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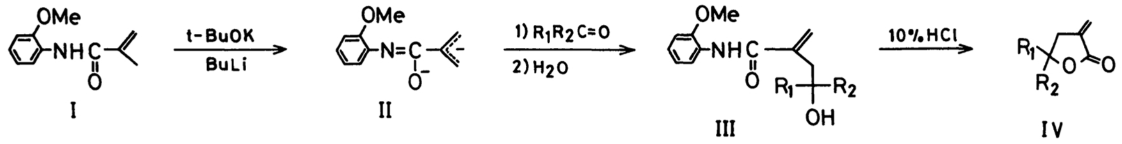
Dianion of *N*-(o-methoxyphenyl)-2-methylpropenamide was successfully generated on treatment of the amide with t-BuOK-BuLi at -78°C in THF and utilized as the key reagent for the synthesis of γ-substituted α-methylene-γ-butyrolactones.

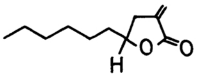
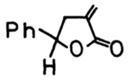
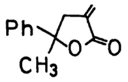
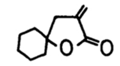
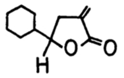
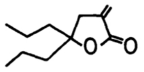
The conversion of carbonyl compounds into α-methylene-γ-butyrolactones is an important synthetic process which has received considerable recent attention.[1] Although several procedures have been developed for such transformation, there is no general method for the synthesis of α-methylene-γ-butyrolactones 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

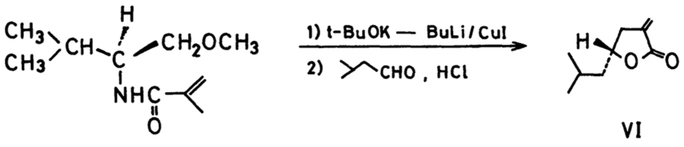
Table 1. Synthesis of α-methylene-γ-butyrolactones

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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References and Notes

1) P. A. Grieco, Synthesis, 1975, 67; R. B. Gammill, C. A. Wilson, and T. A. Bryson, Synth. Commun., 5, 245 (1975).
2) E. Öhler, K. Reininger, and U. Schmidt, Angew. Chem., 82, 480 (1970); L. S. Hegedus, S. D. Wagner, E. L. Waterman, and K. Shiirala-Hansen, J. Org. Chem., 40, 593 (1975); R. M. Carlson and A. R. Oyler, J. Org. Chem., 41, 4065 (1976); R. M. Carlson, Tetrahedron Lett., 1978, 111.
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.
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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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