

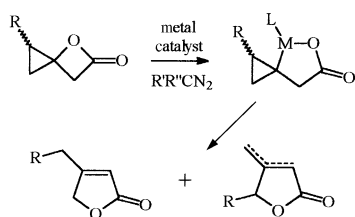
The reaction of cyclic 2-diazo-1,3-dicarbonyl compounds with β - and γ -lactones: formation of benzodioxepinones, benzodioxecinones and benzofurans

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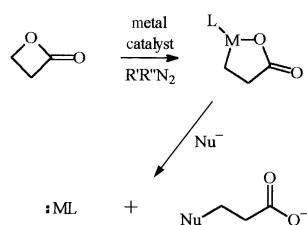
A novel reaction of cyclic 2-diazo-1,3-dicarbonyl compounds with lactones is described which, depending on the structure of the lactone, affords benzodioxepinones, benzodioxecinones or benzofurans.

We have proposed¹ that the key step in the metal-catalysed conversion of spiro[cyclopropane-1,3'-propano-3-lactone]s to furanones² involves the insertion of a metal species into the O-C_{spiro} bond of the lactone ring (Scheme 1). Compounds such as



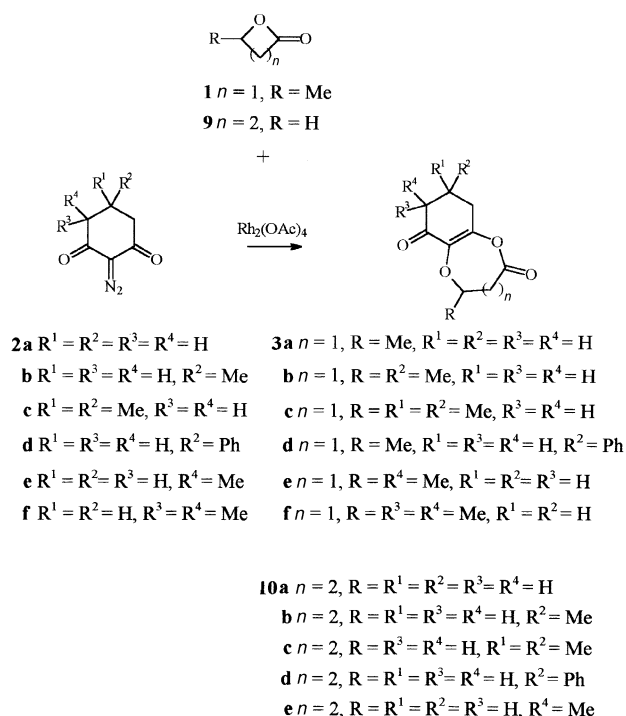
Scheme 1

rhodium acetate and copper acetylacetonate catalyse the reaction, their use being characterised by an induction period which is significantly reduced if a diazo compound is included in the reaction mixture. The novelty of the process suggested that the possibility of its being a general reaction of strained lactone rings, which would result in their activation towards nucleophilic attack and O-alkyl fission (Scheme 2), should be considered.

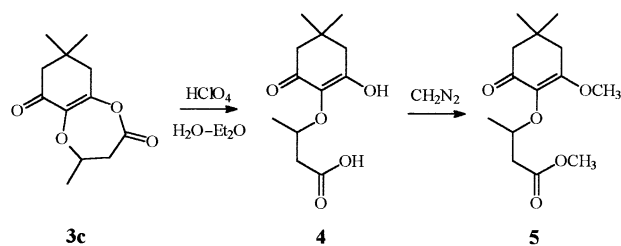


Scheme 2

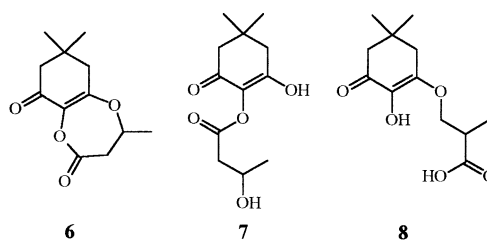
As it appeared possible that the presence of the spiro cyclopropane ring played a role in activating the lactone towards this insertion process, it was not surprising that when β -butyrolactone was heated in the presence of copper acetylacetonate or rhodium acetate, either with or without diazo compounds such as ethyl diazoacetate or diazofluorene, it was recovered unchanged. A reaction did take place, however, when a β -lactone **1** and a cyclic 2-diazo-1,3-dicarbonyl compound **2** were stirred in the presence of rhodium acetate, the product unexpectedly being the dioxepinone **3** (Scheme 3). The structure of dioxepinone **3c** was confirmed by conversion to the acid **4** and its methyl ester **5** (Scheme 4). An X-ray crystal structure of **4** (Fig. 1) unambiguously excluded the possibility that the



