

Cyclisation of Alkynecarboxylic Acids: a Route to an Oxaspirolactone

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Pent-4-ynoic acid, in various alcohols, was cyclised in the presence of yellow mercury(II) oxide to 4,5-dihydro-5-alkoxy-5-methylfuran-2(3*H*)-ones; 8-hydroxyoct-4-ynoic acid was also cyclised in dimethylformamide to 1,6-dioxaspiro[4.5]decan-2-one in good yield.

We have recently reported that various alkynecarboxylic acids are cyclised in aprotic solvents in the presence of a catalytic

amount of yellow mercury(II) oxide to give γ -methylenebutyrolactones in excellent yields.¹ In contrast with these

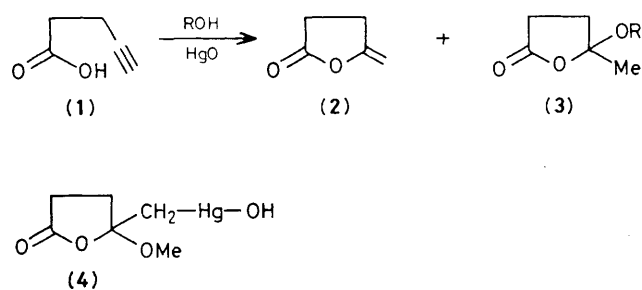


Table 1

	R	Yield, % (2)	(3)
a	Me	0	68
		18	34 ^a
b	Et	0	64
c	Pr ^t	77	Trace
d	Bu ⁿ	31	42
e	Bu ^t	81	Trace

^a Refluxed for 1 h.

results, pent-4-ynoic acid in methanol solution cyclised to give 4,5-dihydro-5-methoxy-5-methylfuran-2(3*H*)-one as the sole product.

Now we report the cyclisation of pent-4-ynoic acid in various alcohols. Furthermore, in order to apply this method to intramolecular double cyclisation reactions, the synthesis of 8-hydroxyoct-4-ynoic acid was carried out and using this alkyne-carboxylic acid a novel and simple synthesis of 1,6-dioxaspiro[4.5]decan-2-one was accomplished.

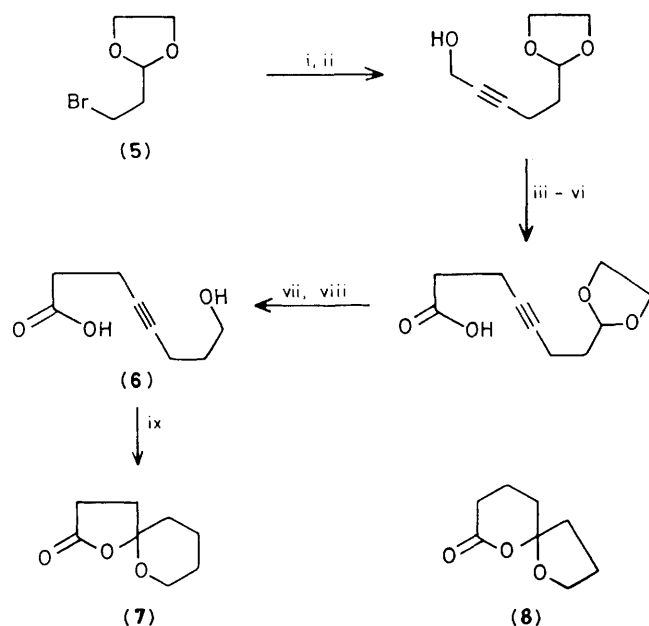
Pent-4-ynoic acid (1) was refluxed in absolute methanol for 4 h in the presence of yellow mercury(II) oxide to give the ether (3a) (68%). The structure of (3a) was assigned from the spectral data.† The yield of (3a) was lower than that of γ -methylenebutyrolactone (2) which was obtained quantitatively by cyclisation in an aprotic solvent. This result may be attributable to the formation of the mercury adduct (4), which was detected by silica gel t.l.c. as highly polar products; however the structure of (4) could not be ascertained from the physical data.‡

Compound (1) was also cyclised in ethanol, propan-2-ol, n-butanol, and 2-methylpropan-2-ol to afford the corresponding cyclic products; the results are listed in Table 1. These results show that the formation of the ether (3) decreased as the alcohol becomes more bulky, *i.e.* the reactivity of the addition of the alcohol to the double bond in the lactone (2) is decreased by steric hindrance.

When the refluxing time for the cyclisation of (1) in methanol was shortened to 1 h (2) and (3a) were obtained in 18 and

† I.r. (neat) 1785 cm^{-1} ; ^1H n.m.r. $\delta(\text{CDCl}_3)$ 1.60(s, 3H), 2.25(m, 2H), 2.55(m, 2H), and 3.35(s, 3H); M^+ , m/z 130(M^+ , 0.76), 99(100), 86(44), and 43(97).

‡ Although the intermediate (4) could not be isolated, a speculative structure for (4) was obtained by comparison with the mercury containing intermediate reported by H. C. Brown (H. C. Brown and G. J. Lynch, *J. Org. Chem.*, 1981, **46**, 531).



Scheme 1. i, $\text{CH}_2\text{=CHLi}\cdot\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2$ in Me_2SO . ii, EtMgBr -tetrahydrofuran (THF), $(\text{CH}_2\text{O})_n$. iii, PBr_3 -pyridine. iv, diethyl malonate, NaH , THF. v, $\text{OH}^-/\text{EtOH-H}_2\text{O}$. vi, H_3O^+ , heat. vii, $\text{HCl-MeOH-H}_2\text{O}$. viii, $\text{NaBH}_4\text{-MeOH}$. ix, HgO -dimethylformamide, reflux.

34% yields, respectively. Isolated compound (2) also gave (3a) on treatment with methanol under the same reaction conditions. These results show that (2) is an intermediate in the formation of the ether (3).

The synthesis of 8-hydroxyoct-4-ynoic acid (6) was carried out from (5), as illustrated in Scheme 1.

The compound (6), m.p. 38–38.5 °C, was cyclised in refluxing dimethylformamide for 2 h in the presence of a catalytic amount of yellow mercury(II) oxide to afford 1,6-dioxaspiro[4.5]decan-2-one (7) (73%). The structure of (7) was indicated by the spectral data.§ In this cyclisation reaction the six-membered lactone (8) was not detected.

Since compounds which contain 1,6-dioxaspiro-[4.5]-decane and -[4.4]nonane structures have been found in several plant species and as insect pheromones,^{2,3} the easily obtained spiro-lactanes can be used to synthesise these natural products.

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References

- M. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1978, 649; M. Yamamoto, *J. Chem. Soc., Perkin Trans. 1*, 1981, 582; M. Yamamoto, S. Tanaka, K. Naruchi, and K. Yamada, *Synthesis*, 1982, 850.
- W. Francke, V. Heeman, B. Gerken, J. A. A. Renwick, and J. P. Vite, *Naturwissenschaften*, 1977, **64**, 590.
- W. Francke, G. Hindorf, and W. Reith, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 862.

§ Spectral data of (7): i.r.(neat) 1770 cm^{-1} ; ^1H n.m.r. $\delta(\text{CCl}_4)$ 1.78(m, 6H), 1.9–2.2(m, 2H), 2.3–2.7(m, 2H), and 3.70(m, 2H); M^+ , m/z 156.0799, calc. 156.0786, relative intensities in parentheses, 156(M^+ , 4), 138(9), 112(77), 111(22), 101(100), 98(63), 83(37), and 52(14).