A New Method for Preparation of *N*-Acetoacetylcarboxamides

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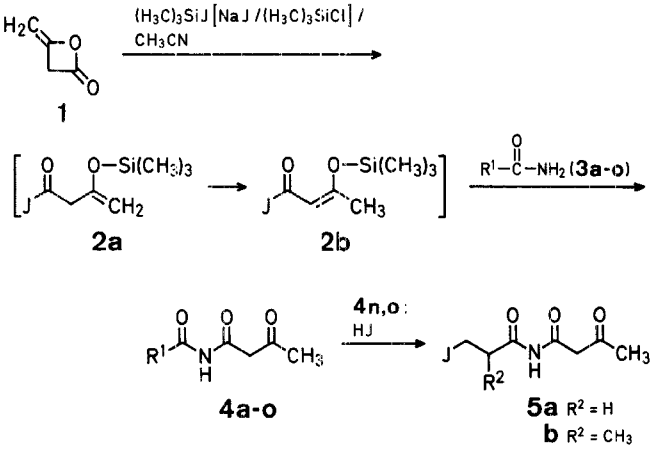
It has been reported[1] that diketene (**1**) reacted with various carboxamides to give the corresponding *N*-acetoacetyl derivatives. However, a reinvestigation[2] of this reaction showed that it did not proceed with consistent success and that no reaction occurred with amides other than acetamide and benzamide. In the course of our studies on 1,3-oxazines, *N*-acetoacetyl derivatives of carboxamides were found to be important as starting materials for the ring transformation reaction[3], which led us to undertake an investigation on the preparation of the *N*-acetoacetyl derivatives. This communication describes a general method for *N*-acetoacetylation of carboxamides **3** using **1** and trimethylsilyl iodide.

Carboxamides **3** smoothly undergo *N*-acetoacetylation with **1** in the presence of trimethylsilyl iodide. Thus, treatment of aliphatic and aromatic amides **3a–k** with **1** in acetonitrile in the presence of trimethylsilyl iodide[4], generated *in situ* from trimethylsilyl chloride and sodium iodide, afforded the corresponding *N*-acetoacetyl derivatives (**4a–k**) in good yields, respectively (Method A). The experimental and spectroscopic data of **4** are summarized in the Table.

The *N*-acetoacetylation seems to proceed as formulated below, involving the formation of the *O*-trimethylsilylated intermediate **2a** and/or **2b** resulting from **1** and trimethylsilyl iodide.



This method also proved effective for the *N*-acetoacetylation of unsaturated amides such as crotonamide (**3l**) and cinnamamide (**3m**). However, similar treatment of acrylamide (**3n**) and methacrylamide (**3o**) exclusively gave rise to the corresponding iododerivatives **5a** and **5b** in place of the expected **4n, o** in 68% and 71% yields, respectively. Products **5a** and **5b** were identified by comparison of their spectral data (I.R., N.M.R.) with those of respective authentic samples which were similarly prepared from **1** and **3p, q** under the conditions described above.

Formation of **5a, b** evidently suggests that the addition reaction between **4n, o** and hydrogen iodide, one of the products, took place in the reaction system. In the reaction of **3n**, removal[5] of the hydrogen iodide by continuously bringing nitrogen into the reaction mixture was carried out (Method B), leading to successful isolation of **4n** in 29% yield along with **5a** (29% yield). Also, in the case of **3o**, **4o** and **5b** were obtained by Method B in 49% and 12% yields, respectively. The results obtained are summarized in the Table. Investigations on the applications of **4** in 1,3-oxazine chemistry are in progress.

