovered unchanged, and a small amount of hydrocarbon products was noted but not further analysed. Conversion of acetates into alcohols was quantitative. Products from bicycloheptanecarboxylic acids were analysed as acetates. Acetates were isolated in *ca.* 65% yield, some acid (*ca.* 30%) was recovered unchanged, and a small amount of hydrocarbon products was detected. Results are given in Tables 1—3.

Stability of Products.—Acetates (11)—(13) were separately treated with lead tetra-acetate and potassium acetate in acetic acid at 90° for 20 h, and were recovered unchanged. Similarly products from bicycloheptanecarboxylic acids were recovered unchanged. Analysis of recovered acids from reaction mixtures showed that each acid gave no other acid under the conditions used.

The possibility of formation of esters by reaction of initially formed olefins under the conditions used was checked. Bicyclo[3.2.1]oct-2-ene in acetic acid with added potassium acetate gave no ester at 90°, but with added lead tetra-acetate a 1 : 1 mixture of (14) and (15) [18] was formed in 30% yield. However, g.l.c. analysis showed these acetates to be absent from the products of decarboxylation. Similarly acetates (16) and (17), products of reaction of bicyclo[2.2.2]oct-2-ene with lead tetra-acetate,[19] were absent. Acetates (18)—(20), products of reaction of 2-methylbicyclo[2.2.1]hept-2-ene with lead tetra-acetate,[20] were absent from products obtained from acids (9) or (10).

DISCUSSION

Bicyclic acids (6)—(8) were chosen for study because of the detailed knowledge of the fate of possible carbonium ions derived from these acids. Products of acetolysis of sulphonate esters (29)—(31) are given in Table 4. It was concluded [17,21] that solvolysis of (29)

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[17] H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, 1968, **90**, 2848.

[18] H. L. Goering, R. W. Greiner, and M. F. Sloan, *J. Amer. Chem. Soc.*, 1961, **83**, 1391.

[19] N. A. LeBel and L. A. Spurlock, *Tetrahedron*, 1964, **20**, 215.

[20] W. F. Erman, *J. Org. Chem.*, 1967, **32**, 765.

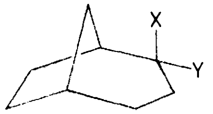
[21] H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, 1968, **90**, 2856, 2862.

or (31) gave products *via* a bridged carbonium ion (32), and (30) gave product *via* a further bridged carbonium ion (33). Little leakage between ions (32) and (33) can occur. With the fate of ions (32) and (33) generated under solvolytic conditions well established, the products of decarboxylation of acids (6)—(8) might be expected to indicate the nature of any intermediate carbonium ion species.

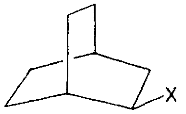
TABLE 4

Products of acetolysis of bicyclo-octyl esters [17,21]

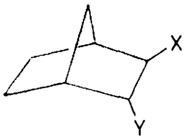
Reactant	Products (%) (11)	(12)	(13)
(29)	45·5	0·6	53·9
(30)	6·6	89·4	4·0
(31)	46·2	0·4	53·4



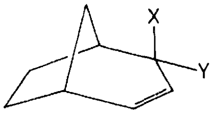
(6) X = CO_2H, Y = H
(7) X = H; Y = CO_2H
(11) X = OAc; Y = H
(12) X = H; Y = OAc
(29) X = $OSO_2C_6H_4Me$-*p*, Y = H
(30) X = H; Y = $OSO_2C_6H_4Me$-*p*
(36) X = $Pb(OAc)_3$; Y = H
(37) X = H; Y = $Pb(OAc)_3$



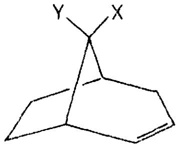
(8) X = CO_2H
(13) X = OAc
(31) X = $OSO_2C_6H_4Me$-*p*
(38) X = $Pb(OAc)_3$



