The Formation of Bicyclic γ-Lactones from γ-Bromoalkylidene Malonates

TRYGVE GULBRANDSEN and
PER KOLSAKER

Chemistry Department, University of Oslo,
Box 1033, Blindern, Oslo 3, Norway

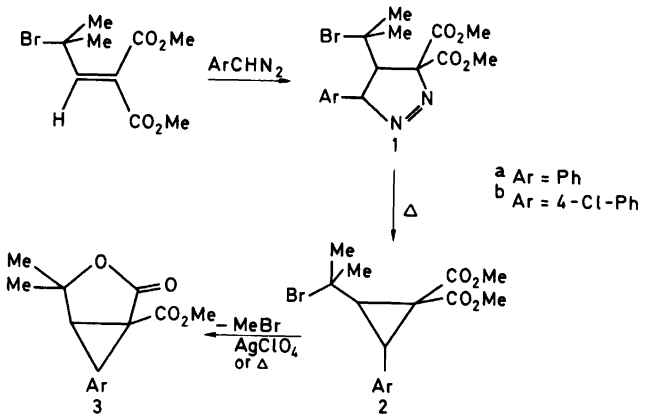
γ-Bromoalkylidene malonates can be converted to α-methoxycarbonyl-$\Delta^{\alpha,\beta}$-butenolides, either thermally[1,2] or by treatment with silver perchlorate.[2]

When dimethyl 2-aryl-3-[1-bromo-1-methylethyl]-1,1-cyclopropanedicarboxylates (*2a* or *2b*), prepared thermolytically from pyrazolines *1*, were left, either neat or in chloroform solution, at room temperature for several months the bicyclic lactones *3* were formed in moderate to good yields (Scheme 1).

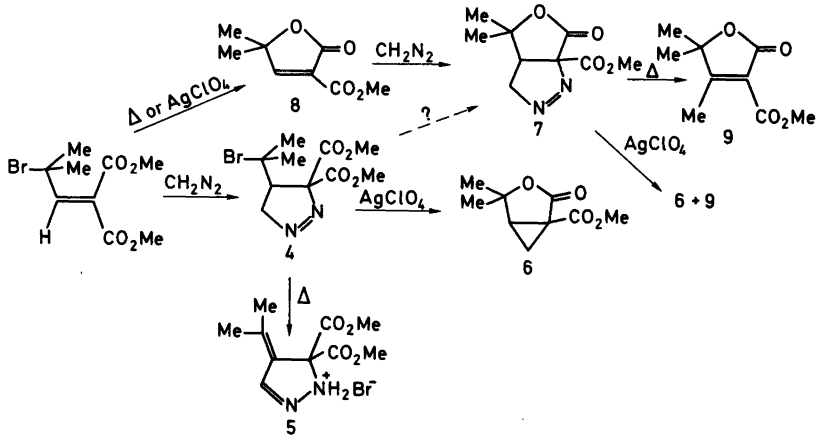
Thermal decomposition of pyrazoline *4* led to the hydrobromide of the exoalkylidene Δ^2-pyrazoline *5*.[3] However, when the same pyrazoline was treated with silver perchlorate at low temperature, the bicyclic lactone *6* was the only product (Scheme 2).

A possible route to *6* could be lactonization to the bicyclic pyrazolinolactone *7* followed by decomposition to *6*. In fact, analogues of *7* have been reported to form mixtures of bicyclic lactones (like *6*) and $\Delta^{\alpha,\beta}$-butenolides upon thermolysis and/or photolysis.[4,5] The butenolides are predominant in the thermolytic process,[4] while photolyses lead to the predominance of bicyclic lactones.[5]

As the reaction of *4* with silver perchlorate proceeded with simultaneous evolution of nitrogen and precipitation of silver bromide, it seemed impossible to synthesize *7* by this method. However, it could be prepared by the addition of diazomethane to butenolide *8*.[4,5] The reaction was complete within



Scheme 1.



Scheme 2.

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1 h while the reaction with dimethyl 2-bromo-2-methylpropylidenemalonate required about 20 h for completion at the same temperature. The reasons for this difference in reactivity are not known, but most likely they are of conformational nature.

