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Metal Catalysed Rearrangement of Cyclopropanespiro-β-lactones to 2-Furanones.

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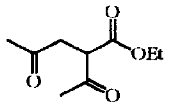
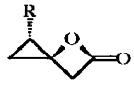
Abstract: The rearrangement of 5-oxo-4-oxaspiro[2.3]hexanes (cyclopropanespiro-β-lactones) to 2(5*H*)-furanones and 2(3*H*)-furanones is shown to be a general reaction which is promoted by metal catalysts. A mechanism is proposed, involving the novel insertion of a metal species into the O-C_β bond of the β-lactone ring, which explains the basic features of the reaction, including its regioselectivity.

The reaction of the exocyclic bond of diketene (**1**) with carbenes and carbenoids[1] from the usual sources (diazo compound/metal catalyst[2]; diazo compound/$h\nu$[3,4];phenyl trihalomethyl mercury[5]) leads in most cases to the formation of 5-oxo-4-oxaspiro[2.3]hexanes in good to poor yield; the reaction of diketene with diazoacetophenone, for example, gives the expected spiro product as a mixture of diastereoisomers (**2a**) and (**3a**). A consideration of the results obtained with diazo compounds in general suggests that the product obtained is a function of the diazo compound used for whereas diazoacetophenone gives only the expected spirolactones under metal catalysis, ethyl diazoacetate is reported to give a mixture of the spirolactone (**2b**) and the furanones (**4b**), (**5b**) and possibly (**6b**) under the same conditions[2], and ethyl diazoacetoacetate, photochemically, only the substituted levulinate (**7**)[4].

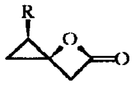

(1)



(7)



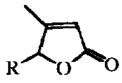
(2)



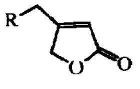
(3)

(2) - (6): a, R = $\mathrm{Ph}\overset{\displaystyle\mathrm{O}}{\overset{\|}{\mathrm{C}}}$ (O below C)

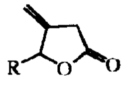
(2) - (6): b, R = $\mathrm{EtO}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}$



(4)



(5)

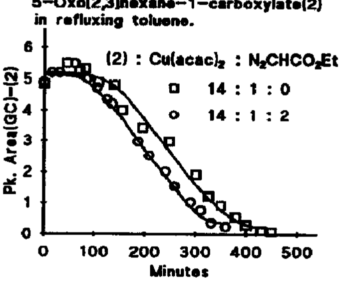


(6)

The formation of the furanones (**4b**), (**5b**) and (**6b**) was unexpected, the suggestion being made that they were formed from the spirolactones (**2b**) and (**3b**) in secondary reactions; however this was neither demonstrated nor considered from the mechanistic point of view. This paper provides evidence that the spirolactone-furanone conversion is a general reaction and attempts to remove some of the mechanistic uncertainty as a preliminary to the synthetic exploitation of the reaction.

The spirolactone **(2b)** and the furanones **(4b)**, **(5b)** and **(6b)**, were originally isolated[2] by fractional distillation of the crude filtered product obtained from the copper powder, or copper(II) sulphate, catalysed reaction of ethyl diazoacetate and diketene; when this reaction was repeated, IR and ^{1}H-NMR spectroscopy showed that the crude product was simply a mixture of the spirolactones **(2b)** and **(3b)**, from which the individual compounds could be isolated by rapid distillation followed by silica gel chromatography, or simply by chromatography alone. The fact that the formation of the furanones **(4b)**, **(5b)** and **(6b)**, could thus be avoided clearly supports the contention that they are indeed formed from the initially formed spirolactones and that this process is at least in part thermal. The possibility that the rearrangement is a simple thermal process is excluded as both **(2b)** and **(3b)** are effectively stable in refluxing toluene (the approximate pot temperature during the fractional distillation of the crude product mixture) and when heated in a sealed tube at 180^0 give product mixtures which do not contain any of the furanones **(Table)**. If however they are heated in the presence of any of a wide range of metal compounds (copper powder, copper(II) sulphate, copper(II) acetylacetonate, rhodium(II) acetate, etc), they are converted to a mixture of the furanones, whose formation during the distillation of the product from the cyclopropanation reaction can thus be explained by the assumption that a soluble metal compound formed in that reaction subsequently catalyses the spirolactone to furanone rearrangement. The possibility clearly exists that such a catalytically active species is formed in a reaction between the metal compound and ethyl diazoacetate and that thus the metal catalysed spirolactone to furanone rearrangement might be further accelerated by the addition of a diazocompound. Appropriate experiments **(Table)** showed that the diazocompound did not effect the rate of the rearrangement but simply reduced or eliminated the induction period which was found to be characteristic of the reaction **(Fig)**. It was also shown that the catalytically active species was not simply functioning as a Lewis acid as the use of boron trifluoride did not lead to furanone formation **(Table)**.