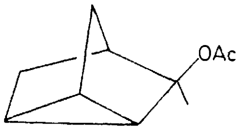
(9) X = Me; Y = CO_2H
(10) X = CO_2H; Y = Me
(21) X = OAc; Y = Me
(27) X = Me; Y = OAc
(41) X = $Pb(OAc)_3$, Y = Me
(42) X = Me; Y = $Pb(OAc)_3$
(44) X = Me; Y = $OSO_2C_6H_4Br$-*p*
(45) X = $OSO_2C_6H_4Br$-*p*; Y = Me
(46) X = Me; Y = NH_2
(47) X = NH_2; Y = Me



(14) X = OAc; Y = H
(15) X = H; Y = OAc



(16) X = OAc; Y = H
(17) X = H; Y = OAc



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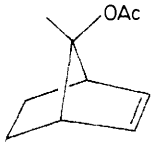

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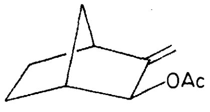

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Product analyses from decarboxylation of acids (6)—(8) are given in Tables 1 and 2. Separate experiments established the stability of products, the failure of acids to epimerise, and the absence of esters derived from olefins under the reaction conditions. Our results establish small differences in products with solvent and between thermal and photo-decomposition but the most striking result is the near identity of product distribution from acids (6) and (7) but the very different product ratio from acid (8).

The similar product distributions from (6) and (7) imply a common intermediate. In accord with earlier observations [3] we conclude that this intermediate is the radical (34). The solvolytic studies [17,21] show that if the fragmentation of a lead carboxylate were a heterolytic process acids (6) and (7) would give different products. Similarly we conclude that acid (8) by initial homolytic fragmentation gives radical (35).

Radicals (34) and (35) can (*a*) give alkyl-lead intermediates (36)—(38), (*b*) give carbonium ions directly by electron transfer to a lead species, (*c*) give saturated hydrocarbons by hydrogen abstraction from the solvent and, (*d*) give esters directly by radical combination. Formation of (13) from (6) or (7) and of (11) from (8) shows the importance of a carbonium ion route, but the formation of more (13) from (8) than that expected on the basis of solvolytic studies,[17,21] shows that a second route, a non-carbonium ion route, competes.

Formation of an alkyl-lead intermediate from a radical and then solvolytic displacement (with or without competitive ion-pair return) could give esters *via* carbonium ion intermediates. Hence the distinction between formation of esters by solvolytic displacement of an organolead intermediate and by electron transfer from a radical to give a carbonium ion captured by solvent is small. In the first case an alkyl-lead intermediate is involved and in the second the alkyl-lead species represents a transition state. In subsequent discussion the intermediate is considered.

In formation of alkyl-lead intermediates both (36) and (37) would be formed from (34) with uncertain specificity [22,23] and (35) would give only (38). Absence of bornane in decarboxylation of acids (3) or (4) shows [10] that hydrogen abstraction is slow and relatively unimportant. Results in Table 1 show that by comparison with products of solvolysis (see Table 4) acid (8) gives *ca.* 50% of products by a carbonium ion pathway and *ca.* 50% by a non-carbonium ion route. With acids (6) and (7) the uncertainty in the expected ratio of (36) to (37) makes analysis more difficult. If there is no effective interconversion of ions (32) and (33) and assuming the same capture ratios for (32) and (33) as observed in acetolysis, the relative importance of carbonium ion and non-carbonium ion routes in decarboxylation of (6) and (7) is similar to that observed for (8).

The non-carbonium ion route must proceed from the

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[22] A. A. Youssef, M. E. Baum, and H. M. Walborsky, *J. Amer. Chem. Soc.*, 1959, **81**, 4709.

