The Thermal Rearrangements of Methylenecyclopropanecarboxylic Acids

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Substituted methylenecyclopropanecarboxylic acids (6) and (7) rearrange thermally in the liquid phase to mixtures of the lactone (10) and the dihydrofuranone (13). The product ratios depend on the positions of the substituents. The parent acid (5) and Feist's acid (1a) decompose thermally in the presence of water to give ethyl methyl ketone and levulinic acid respectively. The mechanistic rationale of the above reactions is based on a competition between ring cleavage and electrophilic addition to the *exo*-double bond.

Although Feist's acid (1a) reported in 1893[1] was the first methylenecyclopropane derivative to be discovered, methylenecyclopropanecarboxylic acids are among the least studied members of this class of strained ring molecules.[2] In contrast the dimethyl ester (1b) [3,4] and many other methylenecyclopropane derivatives [4,5] have been thoroughly studied mainly in connection with the degenerate methylenecyclopropane rearrangement, and the structure of the trimethylenemethane intermediate involved in the rearrangement [6] [see equation (1)].

We report here that methylenecyclopropanecarboxylic acids undergo a variety of thermal reactions which, depending on the substituents, arise either from cyclopropane ring cleavage or from electrophilic addition to the *exo*-double bond.

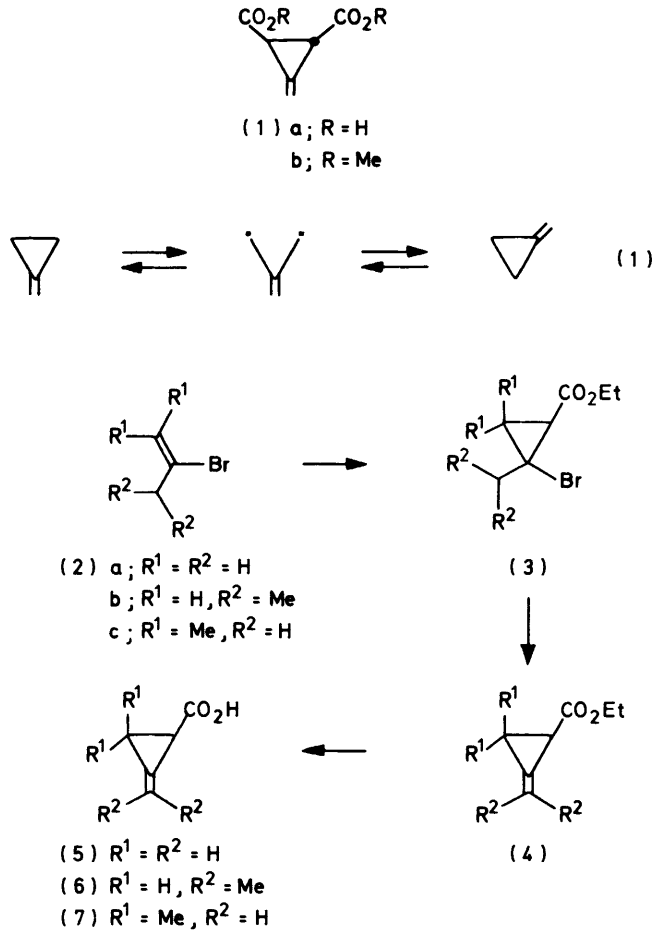
Results and Discussion

The parent acid (5) and the two dimethyl analogues (6) and (7) were prepared from the corresponding vinyl bromides (2) as outlined in Scheme 1. The initial copper-catalysed reaction of ethyl diazoacetate with (2) to form a *Z,E* mixture of the corresponding bromocyclopropanes (3) was carried out by using a modified version of the published procedure.[7] Dehydrobromination of (3) was best achieved under phase-transfer conditions.[8] This method was found superior to others using NaH–ether,[7] powdered KOH [9] or Bu^{t}OK–Me_2SO.[10]

Liquid-phase pyrolysis of neat (6) for ½ h in a sealed Pyrex tube at 180 °C resulted in its ready conversion into a mixture containing the bicyclic lactone (10),[11] the dihydrofuranone (13) [12] and the starting material (6) in a 7 : 1 : 2 ratio. Longer heating at this temperature resulted in the complete disappearance of (6) with no significant change in the (10) : (13) ratio. When the reaction mixture was heated to 300 °C gradual decomposition of (10) occurred. However, interconversion between (10) and (13) under these conditions was not observed.

