Tetrahedron Letters,Vol.28,No.41,pp 4787-4788,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

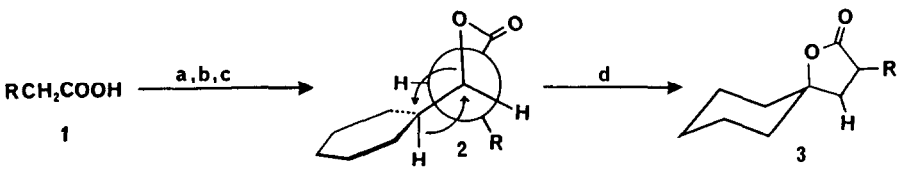
A NEW SYNTHESIS OF SUBSTITUTED SPIRO BUTYROLACTONES VIA DYOTROPIC REARRANGEMENT

T. Howard Black* and William J. DuBay III

Department of Chemistry, Eastern Illinois University
Charleston, Illinois 61920

Spiro butyrolactones bearing various α-substituents have been synthesized in three steps from acetic acid derivatives; the sequence employs a dyotropic rearrangement as its pivotal step.

Spiro lactones have attracted much attention in recent years, and many methods are known for their synthesis.[1] These procedures, however, typically afford only unsubstituted lactones, so that if compounds bearing substituents alpha to the carbonyl are desired (especially those unavailable via enolate alkylation), additional synthetic manipulations are necessary. We have developed a new, expedient, and high-yield method for the preparation of α-substituted spiro butyrolactones (1-oxaspiro[5.4]-decan-2-ones) from cyclohexanecarboxaldehyde and acetic acid derivatives utilizing a dyotropic rearrangement[2] as the pivotal step.



a=2LDA,THF; b= ⟨⟩-CHO; c=$PhSO_2Cl$; d=$MgBr_2$

The three-step sequence, which can be executed quite rapidly, is illustrated above. The β-hydroxy acids available via treatment of substituted acetic acid dianions (from **1** and LDA) with cyclohexanecarboxaldehyde are dehydrated at 0° to afford β-lactones **2**.[3] Brief exposure to magnesium bromide[4] effects the simultaneous sigma bond migrations leading to spiro lactones **3**. Yield data for representative compounds are summarized in Table I.

A fundamental requirement of dyotropic rearrangements is that the migrating bonds be capable of adopting a trans coplanar conformation such that maximum bond overlap occurs in the transition state.[2] Theoretically, all three bonds to the cyclohexyl carbon atom adjoining the lactone ring are capable of migration in the rearrangement step via rotation about the single bond joining the cyclohexyl and lactone moieties. However, it appears that hydride migration is the preferential reaction pathway when appropriate bond alignment can take place.

It is clear that, in the present cases, there is essentially unrestricted rotation around the cyclohexyl-lactone bond. This is a consequence of the trans relationship between the cyclohexane ring and the R-substituent, established during the condensation reaction comprising the first step of this sequence, which affords the threo hydroxy acid almost exclusively.[5]

The preparation of **3a** (R=Me) illustrates the method. The propiolactone **2a** (770 mg, 4.58

Table I[a]

Entry	Suffix	R	1[b]	2[c]	3[d]
1	**a**	Me	93	90	75
2	**b**	Et	100	77	50
3	**c**	OMe	38	74	42
4	**d**	Ph	83	90	76
5	**e**	OPh	62	95	86
6	**f**	SPh	85	91	72

a. All yields pertain to material purified as specified.
b. Yields for β-hydroxy acids after recrystallization from chloroform.
c. Filtered through silica gel.
d. Recrystallized from hexane (if crystalline) or distilled (if oil).

mmol), prepared from 3-cyclohexyl-2-hydroxy-1-methylpropionic acid,[3] was dissolved in anhydrous ether (20 mL) and treated at 20° with magnesium bromide etherate (1.18 g, 4.58 mmol). After 6 hours, the mixture was poured into water and the product isolated via ether extraction. Recrystallization from hexane provided white needles (370 mg, 48% yield); mp 70.5-71° (lit.[6] bp 125-135/0.05 torr); λ_{max} 1768 cm^{-1} (lit.[6] 1765 cm^{-1}).

In conclusion, we feel that our method is advantageous in view of its simplicity, overall yield, and especially ease of placing substituents at the alpha carbon of the lactone ring. Extensions of this methodology are under active investigation.

Acknowledgement: We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

References

1. Canonne, P.; Belanger, D.; Lemay, G.; Foscolos, G.B. J. Org. Chem. **1981**, 46, 3091 and references cited therein.
2. For a review, see Reetz, M.T. Adv. Organomet. Chem. **1977**, 16, 33.
3. Both the hydroxy acids and β-lactones were synthesized according to the method described in Adam, W.; Baeza, J.; Liu, J.-C. J. Am. Chem. Soc. **1972**, 94, 2000.
4. Mulzer, J.; Bruntrup, G. Angew. Chem. Int. Ed. Engl. **1979**, 18, 793.
5. Mulzer, J.; Segner, J.; Bruntrup, G. Tetrahedron Lett. **1977**, 4651.
6. Jacobson, R.M.; Lahm, G.P.; Clader, J.W. J. Org. Chem. **1980**, 45, 395.

(Received in USA 1 June 1987)