A Very Simple Synthesis of α-Substituted β-Ketoamides

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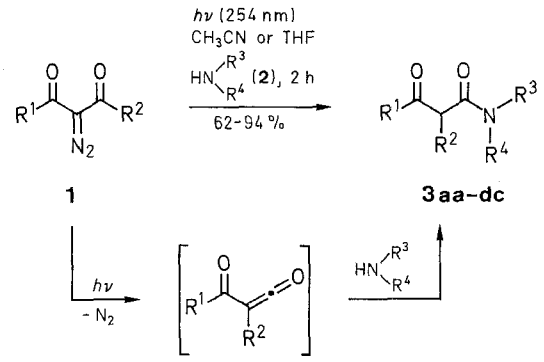
α-Substituted β-ketoamides were prepared in good yields by irradiation of a solution of 2-diazo-1,3-diketones, at 254 nm, in the presence of primary or secondary amines.

The direct conversion of esters to amides is a well-established procedure. Although the aminolysis of β-ketoesters has been reported,[1] we did not obtain the corresponding β-ketoamides in satisfactory yields using this procedure. β-Ketoamides can also be prepared by autocondensation of *N,N*-diethylacetamide,[2] by cyclization of *N*-alkyladipamic esters,[3] or by treatment of carboxylic acid amides with phosgene or phosphoroxy chloride.[4-6] *tert*-Butyl β-ketothioesters in the presence of silver(I) trifluoroacetate,[7] or phenyl isocyanate in the presence of α-acylphosphonium ylides[8] can also lead to β-ketoamides. The easy reaction of amines with ketenes[9] and diketenes[10] produces the corresponding amides and β-ketoamides, respectively.

It has been shown previously that β-ketoketenes, which are intermediates in the Wolff rearrangement of 2-diazo-1,3-diketones,[11] can be trapped efficiently by using alcohols as nucleophiles.[12] We wish to report here that, similarly, α-substituted β-ketoamides **3** can be prepared in very good yields when the Wolff rearrangement of 2-diazo-1,3-diketones **1** is carried out in the presence of amines or amides **2** (Table).

2-Diazo-1,3-diketones were prepared in high yields by reaction of tosyl azide with 1,3-diketones.[13] Irradiation of 2-diazo-1,3-diketones **1** at 254 nm in tetrahydrofuran or dry acetonitrile in the presence of primary, secondary amines or amides **2** led to the corresponding α-substituted β-ketoamides **3**. In the case of cycloalkane-1,3-diones **1b–d**, ring-contracted 2-oxo-1-cycloalkanecarboxamides are obtained. As shown in the Table, the chemical yields are usually higher than 80% and never lower than 60%.

This procedure is convenient, efficient and very general.



1	R^1	R^2	1	R^1	R^2
a	CH_3	CH_3	c	$-CH_2C(CH_3)_2CH_2-$	
b	$-(CH_2)_3-$		d	$-(CH_2)_4-$	

2	R^3	R^4	2	R^3	R^4
a	$CH_2CH=CH_2$	$CH_2CH=CH_2$	e	$-(CH_2)_4-$	
b	H	$CH_2CH=CH_2$	f	$-CH_2CH=CH(CH_2)_2-$	
c	CH_3	$CH_2C\equiv CH$	g	$-C(O)-(CH_2)_3-$	
d	H	$CH_2C\equiv CH$	h	H	H

3-Oxoalkanamides and 2-Oxo-1-cycloalkanecarboxamides 3; Typical Procedure:

To a solution of **1c** (0.2 g, 1.2 mmol, 1 equiv) in dry CH_3CN or THF (50 mL) is added propargylamine (**2d**; 0.199 g, 3.61 mmol, 3 equiv). The solution is irradiated in two quartz tubes (∅ = 1 cm) for 2 h at 254 nm in a merry-go-round equipped with 12 Philips TUV 15 lamps. Evaporation of the solvent gives a residue, which is purified by flash column chromatography (silica gel, 40–63 μ, Merck; eluent: hexane/EtOAc, 60:40). Recrystallization from ether/petroleum ether gives *N-propargyl-4,4-dimethyl-2-oxo-1-cyclopentanecarboxamide* **3cd**; yield: 0.218 g (88%); mp 85–87°C (Table).