Similarly heating the isomeric acid (7) briefly at 180 °C gave a mixture of the isomers (10) and (13) together with the isomeric acid (6). No starting material remained. However, the mixture was relatively richer in (13), the isomer ratio being 1 : 7 : 2 respectively (Scheme 2).

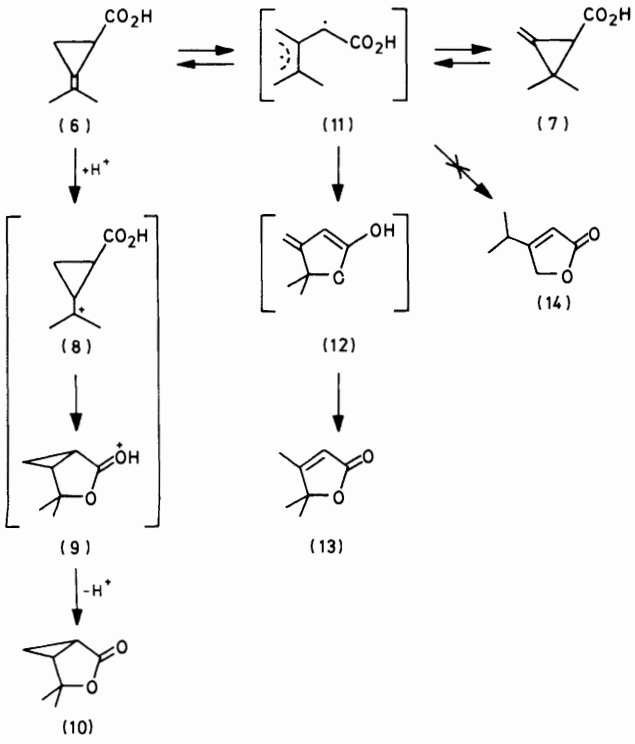
In contrast, no rearrangement products were observed when the parent acid (5) was subjected to pyrolysis under the same conditions. However, heating of (5) for 1 h at 250 °C led to extensive decomposition with concomitant formation of CO_2. The only other volatile product isolated in rather low yield in the pyrolysis was identified as ethyl methyl ketone (17). Similarly, Feist's acid (1a) decomposed upon pyrolysis at 250 °C to give, in addition to CO_2, traces of levulinic acid (18). Dramatically increased yields of both (17) and (18) were, however, obtained when the pyrolyses were conducted in the



Scheme 1

presence of small excesses of water, indicating the involvement of hydrated intermediates at some stage prior to decarboxylation.

Based on the present data and previous mechanistic studies by Doering *et al.*[4] on related methylenecyclopropane rearrangements we propose Scheme 2 as the mechanism of the rearrangement of the acids (6) and (7). This is consistent with our findings as two competitive processes which lead to different products are postulated. The first process involves an acid-catalysed regiospecific intramolecular addition of the carboxylic group across the double bond to produce the lactone (10) *via* the intermediates (8) and (9). In the second process the cyclopropane ring is cleaved to give trimethyl-

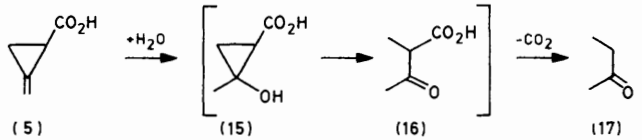


Scheme 2

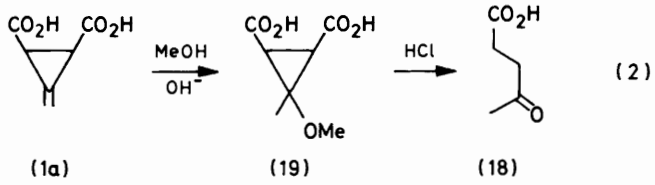
enemethane intermediate (11) * which may either recyclize reversibly to a methylenecyclopropane or rearrange *via* the enol (12), to the dihydrofuranone (13).

It should be noted that the isomeric dihydrofuranone (14) [13] was not formed. Apparently, cyclization of (11) to (14) is much slower than to (13) because of the relatively low spin density on the unsubstituted end of the allylic moiety of (11). Furthermore, from the differences in product ratio observed in the pyrolysis of (6) and (7) we deduce that the relative rates of the rearrangement are strongly dependent on substituent. Formation of the carbocation (8) by protonation of the highly substituted methylene group in (6) is favoured over ring cleavage, resulting in a high proportion of the lactone (10). Conversely, in the acid (7), which is more highly ring substituted, cleavage is preferred over addition and this leads to the predominant formation of (13). It may also be concluded that trimethylenemethane (11) cyclizes through carbon–oxygen bond formation to (13) faster than it does by carbon–carbon interaction to (6). Furthermore, the presence of the acid (6) in the pyrolysis mixture of (7) when all of (7) rearranged clearly indicates that (6) is thermodynamically more stable than (7). This is consistent with the expected higher stability of the more substituted double bond of (6) as compared with the unsubstituted one of (7).