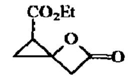
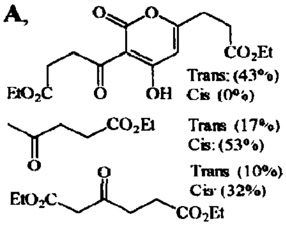
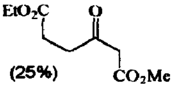
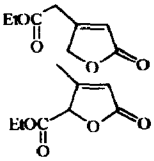
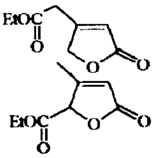
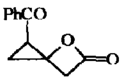
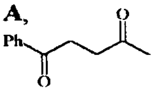
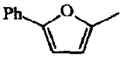
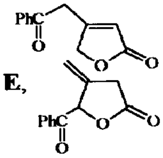
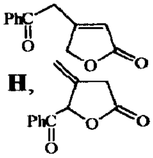
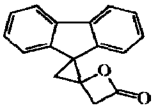
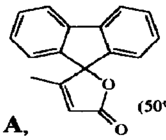
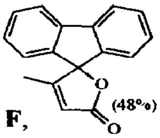
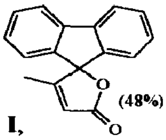
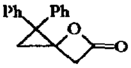
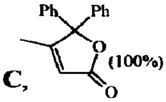
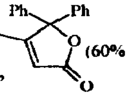
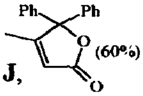
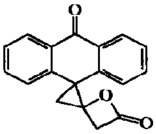
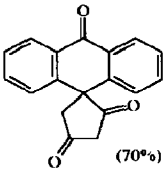
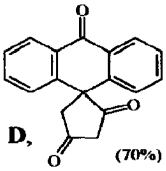
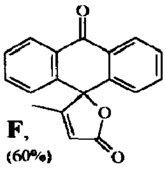
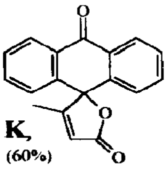
Fig. Rearrangement of Ethyl *trans*-5-Oxo[2,3]hexane-1-carboxylate(2) in refluxing toluene.



Thus it would appear that the spirolactone to furanone rearrangement is a metal catalysed process. A reasonable mechanistic framework would involve the formation of the catalytically active species by the interaction of the metal and diazocompound[6], or, in the absence of the latter, by the initial formation of a metallocycle[7] **(Scheme)** which subsequently breaks down giving the same active species. The induction period observed in the absence of a diazocompound corresponds to the formation of this species in a relatively slow reaction; the diazocompound generates it more efficiently, eliminating the induction period but ultimately giving similar reaction kinetics **(Fig)**.

The proposed mechanism allows the rationalization of all the features of the reaction that have emerged in the course of investigating the behaviour of a range of spirolactones **(Table)**. Thus the higher selectivity for the formation of 2(5*H*)-furanones **(5)** shown by the *trans* spirolactones can be interpreted in terms of the greater steric hindrance encountered in the key intermediate **(II)** during the formation of 2(3*H*)-furanones **(6)**; the *cis* isomer displays no such selectivity, a fact which is entirely in keeping with the structure of the intermediate **(I)** formed in this case. The significant inversion of selectivity which is observed in the rearrangement of the fluorene, diphenyl and anthrone compounds, occurs because of the stability of the intermediate **(III, Scheme)** which facilitates cyclopropane ring cleavage prior to furan ring formation.

