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A ONE-STEP SYNTHESIS OF γ-PYRONES

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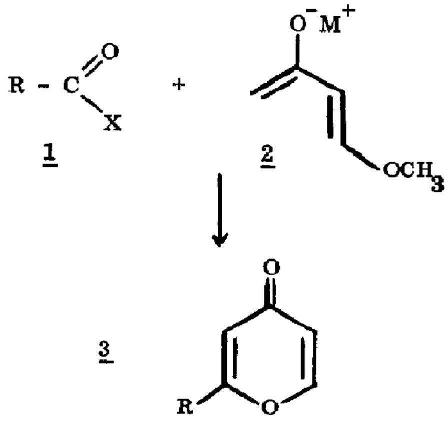
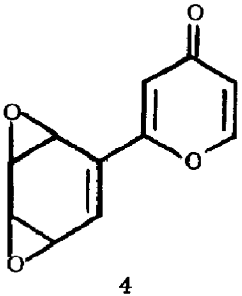
Summary: The potassium enolate of 4-methoxy-3-buten-2-one reacts with acid chlorides anhydrides and acylimidazoles by C-acylation and *in situ* cyclization to afford 2-substituted γ-pyrones directly.

Gamma pyrones are widely distributed in nature and as a consequence, have become accessible in the laboratory by a variety of synthetic methods.[2] Notable among these is the base promoted condensation of vinylogous esters with methyl formate.[3] This reaction first forms an enolic formylketone which subsequently undergoes cyclization in strong acid. As part of our effort to synthesize the acid-labile antibiotic γ-pyrone diepoxide[4] LL-Z1220 4, we sought to develop an alternative construction of such functionalized heterocycles. A recent report by Koreeda and Akagi[5] on this subject now prompts us to disclose related results wherein a one-pot substituted γ-pyrone synthesis has been realized under non-acidic conditions as depicted below.





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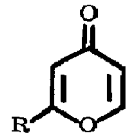
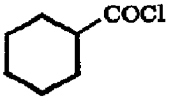
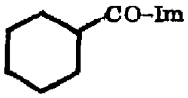
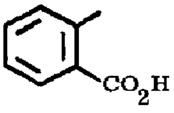
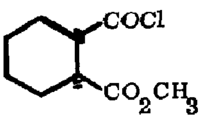
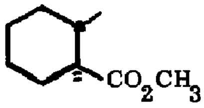
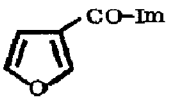
The critical C-acylation of 2 in THF was studied as a function of enolate structure $(Li^+, Na^+ K^+)$ using 1 (R=cyclohexyl, X=Cl) and assayed by direct conversion to 3. Optimum yields were obtained by treating 1 with 2.2 equiv of the potassium enolate of 2 at -78°C,[6] then adding water and stirring for 30 min at rt. Ether extraction afforded the corresponding pyrones as summarize in the Table for six representative cases. Structure 9, postulated to arise from the degradation of LL-Z-1220 in acidic periodate, was prepared from 3-furoic acid imidazole; synthetic material unambigously confirmed its assigned structure.[7]

TABLE

Acylating Agent		(% Yield)
	5 R = cyclohexyl mp 57 - 58°	(23)
 mp 84 - 88°	5	(60)
PhCOCl	6 R = Ph	(82)
phthalic anhydride	7 R = 	(84)
	8 R = 	(27)
	9 R =  mp 136 - 140°	(50)

Im = Imidazole; Pyrones 5, 6 and 9 exhibited spectroscopic properties identical with literature values for these compounds; 7 was further characterized as its methyl ester.

REFERENCES AND FOOTNOTES

1. Fellow of the Alfred P. Sloan Foundation, 1978-1980; Recipient of a Camille and Henry Dreyfus Teacher-Scholar Grant, 1978-1983. 2. R. Livingstone in "Rodd's Chemistry of Carbon Compounds," S. Coffey, ed., Elsevier (Amsterdam, 1977) Vol IV (E) Ch. 20. 3. (a) P. Beak and G.A. Carls, J. Org. Chem., 39, 2678 (1964); (b) I. Takasu and H. Hotta, Chem. Abst., 78 P124442a. 4. D.B. Borders and J.E. Lancaster, J. Org. Chem., 39, 435 (1974). 5. M. Koreeda and H. Akagi, Tetrahedron Lett., 21, 1197 (1980). 6. The enolate was prepared from equimolar amounts of methoxybutenone and potassium tert-butoxide. 7. We wish to acknowledge the National Institutes of Health (CA 17670) for financial support.