Finally, the mechanism postulated for the decarboxylation of the acids (1a) and (5) is outlined in Scheme 3. The necessity of water in the reaction together with simple stoicheiometric considerations indicates initial addition of a water molecule to the double bond of (5) affording the cyclopropanol (15). Under acidic conditions (15) undergoes a typical isomerization [14] to the β-keto-acid (16) which, in turn, readily decarboxylates to (17). Similarly, hydration of Feist's acid (1a)



Scheme 3



followed by isomerization and decarboxylation leads to levulinic acid (18). This mechanism is supported by the previously reported decomposition of (19) in acidic media to give levulinic acid [15] [equation (2)].

Clearly, the absence of radical-stabilizing substituents on the cyclopropane ring and carbonium-stabilizing substituents at the *exo*-methylene group make (1a) and (5) less prone to rearrangements and more liable to intermolecular addition reactions.

Experimental

General.—^{1}H N.m.r. spectra were recorded on Varian Model HA-100 and EM 360A spectrometers; ^{13}C n.m.r. spectra were recorded on a Varian Model CFT-20 instrument. Me_4Si was used as internal standard. I.r. spectra were taken in CCl_4 solutions using a Perkin-Elmer Model 257 spectrometer. Preparative g.l.c. separations were done on a Varian Model 90-P chromatograph. Analytical g.l.c. was performed on a Packard Model 824 chromatograph equipped with an Autolab-system IV computing integrator. The g.l.c. columns used were 6-ft × $\frac{1}{8}$-in glass columns of 10% SE-30 or 20% Carbowax 20M on Chromosorb W. Elemental analyses were determined at the analytical laboratories of the Hebrew University.

2-*Bromo*-3-*methylbut*-1-*ene* (2b).—This compound was prepared according to Gredy [16] by dehydrobromination of 1,2-dibromo-3-methylbutane. An 80% yield of a mixture of (2b) and the corresponding 1-bromo-isomer was obtained in a 1 : 1 ratio (by n.m.r.). Fractional distillation at 100—101 °C through an externally heated 110 cm column filled with glass rings gave 41% of the title compound, δ_H ($CDCl_3$) 1.2 (6 H, d, *J* 7 Hz), 2.5 (1 H, sep, *J* 7 Hz), 5.2 (1 H, d, *J* 2 Hz), and 5.5 (1 H, d, *J* 2 Hz).

2-*Bromo*-3-*methylbut*-2-*ene* (2c).[17,18]—This compound was prepared according to Bachman [17] by dehydrobromination of 2,3-dibromo-3-methylbutane [19] in 68% yield, b.p. 116 °C (lit.,[17] 118—120 °C), δ_H ($CDCl_3$) 1.75 (3 H, s), 1.87 (3 H, s), and 2.25 (3 H, s).[18]

Ethyl 1-*Isopropylidenecyclopropane*-2-*carboxylate* (4b).—To a stirred mixture of (2b) (45 ml), anhydrous $CuSO_4$ (0.8 g), and Cu powder (1.0 g) [20] heated to 90 °C was added dropwise during 10 h a solution of ethyl diazoacetate (50 g, 0.44 mol) in (2b) (45 ml). Excess of (2b) was distilled off at 40 °C (50 mmHg) and the residue taken up in pentane and filtered free from polymeric material and copper salts. Removal of pentane and Kugelrohr distillation at 110 °C (20 mmHg) gave (3b)

* The structure of trimethylenemethane analogues of the intermediate (11) has been thoroughly discussed in ref. 4.

(28.5 g, 28% crude) as a mixture of the (*E*)- and (*Z*)-stereoisomers. The crude material contained *ca.* 10% of fumarate and ethyl bromoacetate (n.m.r.) and was used without purification.