The condensed pyrazolinolactone 7 is rather unstable, decomposing to the $\Delta^{\alpha,\beta}$-butenolide 9 [6] in methanol or benzene solution. However, in the presence of equimolar amounts of silver perchlorate an 80:20 mixture of 6 and 9 was obtained.

The role of silver ions in the decomposition of the Δ^1-pyrazolines is not known, but the possibility of complexation prior to decomposition is supported by the fact that when equimolar amounts of silver perchlorate and pyrazoline 4 were mixed in ethyl acetate solution at −60 °C, precipitation of a white solid took place. When filtered, the solid decomposed spontaneously with gas evolution, leaving behind silver bromide and the bicyclic lactone 6. Complexation of Δ^1-pyrazoline with Cu(II) [7] and formation of a reasonably stable iron−tetracarbonyl-Δ^1-pyrazoline σ-complex [8] have been reported.

Thus, in addition to the earlier reported formation of bicyclic lactones from lactones *via* Δ^1-pyrazolines,[4,5] it has now been demonstrated that the cyclopropane ring may be formed first, followed by lactonization either thermally or promoted by silver perchlorate.

Experimental. General. Melting points (uncorrected) were determined on a micro hot-stage. IR spectra were recorded on a Perkin-Elmer 457 Grating Infrared Spectrophotometer, ^{1}H NMR spectra on a Varian A60A spectrometer, ^{13}C NMR spectra on a FT NMR JEOL FX-60 spectrometer and mass spectra on an AEI MS 902 instrument. Elemental analyses were performed by I. Beetz, West Germany.

Δ^1-pyrazolines 1a, 1b, 4 and *7* were made by adding an ether solution of the proper diazoalkane to dimethyl 2-bromo-2-methylpropylidenemalonate (*1a, 1b, 4*) or γ,γ-dimethyl-α-methoxycarbonyl-$\Delta^{\alpha,\beta}$-butenolide (*7*).

Dimethyl 4-(1-bromo-1-methylethyl)-4,5-dihydro-5-phenyl-3H-pyrazole-3,3-dicarboxylate (1a). The reaction was run at −20 °C for 15 days, nitrogen atmosphere. Yield 64 %, m.p. 104−105 °C (dec.) (ether−pentane). Found: C 50.14; H 4.96, N 7.31. Calc. for $C_{16}H_{19}BrN_2O_4$: C 50.60; H 4.96; N 7.16. ^{1}H NMR ($CDCl_3$): δ 7.3 (5H, m), 5.77 (1H, d, J=10.0 Hz), 4.00 (3H, s), 3.82 (3H, s), 3.12 (1H, d, J=10.0 Hz), 1.93 (3H, s), 1.47 (3H, s). IR (KBr) 1760 and 1550 cm^{-1}. MS (IP 70 eV, *m/e*, rel. int.): 233 (M − N_2 − $CBrMe_2$, 100).

Dimethyl 4-(1-bromo-1-methylethyl)-5-(4-chlorophenyl)-4,5-dihydro-3H-pyrazole-3,3-dicarboxylate (1b). Reaction was run at −20 °C for 15 days, nitrogen atmosphere. Yield 81 %, m.p. 103−107 °C (dec.) (ether−pentane). Anal. $C_{16}H_{18}BrClN_2O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 7.3 (4H, 2d), 5.75 (1H, d, J=10.0 Hz), 4.00 (3H, s), 3.82 (3H, s), 3.07 (1H, d, J=10.0 Hz), 1.92 (3H, s), 1.48 (3H, s). IR (KBr): 1750 and 1545 cm^{-1}.

Dimethyl 4-(1-bromo-1-methylethyl)-4,5-dihydro-3H-pyrazole-3,3-dicarboxylate (4). Reaction run for 20 h at 0 °C. Yield 89 %. M.p. 67−68 °C (ether−pentane). Anal. $C_{10}H_{15}BrN_2O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 3.91 (3H, s), 3.75 (3H, s) ABX-system: ν_A 5.04, ν_B 4.59, ν_X 3.00, J_{AX}=8.5 Hz, J_{BX}=10.0 Hz, J_{AB}=18.0 Hz, 1.88 (3H, s), 1.84 (3H, s).