***N*-Acetoacetylation of Carboxamides 3; General Procedure:**

Method A: To an ice-bath cooled solution of **3** (10 mmol), sodium iodide (1.95 g, 13 mmol) and **1** (1.09 g, 13 mmol) in dry acetonitrile (30 ml) is added dropwise a solution of trimethylsilyl chloride (1.41 g, 13 mmol) in dry acetonitrile (10 ml) with stirring. After completion of the addition, the cooling bath is removed and stirring is continued at room temperature for 2 h. The mixture is evaporated under aspirator vacuum followed by extraction with chloroform (3 × 20 ml). The chloroform layer is washed successively with 10% sodium thiosulfate solution (20 ml) and water (20 ml), then dried with anhydrous magnesium sulfate. Evaporation of the chloroform layer gives the crude product **4**, which is purified by recrystallization from the solvent indicated in the Table.

Method B: To a stirred solution of sodium iodide (1.5 g, 10 mmol) and **1** (0.84 g, 10 mmol) in dry acetonitrile (20 ml), cooled with an ice-bath, is successively added dropwise a solution of trimethylsilyl chloride (1.09 g, 10 mmol) in dry acetonitrile (10 ml) and a solution of **3n** (0.71 g, 10 mmol) in dry acetonitrile (20 ml). During the addition of **3n**, nitrogen is passed into the reaction mixture. Cooling, stirring, and passage of nitrogen are continued for further 10 h. The resultant mixture is evaporated under aspirator vacuum, followed by extraction with chloroform (3 × 20

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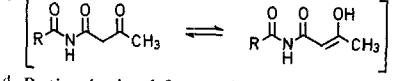
Table. *N*-Acetoxyacetylcarboxamides **4** and **5**