A mixture of crude (3b) (10 g, 42 mmol) in CH_2Cl_2 (30 ml) was stirred at room temperature with 50% aqueous NaOH (20 ml) and benzyltriethylammonium chloride (100 mg). G.l.c. analysis after *ca.* 2 h indicated that no (3b) was left. The organic phase was washed with 5% aqueous HCl and brine and dried (Na_2SO_4). Removal of CH_2Cl_2 and Kugelrohr distillation at 70 °C (20 mmHg) gave the title compound (2 g, 30%). The ^1H n.m.r. spectrum of the product was identical with that in the literature.[5b]

Ethyl 3,3-*Dimethyl*(*methylene*)*cyclopropane*-2-*carboxylate* (4c).—As above, ethyl diazoacetate (15 g, 132 mmol) in (2c) (40 ml) was added at 90 °C to a mixture of (2c) (40 ml), anhydrous $CuSO_4$ (250 mg), and Cu powder (1.0 g) to give the stereoisomeric mixture of (3c) (7.3 g, 24% crude) which was Kugelrohr distilled at 82 °C (3.5 mmHg). A solution of crude (3c) (1.5 g, 6.4 mmol) in CH_2Cl_2 (50 ml) was dehydrobrominated as above by treatment with 50% aqueous NaOH (10 ml) and benzyltriethylammonium chloride (50 mg). Kugelrohr distillation at 70 °C (30 mmHg) gave the titled compound (750 mg, 76%). The ^1H n.m.r. spectrum of the product was identical with that in the literature.[5b]

1-*Isopropylidenecyclopropane*-2-*carboxylic Acid* (6).—A mixture of (4b) (1.9 g, 9.7 mmol) and 10% aqueous KOH (35 ml) was stirred at ambient temperature until all the ester dissolved. The aqueous solution was extracted with ether, acidified with dilute aqueous HCl and extracted again with ether. The ethereal solution was washed with brine, dried over anhydrous Na_2SO_4, and distilled at 90 °C (3 mmHg) to give the title compound (1.4 g, 90%) which crystallized with time at m.p. 70—72 °C; δ_H (CCl_4) 1.8 (8 H, m), 2.0—2.5 (1 H, m), 11.5 (1 H, bs); δ_C ($CDCl_3$) δ 12.54 (C-3), 18.02 (C-2), 22.12 (2 × CH_3), 116.02 (C-1), 123.91 (CMe_2), and 179.94 p.p.m. (CO_2H); $\nu_{max.}$ (CCl_4) 2 950br, and 1 680 cm^{-1} (Found: C, 66.25; H, 7.85. Calc. for $C_7H_{10}O_2$: C, 66.65; H, 7.99%).

3,3-*Dimethyl*(*methylene*)*cyclopropane*-2-*carboxylic Acid* (7).—As above, compound (4c) (2 g, 13 mmol) was treated with 10% aqueous KOH (10 ml) to give the title compound (1.4 g, 83%) which was Kugelrohr distilled at 110 °C (0.3 mmHg); it solidified with time (m.p. 38 °C), δ_H (CCl_4) 1.35 (3 H, s), 1.39 (3 H, s), 1.98 (1 H, t, *J* 2.0 Hz), 5.45 (2 H, t, *J* 2.0 Hz), and 12.1 (1 H, s); $\nu_{max.}$ (CCl_4) 2 950br and 1 680 cm^{-1} (Found: C, 66.85; H, 7.85. Calc. for $C_7H_{10}O_2$: C, 66.65; H, 7.99%), δ_C ($CDCl_3$) 18.19, 26.06 (2 × CH_3), 27.70 (C-3), 30.06 (C-2), 103.21 (CH_2), 141.23 (C-1), and 177.72 p.p.m. (CO_2H).

Pyrolyses: General Procedures.—Acids were sealed in a U-shaped tube (5 cm × 4 mm i.d.) and pyrolysed in a Kugelrohr oven. At the end of the pyrolysis one arm of the tube was cooled externally and the pyrolysate distilled into the cold arm. The tube was then opened and the condensed mixture analysed by g.l.c.

4,4-*Dimethyl*-3-*oxabicyclo*[3.1.0]*hexane*-2-*one* (10) [11] and 4,5,5-*Trimethylfuran*-2(5H)-*one* (13).[12]—*Pyrolysis of* (6). Heating of (6) (20 mg, 0.13 mmol) at 180 °C for 1 h gave a 7 : 1 mixture (17 mg, 85%) of (10) and (13) which was separated by g.l.c.; the compounds were identified by their ^1H n.m.r. spectra in $CDCl_3$: (10) δ 0.8—1.30 (2 H, m), 1.2 (3 H, s), and 1.6—2.0 (2 H, m); [11] (13) δ 5.6 (1 H, q, *J* 2 Hz), 2.05 (3 H, d, *J* 2 Hz), and 1.45 (6 H, s).[12b]

Pyrolysis of (7). As above, heating of (7) (47 mg, 0.32 mmol) afforded a 1 : 7 mixture (39 mg, 70%) of (10) and (13) by ^1H n.m.r.[11,12]