Methyl 5,5-dimethyl-3-oxo-2a,3,5a,6-tetrahydro-5H-furo[3,4-c]-pyrazole-2a-carboxylate (7). Yield 96 %, m.p. 57−59 °C (dec.). ^{1}H NMR ($CDCl_3$): δ 3.87 (3H, s), ABX-system: ν_A 5.05, ν_B 4.75, ν_X 3.08, J_{AX}=4 Hz, J_{BX}=2 Hz, J_{AB}=19 Hz. ^{13}C NMR (15.0 MHz, $CDCl_3$ at −20 °C): δ 164.5 (2×C=O), 106.5 (C2a), 85.3 (C5), 82.5 (C6), 54.3 (MeO), 45.0 (C5a), 30.8 and 24.4 (2×Me). IR: Decomposes.

Decomposition of Δ^1-pyrazolines. Dimethyl 2-(1-bromo-1-methylethyl)-3-phenyl-1,1-cyclopropanedicarboxylate (2a). A solution of *1a* was heated in toluene at 60 °C for 2 h. After evaporation of the solvent a colorless oil was obtained. M.p. 61−62 °C (heptane). Yield 95 %. ^{1}H NMR ($CDCl_3$): δ 7.28 (5H, s), 3.80 (3H, s), 3.47 (3H, s) 3.42 and 3.02 (2H, AB-quart. J=9.0 Hz), 1.95 (3H, s), 1.82 (3H, s).

Dimethyl 2-(1-bromo-1-methylethyl)-3-(4-chlorophenyl)-1,1-cyclopropanedicarboxylate (2b). Treating *1b* in the same way as *1a* gave *2b* in 65 % yield (after recrystallization). M.p. 53−55 °C (ether−pentane). Anal. $C_{16}H_{18}BrClO_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 7.23 (4H, s), 3.78 (3H, s), 3.47 (3H, s), 3.43 and 3.02 (2H, AB-quart. J=9.0 Hz), 1.95 (3H, s), 1.77 (3H, s). IR (KBr): 1735 cm^{-1}.

Dimethyl 4-isopropylidene-2,3-dihydro-4H-pyrazolium-3,3-dicarboxylate bromide (5). On refluxing *4* in benzene for a few minutes, *5* precipitates from the boiling solution. Essentially quantitative yield. Treatment of *5* with aqueous sodium bicarbonate−ether gave *the free base.* M.p. 76−77 °C. Anal. $C_{10}H_{14}N_2O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 7.15 (1H, s), ~6.5 (1 H, broad, s), 3.70 (6 H, s), 1.97 (3 H, s), 1.90 (3H, s). IR (KBr): 1650 and 1550 cm^{-1}. MS (IP 70 eV, *m/e*): 226 (M).

Methyl 4,4-dimethyl-2-oxo-3-oxa-[3.1.0]-bicyclohexane-1-carboxylate (6). To a solution of *4* (0.81 g, 2.6 mmol) in ethyl acetate (15 ml) cooled to −40 °C was added silver perchlorate monohydrate (0.65 g, 2.9 mmol) dissolved in ethyl acetate (10 ml). Warming the solution to −30 °C caused precipation of silver bromide and evolution of nitrogen. The solution was warmed to room temperature, silverbromide (0.49 g) filtered off, and the filtrate carefully washed with water. After drying ($MgSO_4$), the solvent was removed. The residue was chromatographed through a short column of SiO_2 using a

1:1 mixture of chloroform–dichloromethane as eluting solvent. Yield 73 %, m.p. 47–48 °C (dichloromethane–pentane). Anal. $C_9H_{12}O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 3.78 (3H, s), 2.5 (1H, m), 1.8 (2H, m), 1.52 (3H, s), 1.37 (3H, s). ^{13}C NMR (15.0 MHz, $CDCl_3$): 169.6 (C2), 167.3 and 52.8 (CO_2Me), 80.9 (C4), 37.7 (C5), 31.4 (C1), 29.1 and 23.8 (2 × Me), 19.9 (C6). IR (KBr): 1780, 1730 cm^{-1}. MS [IP 70 eV, *m/e* (% rel. int.)]: 184 (4, M), 169 (100, [M–15]).

