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DIANION OF *N*-(o-METHOXYPHENYL)-2-METHYLPROPENAMIDE: A NEW REAGENT FOR THE CONVENIENT SYNTHESIS OF α-METHYLENE-γ-BUTYROLACTONES FROM CARBONYL COMPOUNDS

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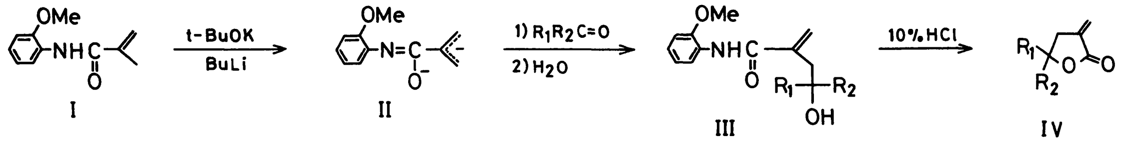
Dianion of *N*-(o-methoxyphenyl)-2-methylpropenamide was successfully generated on treatment of the amide with t-BuOK-BuLi at -78°C in THF and utilized as the key reagent for the synthesis of γ-substituted α-methylene-γ-butyrolactones.

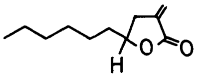
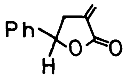
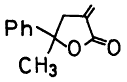
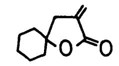
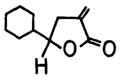
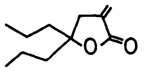
The conversion of carbonyl compounds into α-methylene-γ-butyrolactones is an important synthetic process which has received considerable recent attention.[1] Although several procedures have been developed for such transformation, there is no general method for the synthesis of α-methylene-γ-butyrolactones using carbanions derived from α,β-unsaturated amides.[2] The generation of the stable carbanions from α,β-unsaturated amides is difficult owing to the tendency of these carbanions to undergo facile Michael addition to the starting amides.[3]

We report herein the successful generation of the stable carbanion of *N*-(o-methoxyphenyl)-2-methylpropenamide (I) and its application to the synthesis of γ-substituted α-methylene-γ-butyrolactones.[4,5]



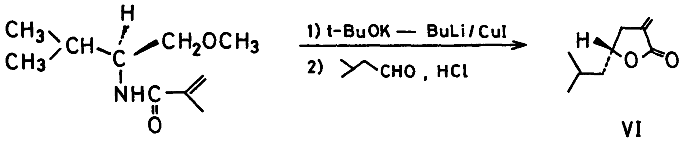
A typical procedure for the conversion of acetophenone into γ-methyl-α-methylene-γ-phenyl-γ-butyrolactone (IVc) is as follows. To a suspension of t-BuOK (44 mmol) in dry THF (60 ml) at -78°C under N_2 was added a solution of I (20 mmol) in 5 ml of THF. After 10 min, butyllithium (44 mmol) was added and the resulting orange suspension was stirred for 30 min. Acetophenone (22 mmol) in 5 ml of THF was then added. Product isolation and purification by chromatography gave a 59% yield of IIIc as a viscous oil; ^{1}H-NMR(CCl_4) δ 8.30(m, 2H), 7.10(m, 8H), 5.55(s, 1H), 4.98(s, 1H), 4.95(m, 1H), 3.80(s, 3H), 2.76(m, 2H), 1.53(s, 3H). Hydrolysis of IIIc in 10% hydrochloric acid afforded an 89% yield of IVc; ^{1}H-NMR ($CDCl_3$) δ 7.30(m, 5H), 6.16(t, 1H), 5.55(t, 1H), 3.13(t, 2H), 1.70(s, 3H); IR(neat) 1752(COO), 1660(C=C) cm^{-1}. Anal. Found: C, 76.52; H, 6.59%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.44%. Other examples of this new procedure are listed in

Table 1. Synthesis of α-methylene-γ-butyrolactones

Carbonyl compound	III, Yield(%)[a]	IV, Yield(%)[a,b]	Mp, °C
Heptanal	57 (IIIa)	 (IVa) 88	oil[c]
Benzaldehyde	46 (IIIb)	 (IVb) 80	54-55[d]
Acetophenone	59 (IIIc)	 (IVc) 89	oil[c]
Cyclohexanone	55 (IIId)	 (IVd) 87	oil[c]
Cyclohexanecarbaldehyde	45 (IIIe)	 (IVe) 88	55-56
4-Heptanone	56 (IIIf)	 (IVf) 88	oil[c]

a) Isolated yields. b) All products gave satisfactory analytical results and spectral data. c) Purified by column chromatography since distillation led to decomposition.
d) Lit.[2] 49-54°C.

Table 1. This strategy can also be applied to the asymmetric synthesis of α-methylene-γ-butyrolactone. The chiral amide (V) was conveniently prepared from L-valine. 3-Methylbutanal was treated with the dianion prepared from V in the presence of 1.1 equiv of CuI and the resulting adduct was then heated under reflux in 10% hydrochloric acid. The desired lactone VI was thus obtained in 16% overall yield (12% optical purity).[6]



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VI

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References and Notes

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3) W. Bannwarth, R. Eidenschink, and T. Kauffmann, Angew. Chem. Int. Ed. Engl., 13, 468 (1974); J. E. Baldwin and W. A. Dupont, Tetrahedron Lett., 1980, 1881.
4) A report describing the β'-lithiation of α,β-unsaturated amides has recently appeared. P. Beak and D. J. Kempf, J. Am. Chem. Soc., 102, 4550 (1980); see also J. A. Oakleaf, M. T. Thomas, A. Wu, and V. Snieckus, Tetrahedron Lett., 1978, 1645.
5) Reported in April 1980 at the Meeting of the Japan Chemical Society, Osaka. Abstracts II, p 1023.
6) Based on $[\alpha]_D$ +67.0° (c 1.44, EtOH); see K. Mori, Tetrahedron, 32, 1101 (1976).

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