[23] W. Kraus, *Annalen*, 1965, **685**, 97.

radical and give ester directly, as mentioned above, or from an alkyl-lead intermediate with either retention or inversion of configuration. The products obtained from acids (6)—(8) fail to discriminate between the stereochemical possibilities. In order to distinguish between these processes acids (9) and (10) have been examined. The carbonium ions, which might be derived from these acids have been carefully studied,[15,24] and the methyl group will influence the direction of attack upon the radicals (39) and (40) and hence control the formation of alkyl-lead intermediates. Radical (39) should give entirely intermediate (41) and radical (40) both [25] (42) and (43).

Decarboxylation of (9) or (10) gives a complex mixture of acetates, partially analysed by g.l.c. on capillary columns. Comparison with authentic acetates (21),[16] (23),[15] (27),[15] and (28) [16] and with mixtures of acetates obtained by solvolysis (kindly supplied by Professor J. A. Berson) gave the results shown in Table 3. Acetates (23)—(25) were incompletely resolved. These results establish the importance of a carbonium ion pathway but comparison of the product distribution with those obtained [24] by solvolytic and deaminative routes show significant differences (Table 5). All the acetates expected from a carbonium ion pathway are observed but ratios of Wagner–Meerwein related pairs, *e.g.* (21) and (22), differ.

TABLE 5

Products from acetolysis and deamination of methyl norbonyl derivatives

Reactant	Conditions	Products (%) (21)	(22)	(25)	(26)	(23)	(24)	(49)	(27)	(28)
(44)	AcOH–NaOAc	18	17	14	16	5	28	3·4	0	0
(45)	AcOH–NaOAc	30	31	11	12	0	8	7	0	0
(46)	$NaNO_2$–AcOH	5·7	6·1	3·5	5·5	4·3	46·4	0	28·4	0
(47)	$NaNO_2$–AcOH	Acetates 21	14	1	1	0	1	1	0	0
		Alcohols 34	23	1	1	1	1	1	0	0

Acetate (27) is obtained in decarboxylation of acid (9), in deamination of amine (46), but not in acetolysis of (44). Acetate (27) must be a product of a non-carbonium ion pathway as noted in the deamination of (46). It can be formed by collapse of the organolead intermediate (42) with retention of configuration or by substitution with inversion in (43). The latter is unlikely because of the considerable hindrance to *endo*-attack and the alternative of collapse of (42) is preferred with retention of configuration.

Similarly a non-ionic mechanism for collapse of the intermediate (41) with retention of configuration to give acetate (21) may be detected. Absence of acetate (28) shows that intermediate (41) fails to give esters by displacement with inversion of configuration. Decarboxylation of (10) gives more (21) than anticipated from the typical capture ratio to give the Wagner–Meerwein pair (21) and (22). Again a collapse with retention of configuration whereby (41) gives (21) is indicated. Results in Table 5 indicate that both (9) and (10) undergo decarboxylation by competitive processes leading from organolead intermediates to acetates by an ionic mechanism and a non-ionic mechanism requiring retention of configuration.

Our results adequately account for the earlier results of Corey and Casanova,[9] and of Gream and Wege.[10] In decarboxylation of *exo*- or *endo*-norbornane-2-carboxylic acid [9] almost exclusive formation of an *exo*-alkyl-lead intermediate is expected. Competitive heterolysis to give the non-classical norbornyl cation and hence racemic product and substitution with retention of configuration to give the chiral *exo*-acetate account for the major products.

Decarboxylation [10] of acids (3) and (4) are expected to give mainly the *endo*-alkyl-lead intermediate on the basis of recent stereochemical studies.[26] The formation of *endo*-acetate (48), a product not observed in acetolysis of (5) and hence a product of a non-ionic pathway is by collapse of the *endo*-alkyl-lead intermediate with retention of configuration. Other products are those expected of an ionic pathway. We therefore conclude that in all the reported decarboxylations of bicyclic acids, products may be adequately accounted for by a carbonium ion pathway and a non-ionic pathway in which retention of configuration is observed from alkyl-lead intermediate to acetate product. Earlier schemes [9,10] requiring competitive formation of classical and non-classical carbonium ions are unnecessary.

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