Product No.	R[1]	Yield [%][a] (Method)	m.p. [°C] (solvent)	Molecular formula[b] or Lit. m.p. [°C]	Ratio[c,d] keto:enol	I.R. (KBr)[e] ν [cm^{-1}]	^{1}H-N.M.R. (60 MHz, $CDCl_3$)[f] δ [ppm] R[1]	NH	keto CH_3	keto CH_2	enol CH_3	enol —CH—	enol OH
4a	CH_3	62 (A)	86–86.5° (ether)	88–89°[6]	5:1	1740; 1700 (sh)	2.23 (s, 3H)	9.60 (br)	2.33	3.83	2.07	5.90	13.40
4b	C_2H_5	77 (A)	116–117° (C_2H_5OH)	116–117°[6]	4:1	1730; 1700 (sh)	1.16 (t, 3H, J=8 Hz); 2.35 (q, 2H, J=8 Hz)	9.40 (br)	2.33	3.83	2.03	6.00	13.43
4c	n-C_3H_7	70 (A)	95–95.5° (40–70° PE/ether)	$C_8H_{13}NO_3$ (171.2)	5:1	1740; 1700 (sh)	0.93 (t, 3H, J=6 Hz); 1.8 (m, 2H); 2.24 (t, 2H, J=6 Hz)	9.43 (br)	2.33	3.86	2.00	6.07	13.40
4d	i-C_3H_7	64 (A)	82–84° (40–70° PE/ether)	81–82°[6]	4:1	1720; 1700 (sh)	1.17 (d, 6H, J=8 Hz); 2.7 (m, 1H)	9.10 (br)	2.30	3.90	2.03	6.23	13.60
4e	t-C_4H_9	81 (A)	110–111° (ether)	$C_9H_{15}NO_3$ (185.2)	7:1	1720; 1690	1.23 (s, 9H)	8.93 (br)	2.27	3.93	2.00	6.40	13.66
4f	$C_6H_5CH_2$	82 (A)	146–147° (C_2H_5OH)	147–148°[7]	4:1	1740; 1720	3.83 (s, 2H); 7.37 (s, 5H_{arom})	9.67 (br)	2.43	4.00	2.13	6.27	—[g]
4g	C_6H_5	86 (A)	120–121° (C_6H_6)	123–124°[4]	7:3	1710; 1680	7.4–8.2 (m, 5H_{arom})	9.70 (br)	2.34	4.07	2.10	6.63	13.65
4h	4-H_3C—C_6H_4	83 (A)	144–145° (C_6H_6)	$C_{12}H_{13}NO_3$ (219.2)	5:1	1720 (sh); 1700	2.40 (s, 3H); 7.2–7.8 (m, 4H_{arom})	9.23 (br)	2.32	4.00	2.07	6.53	13.63
4i	4-H_3CO—C_6H_4	90 (A)	136.5–138° (C_6H_6)	$C_{12}H_{13}NO_4$ (235.2)	6:1	1720; 1700; 1680	3.93 (s, 3H); 6.9–8.0 (m, 4H_{arom})	—	2.43	4.17	2.17	6.53	—[g]
4j	4-Cl—C_6H_4	88 (A)	148–149° (C_6H_6)	$C_{11}H_{10}ClNO_3$ (239.6)	7:1	1720; 1700; 1680	6.9–8.0 (m, 4H_{arom})	—	2.47	4.15	2.17	6.50	—[g]
4k	4-O_2N—C_6H_4	86 (A)	149–150° (CH_3OH)	$C_{11}H_{10}N_2O_5$ (250.2)	6:1	1710; 1680	8.0–8.6 (m, 4H_{arom})	—	2.50	4.53	2.20	6.60	—[g]
4l	H_3C—CH=CH	77 (A)	108–109° (ether)	$C_8H_{11}NO_3$ (169.2)	2:1	1715; 1640	1.97 (dd, 3H, J=2, 7 Hz); 6.17 (dd, 1H, J=2, 15 Hz); 7.05 (dq, 1H, J=7, 15 Hz)	9.70 (br)	2.30	4.00	2.10	6.10	13.60
4m	C_6H_5—CH=CH	80 (A)	114–115° (C_6H_6)	$C_{13}H_{13}NO_3$ (231.2)	5:2	1720; 1670; 1630	6.80 (d, 1H, J=14 Hz); 7.2–7.6 (m, 5H_{arom}); 7.60 (d, 1H, J=14 Hz)	9.73 (br)	2.37	3.93	2.00	6.13	13.6
4n	H_2C=CH	29 (B)	125–125.5° (hexane)	$C_7H_9NO_3$ (115.2)	10:3	1720; 1700 (sh); 1630	5.7–6.6 (m, 3H)	9.57 (br)	2.33	3.97	2.05	6.20	13.50
4o	H_2C=C(CH_3)	49 (B)	52–52.5° (ether)	$C_8H_{11}NO_3$ (169.2)	7:2	1720; 1710 (sh); 1675	2.00 (s, 3H); 5.47 (s, 1H); 5.90 (s, 1H)	9.00 (br)	2.30	3.97	2.08	6.37	13.73
5a	R^2=H	68 (A) 29 (B)	134–135° (C_2H_5OH)	$C_7H_{10}JNO_3$ (283.1)	5:1	1740; 1720; 1700 (sh)	3.3 (m, 4H)	9.80 (br)	2.40	4.00	2.10	6.00	—[g]
5b	R^2=CH_3	71 (A) 12 (B)	98–99.5° (40–70° PE/ether)	$C_8H_{12}JNO_3$ (297.1)	3:1	1740 (sh); 1720	1.30 (d, 3H, J=7 Hz); 2.7–3.4 (m, 3H)	9.23 (br)	2.30	3.87	2.05	6.10	13.43

[a] Yield of pure, isolated product.

[b] All new compounds gave satisfactory microanalyses: C ±0.30; H ±0.13; N ±0.29.

[c] 

[d] Ratio obtained from relative intensities of the signals in the ^{1}H-N.M.R. spectra.

[e] Recorded on a Shimazu IR-400 instrument.

[f] Recorded on a Hitachi R-24B instrument at 60 MHz with TMS as internal standard.

[g] In 10:1 $CDCl_3$/CF_3COOH solution.

ml). The chloroform layer is washed successively with 10% sodium thiosulfate solution (20 ml) and water (20 ml), then dried with anhydrous magnesium sulfate. Evaporation of the chloroform layer gives a mixture of **4n** and **5a**, which are separated and purified by fractional recrystallization.

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