Scheme 3



Scheme 4



product of the reaction was the isomeric dioxepinone **6**, which would have given either **7** or **8** on hydrolysis. Although the yields of dioxepinone obtained are in all cases low, a large amount of polymeric material being formed as well, the reac-

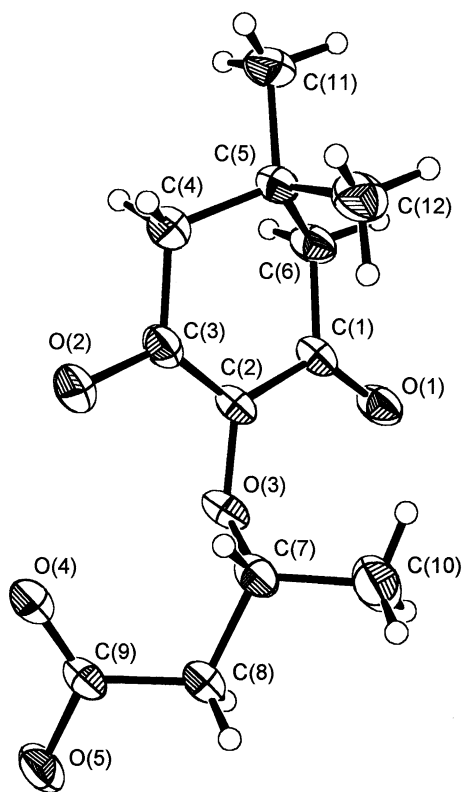
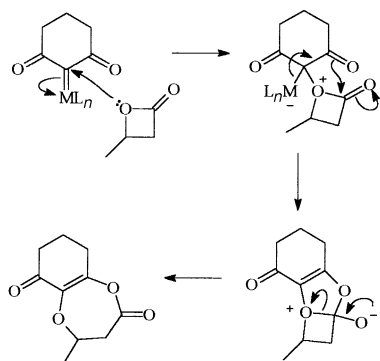


Fig. 1 ORTEX drawing (40% ellipsoids) of **4**

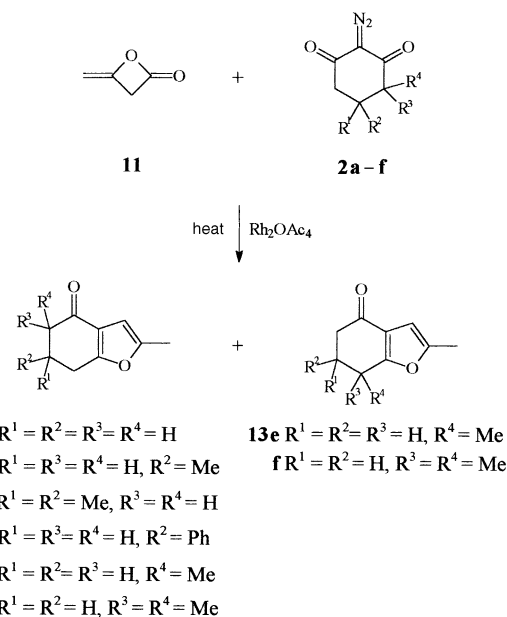
tion is experimentally simple and appears to be quite general; it is also moderately regioselective (Table 1).

Remarkably, the dioxecinones **10** are formed in the analogous rhodium acetate-catalysed reactions of cyclic 2-diazo-1,3-dicarbonyl compounds with the γ -lactone **9** (Table 1). The yields obtained are even lower than with β -butyrolactone, suggesting that ring strain is an important activating factor for the reaction. The formation of the benzodioxepinones and benzodioxecinones can be understood in terms of nucleophilic attack by the lactone on an electrophilic carbenoid (Scheme 5).