Table. 3-Oxoalkanamides and 2-Oxo-1-cycloalkanecarboxamides **3** Prepared

Product	Yield (%)	mp (°C) (solvent)	Molecular Formula[a]	IR ($CHCl_3$) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS)
3aa	65	oil	$C_{11}H_{17}NO_2$ (195.2)	1700, 1640, 1620	1.4 (d, 3H, J = 7); 2.1 (s, 3H); 3.6 (q, 1H, J = 7); 3.8–4.3 (m, 4H); 4.9–6.0 (m, 6H)	14.0; 27.2; 48.2; 49.4; 51.6; 177.5; 132.7; 170.5; 205.2
3ba	62	oil	$C_{12}H_{17}NO_2$ (207.2)	1730, 1620, 1430, 1410	1.6–2.6 (m, 6H); 3.4 (t, 1H, J = 10); 3.6–4.3 (m, 4H); 5.0–5.3 (m, 4H); 5.6–5.8 (m, 2H)	21.6; 27.6; 38.7; 49.4; 52.1; 117.0; 133.4; 169.1; 214.8
3bc	88	oil	$C_{10}H_{13}NO_2$ (179.2)	3300, 1730, 1630	1.7–2.6 (m, 6H); 3.0 (s, 3H); 3.3–3.6 (m, 3H); 3.7–4.6 (m, 2H)	20.9; 27.1; 33.8; 36.7; 38.5; 39.5; 51.9; 72.0; 168.5; 214.7
3cb	94	oil	$C_{11}H_{17}NO_2$ (195.2)	3380, 1725, 1665, 1645	1.0 (s, 3H); 1.1 (s, 3H); 2.0–2.4 (m, 4H); 3.2 (t, 1H, J = 9); 3.8–3.9 (m, 2H); 5.0–5.2 (m, 2H); 5.7–5.8 (m, 1H); 6.8 (br s, 1H)	27.9; 28.8; 34.1; 39.4; 42.0; 53.7; 53.8; 116.2; 134.1; 166.9; 216.7
3cd	88	85–87 (Et_2O/PE[b])	$C_{11}H_{15}NO_2$ (193.2)	3380, 3310, 1725, 1610	1.0 (s, 3H); 1.1 (s, 3H); 2.0–2.3 (m, 5H); 3.2 (t, 1H, J = 9.5); 3.9–4.1 (m, 2H); 7.0 (br s, 1H)	27.8; 28.8; 29.3; 34.0; 39.2; 53.6; 53.6; 71.6; 79.4; 166.8; 215.9
3ca	91	oil	$C_{14}H_{21}NO_2$ (235.3)	1740, 1650, 1635	1.0 (s, 3H); 1.2 (s, 3H); 1.8–1.9 (m, 1H); 2.1 (d, 1H, J = 17.5); 3.6 (dd, 1H, J = 10.5, 8.5); 3.6–3.8 (m, 2H); 4.2–4.3 (m, 2H); 5.1–5.2 (m, 4H); 5.6–5.8 (m, 2H)	28.1; 29.1; 34.4; 41.0; 48.5; 49.4; 51.5; 53.5; 116.5; 117.0; 132.7; 133.3; 169.0; 214.1
3cc	88	oil	$C_{12}H_{17}NO_2$ (207.2)	3310, 1740, 1640	1.0 (s, 3H); 1.1 (s, 3H); 1.8–2.4 (m, 5H); 3.1 (s, 3H); 3.6–3.7 (m, 1H); 3.8–4.6 (m, 2H)	28.1; 29.1; 34.3; 35.0; 36.9; 40.6; 51.4; 53.5; 72.0; 78.6; 168.5; 213.4
3ce	74	oil	$C_{12}H_{19}NO_2$ (209.2)	1740, 1625	1.0 (s, 3H); 1.1 (s, 3H); 1.7–2.0 (m, 5H); 2.0 (d, 1H, J = 17.6); 2.2 (d, 1H, J = 17.6); 2.3 (dd, 1H, J = 12.7, 10.8); 3.3–3.5 (m, 4H); 3.7–3.8 (m, 1H)	24.4; 25.9; 28.1; 29.0; 34.3; 40.3; 46.1; 46.9; 53.3; 53.5; 167.1; 214.1
3cf	85	67–69 (Et_2O/PE)	$C_{13}H_{19}NO_2$ (221.3)	1740, 1660, 1625	1.0 (s, 3H); 1.2 (s, 3H); 1.8–2.4 (m, 6H); 3.5–3.7 (m, 3H); 3.8–4.2 (m, 2H); 5.5–5.9 (m, 2H)	26.0; 28.1; 29.1; 34.2; 40.6; 43.2; 45.4; 51.1; 53.5; 124.3; 124.9; 167.2; 217.5
3cg	67	oil	$C_{12}H_{17}NO_3$ (223.2)	1740, 1685	1.1 (s, 3H); 1.2 (s, 3H); 1.9–2.3 (m, 6H); 2.5–2.7 (m, 2H); 3.7–3.9 (m, 2H); 4.9 (t, 1H, J = 10)	17.0; 28.1; 29.3; 33.9; 34.5; 40.2; 46.0; 53.2; 54.8; 170.2; 175.7; 212.2
3dc	66	oil	$C_{11}H_{15}NO_2$ (193.2)	3300, 1700, 1640	1.6–2.4 (m, 9H); 2.5–2.6 (m, 1H); 2.9 (s, 3H); 3.5–4.6 (m, 2H)	23.5; 27.0; 30.3; 33.7; 36.6; 39.5; 41.9; 54.6; 73.1; 169.4; 207.1
3ch	62	69–71 (Et_2O/PE)	$C_8H_{13}NO_2$ (155.2)	3680, 3500, 3380, 1735, 1690	1.0 (s, 3H); 1.2 (s, 3H); 2.0–2.4 (m, 4H); 3.3 (t, 1H, J = 10.5); 6.8 (br s, 1H)	27.5; 28.5; 33.7; 38.9; 53.2; 53.5; 169.6; 215.2