α-Methoxycarbonyl-β-methyl-γ,γ-dimethyl-Δ^{α,β}-butenolide (9). A solution of 7 in methanol or benzene was heated at 50 °C until the gas evolution ceased (about 10 min). Evaporation of solvent gave a product shown by TLC and ^{1}H NMR to be identical to 9.[6] Yield was essentially quantitative.

Reaction of 7 *with silver perchlorate.* Compound 7 was dissolved in ethyl acetate and cooled to −78 °C and equimolar amounts of silver perchlorate monohydrate was added. Gas evolution first became visible by warming up to about room temperature. Evaporation of solvent gave a residue containing approx. 80 % *6* and 20 % *9* (TLC and ^{1}H NMR).

Bicyclic lactones from cyclopropanes (2). Methyl 4,4-dimethyl-2-oxo-6-phenyl-3-oxa-[3.1.0]-bicyclohexane-1-carboxylate (3). After several months standing at room temperature, *2a* was converted, almost completely, to the bicyclic lactone *3a*. Yield 86 % (after recrystallization). M.p. 138–141 °C (chloroform–pentane). Anal. $C_{15}H_{16}O_4$: C, H. ^{1}H NMR ($CDCl_3$): δ 7.27 (5H, s), 3.52 (3H, s), 3.08 and 2.95 (2H, AB-quart, J = 6.0 Hz), 1.60 (3H, s), 1.48 (3H, s). IR (KBr): 1770 and 1720 cm^{-1}.

*Methyl 6-(4-chlorophenyl)-4,4-dimethyl-2-oxo-3-oxa-[3.1.0]-bicyclohexane-1-carboxylate (*3b*).* Likewise, left for three months at room temperature *2b* was converted to *3b*. Yield 30 % (after recrystallization). M.p. 147–148 °C (chloroform–pentane). Anal. $C_{15}H_{15}ClO_4$: C, H. ^{1}H NMR ($CDCl_3$): $\delta \sim 7.3$ (4H, m), 3.58 (3H, s), 3.05 and 2.92 (2H, AB-quart., J = 6.0 Hz), 1.60 (3H, s), 1.50 (3H, s). ^{13}C NMR (15.0 MHz, $CDCl_3$): δ 169.1 (C2), 164.3 and 52.9 (CO_2Me), 134.5–130.9(2)–130.3(2)–129.0 (aryl), 81.7 (C4), 40.0 (C1), 37.8 (C5), 36.2 (C6), 29 and 24 (2 × Me). IR ($CHCl_3$): 1775 and 1720 cm^{-1}.

Reaction of 2b *with silver perchlorate.* To solution of *2b* (50 mg) in ethyl acetate (1 ml) was added an equimolar amount of silver perchlorate monohydrate in ethyl acetate (1 ml) at room temperature. Precipation of silver bromide occurred immediately. After filtration, the filtrate was washed carefully with water, dried ($MgSO_4$) and the solvent was removed. The residue was shown by ^{1}H NMR to be the bicyclic lactone *3b*, contaminated with about 5 % of what is thought to be the corresponding 2-isopropenyl cyclopropane derivative (loss of HBr).

1. Verhe, R., De Kimpe, N., De Buyck, L., Courtheyn, D. and Schamp, N. *Bull. Soc. Chim. Belg. 87* (1978) 215.
2. Berg, A. and Kolsaker, P. *Acta Chem. Scand. B 32* (1978) 665.
3. Kolsaker, P., Storesund, H. J. and Wøien, G. *To be published.*
4. Franck-Neumann, M. *Angew. Chem. 80* (1968) 42.
5. Pelletier, S. W., Djarmati, Z., Lajsik, S. D., Micovic, I. V. and Yang, D. T. C. *Tetrahedron 31* (1975) 1659.
6. Kolsaker, P. and Berg, A. S. *Acta Chem. Scand. B 33* (1979) 755.
7. Tortschanoff, K., Kisch, H. and Polansky, O. E. *Justus Liebigs Ann. Chem.* (1975) 449.
8. Kisch, H. *J. Organomet. Chem. C 38* (1972) 19.

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