Table

Spiro-β-lactone	Thermal	Lewis Acid Catalysed	Metal Catalysed	Diazocompound/ Metal Catalysed
	Conditions, Products (yield)	**Conditions,** Products (yield)	**Conditions,** Products (yield)	**Conditions,** Products (yield)
 Cis or Trans	**A**,  Trans: (43%) Cis (0%) Trans (17%) Cis: (53%) Trans (10%) Cis (32%) **B**, Trans: no reaction Cis: < 5% ethyl levulinate	**C**,  (25%)	**E**,  90-95%, Trans 1 9 : 1 Cis: 1.2 : 1	**H**,  90-95%, Trans 2 2 1 Cis. 1 2 1
 Cis or Trans	**A**,  (20%)  (5%) **B**, Trans or cis no reaction	**C**, Complex mixture of products	**E**,  90-95%; Trans. 2.1 : 1 Cis: 1 4 . 1	**H**,  80%, Trans 2.5 1 Cis 1.3 1
	 **A**, (50%) **B**, no reaction.	**D**, Complex mixture of products	 **F**, (48%)	 **I**, (48%)
	 **C**, (100%) **B**, no reaction.	**D**, Complex mixture of products	 **G**, (60%)	 **J**, (60%)
	 **B**, (70%) **A**, complex mixture of products.	 **D**, (70%)	 **F**, (60%)	 **K**, (60%)

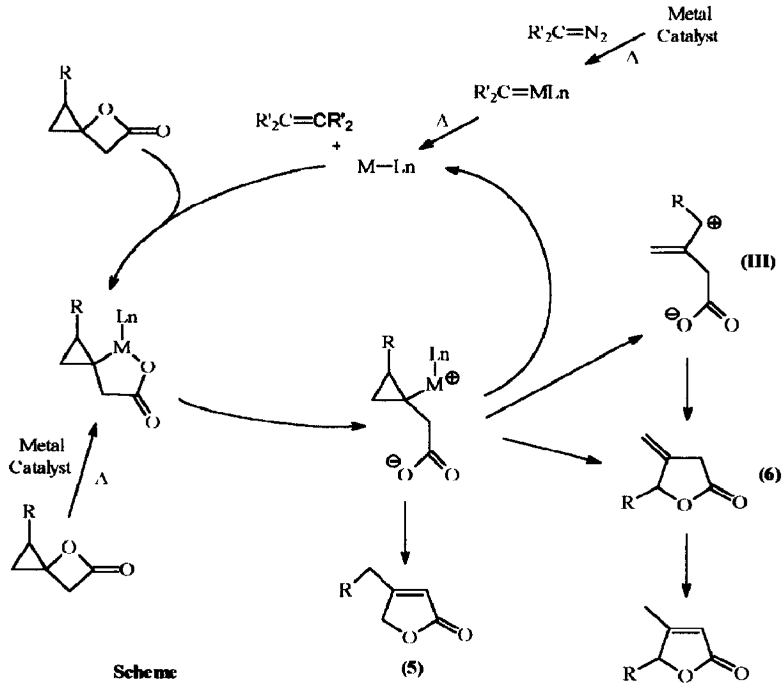
Conditions:

Thermal: A, 180°,sealed tube, ~50min; **B**, refluxing toluene, ~32h

Lewis Acid Catalysed: C, $BF_3.Et_2O$, CH_2Cl_2, 24h; **D**, $BF_3.Et_2O$, Et_2O, 24h

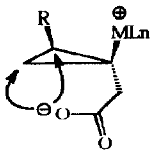
Metal Catalysed: E, $Cu(AcAc)_2$, refluxing toluene, ~6h; **F**, $Cu(AcAc)_2$, refluxing toluene, ~6h, SiO_2; **G**, $Cu(AcAc)_2$, refluxing toluene, ~5h, SiO_2

Metal/Diazocompound Catalysed: H, $Cu(AcAc)_2$, N_2CHCO_2Et, refluxing toluene, 5h; **I**, $Cu(AcAc)_2$, N_2CHCO_2Et, refluxing toluene, 15min, SiO_2; **J**, $Cu(AcAc)_2$, diazofluorene, refluxing toluene, 5h, SiO_2; **K**, $Cu(AcAc)_2$, N_2CHCO_2Et, refluxing toluene, 10min, SiO_2

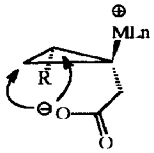


Scheme

(I)



(II)



The behaviour of these cyclopropanespiro-β-lactones under metal catalysis is thus consistent with a mechanistic scheme which is based on the insertion of a metal species into the O-C_β bond of diketene; in contrast, the thermal or Lewis acid catalysed reactions of these compounds leads to a wide range of products, the formation of which will be discussed elsewhere. The synthetic potential of this reaction is currently under investigation.

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