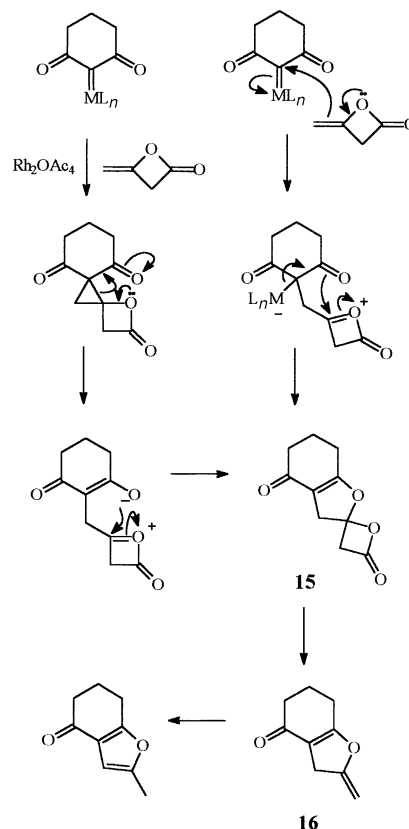
Scheme 5

In view of the above results, it might be expected that the reaction of cyclic 2-diazo-1,3-dicarbonyl compounds with diketene **11** would give products resulting from either cyclopropanation of the exocyclic double bond or insertion of the metal into the O–C bond, or possibly both. In fact the reaction ultimately results in the formation of the benzofurans **12** and **13** (Scheme 6), a process which is quite general but of moderate regioselectivity (Table 2). The diketene is here behaving as a vinyl acetate equivalent, Pirrung having shown³ that vinyl acetate reacts with these diazo compounds to give benzofurans. The isolation of products with exocyclic double bonds **16** (Scheme 6) which, with the exception of **14** (Table 2), isomerise to benzo-



Scheme 6

furans during chromatography or on standing, provides an indication of how the reaction proceeds. Such products could be formed from **15** by the thermal elimination of carbon dioxide (Scheme 7); this reaction is reported⁴ to involve the



Scheme 7

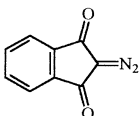
build up of positive charge at C(4), and thus could be facilitated by a resonance interaction with the oxygen of the dihydrofuran ring. Although **15** could be a rearrangement product of an initially formed spiro[cyclobutane-1,3'-propano-3'-lactone] (Scheme 7), such behaviour would not be consistent with that observed for other such compounds which form furanones under these conditions. The metal-catalysed reactions of cyclic 2-diazo-1,3-dicarbonyl compounds are often significantly

Table 1 The Rh₂(OAc)₄ catalysed reaction of 2-diazo-1,3-dicarbonyl compounds with β- and γ-lactones

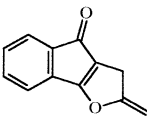
Lactone	Diazo compound	Product	Yield (%)
1	2a	3a	22
1	2b	3b	18
1	2c	3c	26
1	2d	3d	18
1	2e	3e	6
1	2f	3f	16
9	2a	10a	5
9	2b	10b	5
9	2c	10c	3
9	2d	10d	8
9	2e	10e	3

Table 2 The reaction of 2-diazo-1,3-dicarbonyl compounds with diketene

Diazo compound	Product (yield, %)
2a	12a (29)
2b	12b (44)
2c	12c (46)
2d	12d (43)
2e	12e (35), 13e (6)
2f	12f (28), 13f (14)



2a



14 (37)

different⁵ from those of other α-diazo carbonyl compounds, giving rise to metal carbenoids which display formal dipolar character. Thus an alternative route to **15** involving an effective dipolar cycloaddition to the exocyclic double bond of diketene (Scheme 7) may be in operation in this case.

In an attempt to improve the poor yields obtained in these exploratory experiments, reactions were carried out using rhodium trifluoroacetate as catalyst (Table 3). These results indicate that the reactions may be more complex than the proposed mechanisms suggest, but also that it may be possible to significantly improve the yields by a more appropriate choice of catalyst. Catalyst and reaction condition studies, and the possibility of extending the reaction to cover other systems such as lactams, are currently under way.

Experimental

The following are sample procedures.

4,8,8-Trimethyl-3,4,6,7,8,9-hexahydro-2H-1,5-benzodioxepine-2,6-dione 3c

2-Diazo-5,5-dimethylcyclohexane-1,3-dione (2.0 g, 0.012 mol) and Rh₂(OAc)₄ (3 mg, 6.8 μmol) were added to freshly distilled β-butyrolactone (7.0 g, 0.08 mol) and the mixture was stirred at room temp. for 15 h, at which point the diazo compound had completely reacted (checked by IR). After most of the excess β-butyrolactone had been removed by distillation (0.5 mmHg, 50 °C), the oily residue was dissolved in chloroform and was placed on a column of silica gel (30 g). Elution with diethyl ether–light petroleum (bp 40–60 °C) (1 : 1) gave some residual β-butyrolactone and a trace amount of *trans*-but-2-enoic acid; further elution with diethyl ether gave, after removal of the solvent, an oil (1.6 g). Light petroleum (bp 40–60 °C) was added to this oil and the mixture was heated on a steam bath, EtOH being added until dissolution occurred. The resulting solution was cooled in an ice–salt bath to give **3c** (0.7 g, 26%), mp 74–76 °C (Found: C, 63.9; H, 7.0. C₁₂H₁₆O₄ requires C, 64.3; H, 7.2%); ν_{max}(Nujol)/cm⁻¹ 1785 (vinyl ester), 1671 (α,β-unsaturated

Table 3 The effect of catalyst structure on the reaction of 2-diazo-5,5-dimethylcyclohexane-1,3-dione with lactones