Levulinic acid (18). A mixture of Feist's acid [21] (40 mg, 0.28 mmol) and water (10 mg) was heated at 250 °C for 1 h. G.l.c. analysis of the collected material (27 mg, 80%) showed a single product identified by ^1H n.m.r. as (18).[22a]

Ethyl methyl ketone (17). As above, the acid (5) [7] (20 mg, 0.20 mmol) and water (10 mg) heated at 300 °C for 1 h afforded the title compound (4 mg, 20%).[22b]

References

1 F. Feist, *Ber.*, 1893, **26**, 747.
2 D. Lloyd, 'Topics in Carbocyclic Chemistry,' Logos Press, London, 1969, vol. 1, pp. 249; J. Meinwald, J. W. Wheeler, A. A. Nimetz, and J. S. Liu, *J. Org. Chem.*, 1965, **30**, 1038.
3 E. F. Ullman, *J. Am. Chem. Soc.*, 1960, **82**, 505.
4 W. von E. Doering and H. D. Roth, *Tetrahedron*, 1970, **26**, 2825 and references cited therein; W. von E. Doering and L. Birladeanu, *Tetrahedron*, 1973, **29**, 499.
5 (*a*) J. P. Chesick, *J. Am. Chem. Soc.*, 1963, **85**, 2720; J. J. Gajewski, *J. Am. Chem. Soc.*, 1968, **90**, 7178; A. S. Kende and E. R. Riecke, *J. Am. Chem. Soc.*, 1972, **94**, 1397; Z. Goldschmidt and S. Mauda, *Tetrahedron Lett.*, 1976, 4183; J. J. Gajewski and S. K. Chou, *J. Am. Chem. Soc.*, 1977, **99**, 5696; J. A. Berson, *Acc. Chem. Res.*, 1978, **11**, 446; (*b*) X. Creary, *J. Org. Chem.*, 1978, **43**, 1777.
6 F. Weiss, *Q. Rev. Chem. Soc.*, 1970, **24**, 278; P. Dowd, *Acc. Chem. Res.*, 1972, **5**, 242; D. A. Dixon, R. Foster, T. A. Halgren, and W. N. Lipscomb, *J. Am. Chem. Soc.*, 1978, **100**, 1359 and references therein.
7 E. F. Ullman and W. J. Fanshawe, *J. Am. Chem. Soc.*, 1961, **83**, 2379.
8 E. V. Dehmlow, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 170; 1977, **16**, 493; M. S. Newman, B. Dhawan, M. M. Hashem, V. K. Khanna, and J. M. Springer, 1976, **41**, 3925; E. V. Dehmlow and M. Lissel, *Synthesis*, 1979, 372.
9 J.-L. Derocque, F.-B. Sunderman, N. Youssif, and M. Hanack, *Liebigs Ann. Chem.*, 1973, 419.
10 S. Arora and P. Binger, *Synthesis*, 1974, 801.
11 W. Ando, I. Imai, and T. Migita, *J. Org. Chem.*, 1972, **37**, 3596.
12 (*a*) J. M. Morrow and D. W. Wooley, *J. Am. Chem. Soc.*, 1959, **81**, 4951; (*b*) T. C. McMorris, *J. Org. Chem.*, 1970, **35**, 458.
13 M. Franck-Newmann, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 65.
14 C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Am. Chem. Soc.*, 1966, **88**, 3347.
15 F. R. Goss, C. K. Ingold, and J. F. Thorpe, *J. Chem. Soc.*, 1925, **127**, 460.
16 B. Gredy, *Bull. Soc. Chim. Fr.*, 1935, [5], **2**, 1951.
17 J. K. Farrell and G. B. Bachman, *J. Am. Chem. Soc.*, 1935, **57**, 1281.
18 C. V. Pittman Jun. and W. G. Miller, *J. Am. Chem. Soc.*, 1973, **95**, 2947.
19 F. C. Whitmore, W. L. Evers, and H. R. Rothrock, *Org. Syn.*, Coll. Vol. 2, 1943, 408.
20 A. I. Vogel, 'A Text Book of Practical Organic Chemistry,' Longman, 1959, 3rd. edn., p. 192.
21 A. T. Blomquist and D. T. Longone, *J. Am. Chem. Soc.*, 1959, **81**, 2012.
22 (*a*) C. J. Pouchert and J. R. Campbell, 'The Aldrich Library of NMR Spectra,' vol. 2, p. 179; (*b*) p. 105.

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