[a] Satisfactory microanalyses were obtained: C ±0.25, H ±0.12, N ±0.13.

[b] PE = petroleum ether.

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(1) Labelle, M., Gravel, D. *J. Chem. Soc. Chem. Commun.* **1985**, 105.
(2) Montagne, M. *C.R. Acad. Sci.* **1931**, *192*, 111.
Utzinger, G.E. *Helv. Chim. Acta* **1952**, *35*, 1359.
(3) Johnson, D.H. *J. Chem. Soc.* **1958**, 1624.
(4) Seefelder, M. *German Patent* 1089760 (1958), Badische Anilin-and-Soda-Fabrik A.G.; *C.A.* **1962**, *56*, 1326.
(5) Bredereck, H., Gompper, R., Klemm, K. *Chem. Ber.* **1959**, *92*, 1456.
(6) Eilingsfeld, H., Seefelder, M., Weidinger, H. *Angew. Chem.* **1960**, *72*, 836.
(7) Ley, S.V., Woodward, P.R. *Tetrahedron Lett.* **1987**, *28*, 3019.
(8) Bestmann, H.J., Kumar, K. *Chem. Ber.* **1983**, *116*, 2708.
(9) Sauer, J.C. *J. Am. Chem. Soc.* **1947**, *69*, 2444.
Sauer, J.C. *US Patent* 2323938 (1944), E.I. du Pont de Nemours Co.; *C.A.* **1944**, *38*, 266.
(10) Clemens, R.J. *Chem. Rev.* **1986**, *86*, 241.
Borrmann, D., in: *Houben-Weyl*, 4th ed., Vol. VII/4, Georg Thieme Verlag, Stuttgart, 1968, p. 53.
(11) Whittaker, D., in: *The Chemistry of Diazonium and Diazo Compounds*, Patai, S. (ed.), John Wiley & Sons, New York, 1978, 593–644.
(12) Kunish, F., Hobert, K., Welzel, P. *Tetrahedron Lett.* **1985**, *26*, 5433.
Froborg, J., Magnusson, G. *J. Am. Chem. Soc.* **1978**, *100*, 6728.
(13) Moriarty, R.M., Bailey, B.R., III, Prakash, O., Prakash, I. *J. Am. Chem. Soc.* **1985**, *107*, 1375.
Regitz, M. *Angew. Chem.* **1967**, *79*, 786; *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 733.