Lactone	Catalyst	t/h	Yield (%)
1	Rh ₂ (OAc) ₄	110	26
1	Rh ₂ (OCOCF ₃) ₄	15	13
10	Rh ₂ (OAc) ₄	12	3
10	Rh ₂ (OCOCF ₃) ₄	110	15
11	Rh ₂ (OAc) ₄	18	46
11	Rh ₂ (OCOCF ₃) ₄	96	18

ketone) and 1638 (alkene); δ_H(270 MHz; CDCl₃) 1.14 (3 H, s, 8-Me), 1.15 (3 H, s, 8-Me), 1.41 (3 H, d, *J* 6.3, † 4-Me), 2.41 (2 H, s, 7-H₂), 2.51 (2 H, s, 9-H₂), 2.66 (1 H, dd, *J* 6.2 and 13.0, 3-H), 3.00 (1 H, dd, *J* 6.0 and 13.0, 3-H), 4.86 (1 H, m, 4-H).

9,9-Dimethyl-2,3,4,5,7,8,9,10-octahydro-1,6-benzodioxecine-2,7-dione 10c

As described above and using rhodium(II) trifluoroacetate dimer (3 mg, 4.6 μmol) as catalyst, 2-diazo-5,5-dimethylcyclohexane-1,3-dione (2.0 g, 0.012 mol) reacts in 110 h with γ-butyrolactone (10.0 g, 0.116 mol) to give 9,9-dimethyl-2,3,4,5,7,8,9,10-octahydro-1,6-benzodioxecine-2,7-dione **10c** (0.37 g, 16%), mp 133–134 °C (Found: C, 64.1; H, 7.0. C₁₂H₁₆O₄ requires C, 64.3; H, 7.2%); ν_{max}(Nujol)/cm⁻¹ 1769 (vinyl ester), 1675 (α,β-unsaturated ketone) and 1641 (alkene); δ_H(270 MHz; CDCl₃) 1.14 (6 H, s, 8-Me), 2.04 (2 H, m, 4-CH₂), 2.37 (2 H, s, 8-CH₂), 2.49 (2 H, s, 10-H₂), 2.56 (2 H, m, 3-CH₂) and 3.94 (2 H, t, *J* 5.9, 5-CH₂).

2,6,6-Trimethyl-4,5,6,7-tetrahydro-1-benzofuran-4-one 12c

2-Diazo-5,5-dimethylcyclohexane-1,3-dione (2.5 g, 0.015 mol) and Rh₂(OAc)₄ (3 mg, 6.8 μmol) were added to freshly distilled diketene (8.0 g, 0.1 mol) and the mixture was stirred at room temp. for 22 h, at which point the diazo compound had completely reacted (checked by IR). After the excess diketene had been removed at room temp. (0.1 mmHg), Kugelrohr distillation (bath temperature: 80–140 °C, 0–1 mmHg) of the residue gave 2,6,6-trimethyl-4,5,6,7-tetrahydro-1-benzofuran-4-one **12c** (1.2 g, 46%), mp 74–76 °C (lit.⁶ 74–75 °C) (¹H NMR analysis of the crude product obtained after removal of excess diketene showed it to be a 2 : 1 mixture of the title compound and 2-methylene-6,6-dimethyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one); δ_H(270 MHz; CDCl₃) 3.48 (2 H, m, 3-CH₂), 4.43 and 4.78 (each 1 H, each q, *J*_{gem} = *J*_{long-range} = *J*_{long-range} 2.6, C=CH₂).

Crystal data and structure refinement for 4

C₁₂H₁₆O₅, *M* = 240.25, monoclinic, space group *P*2₁/*n*, *a* = 11.447(2), *b* = 9.566(2), *c* = 11.666(2) Å, β = 100.450(10)°, *V* = 1256.3(4) Å³, *Z* = 4, *D*_c = 1.270 Mg m⁻³, *F*(000) = 512, μ(Mo-Kα) = 0.099 mm⁻¹, crystal size 0.45 × 0.33 × 0.28 mm.

Intensity data were collected at 293 K on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated radiation, λ = 0.71069 Å. Data were corrected for Lorentz and polarisation effects but not for absorption. The structure was solved by direct methods using SHELXS-86,⁷ and refined by full-matrix least-squares on *F*² using SHELXL-93.⁸ SHELX operations were rendered paperless using ORTEP which was also used to obtain the drawing.⁹ Hydrogen atoms were included in calculated positions with thermal parameters 30% larger than the atom to which they were attached. The two hydroxy hydrogens were not included in the refinement model. Refinement with 156 parameters and 3652 independent reflections in the range 2.29 < θ < 29.96° gave *R*₁ = 0.0816 and *wR*₂ = 0.2519. The relatively high *R* index, and the residual peak at 1.052 e Å⁻³ which occurs at 0.98 Å from C(7), are both due to the weak diffraction obtained from the crystal of **4**.

† *J* values are given in Hz.

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/74.

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