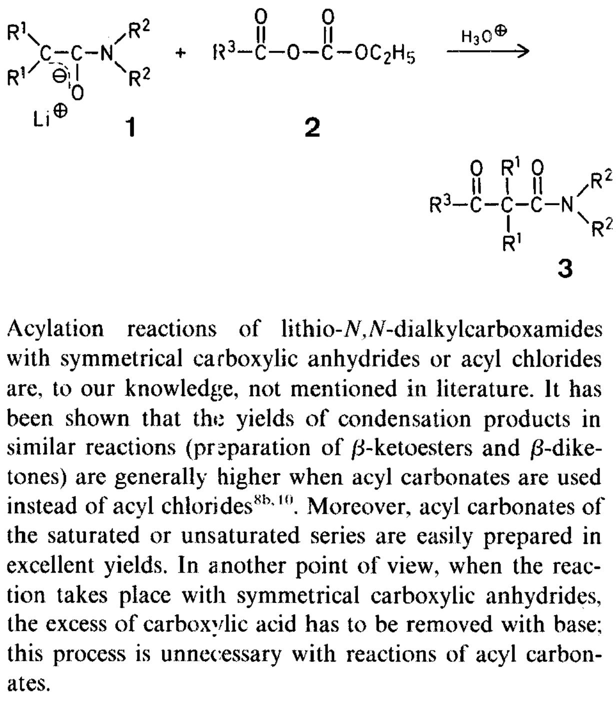
Synthesis of *N*,*N*-Dialkyl-3-oxoalkanamides

Claude Goasdoue, René Couffignal

Laboratoire de Synthèse Organométallique, Université Pierre et Marie Curie, Bâtiment F, 4, Place Jussieu, F-75230 Paris Cédex 05, France

N,*N*-Dialkyl-3-oxoalkanamides **3** have not been intensively studied in recent years. They are, however, interesting compounds which have insect repellent properties[1a–f]. They are generally prepared by the self-condensation of *N*,*N*-dialkylcarboxamides with either sodium metal[1b,2] or Grignard reagents[3] or also by the reaction of a secondary amine with a β-ketoester[1b,4]. Compounds **3** can also be prepared by alkylation of dimetallated *N*,*N*-dimethylacetoacetamide[5]. This latter report prompted us to report our results for the acylation reaction of lithio-*N*,*N*-dialkylcarboxamides **1** by the acyl carbonates **2**, structural analogues of mixed anhydrides.



Acylation reactions of lithio-*N*,*N*-dialkylcarboxamides with symmetrical carboxylic anhydrides or acyl chlorides are, to our knowledge, not mentioned in literature. It has been shown that the yields of condensation products in similar reactions (preparation of β-ketoesters and β-diketones) are generally higher when acyl carbonates are used instead of acyl chlorides[8b,10]. Moreover, acyl carbonates of the saturated or unsaturated series are easily prepared in excellent yields. In another point of view, when the reaction takes place with symmetrical carboxylic anhydrides, the excess of carboxylic acid has to be removed with base; this process is unnecessary with reactions of acyl carbonates.

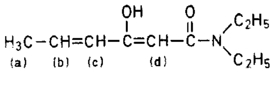
Table 1. *N*,*N*-Dialkyl-3-oxoalkanamides **3**

R^1	R^2	R^3	Yield [%]	b.p./torr or m.p.	Molecular formula[a]	I.R. (KBr)[b] ν [cm^{-1}]
CH_3	CH_3	n-C_3H_7	78	122–124°/12	$C_{10}H_{19}NO_2$ (185.3)	1710; 1640
CH_3	CH_3	c-C_6H_{11}	68	100°/0.06	$C_{13}H_{23}NO_2$ (225.3)	1700; 1635
CH_3	CH_3	C_6H_5	85	m.p. 105°	$C_{13}H_{17}NO_2$ (219.3)	1670; 1620
H	C_2H_5	$H_3C—CH=CH$	35	73–76°/0.03	$C_{10}H_{17}NO_2$ (183.2)	1660; 1590

[a] All new products gave satisfactory microanalyses (C, ±0.1; H, ±0.3; N, ±0.3) and ^{1}H-N.M.R. spectra were consistent with the structure assigned.

[b] The I.R. spectra were recorded on a Perkin Elmer 257 spectrometer.

Table 2. ^{1}H-N.M.R. Data for *N*,*N*-Diethyl-3-hydroxy-2,4-hexadienamide (**6b**)



$$H_3C-CH=CH-\overset{OH}{\overset{|}{C}}=CH-\overset{O}{\overset{\|}{C}}-N(C_2H_5)_2$$

Assignment	H(a)	H(d)	H(c)	H(b)
Chemical Shift δ [ppm]	1.8 (m, 3H)	5.0 (s, 1H)	5.8 (m, 1H)	6.5 (m, 1H)

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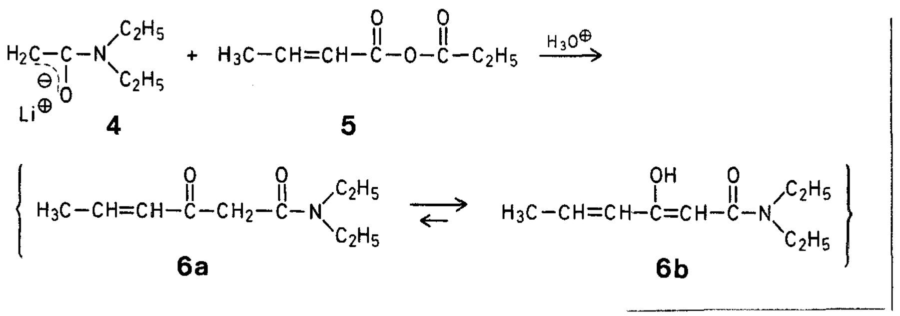

The condensation of the lithio-*N*,*N*-diethylacetamide (**4**) with the unsaturated acyl carbonate **5**, prepared from *trans*-2-butenoic acid and ethyl carbonochloridate, leads to the 3-oxo-4-alkenamide **6**.

The ^1H-N.M.R. spectra of **6** showns that it exists only in the enolic form **6b** (*N*,*N*-diethyl-3-hydroxy-2,4-hexadienamide). No signal can be attributed to the ketoamide form **6a**. Finally, the structure analogy between compound **6** and the 3-oxo-4-alkenoates $R^1-CH=CH-CO-CH_2-COOR$ led us to expect that **6** could be a useful synthon in cyclic and heterocyclic chemistry for cyclisation reactions[6].

Acyl Carbonates 2; General Procedure[7,8a,8b]**:**

A commercial carboxylic acid R^3-COOH (0.1 mol) in tetrahydrofuran (75 ml) is treated with triethylamine (0.11 mol) in tetrahydrofuran (75 ml). This solution is cooled to −10 to −20° and ethyl carbonochloridate (0.11 mol) in tetrahydrofuran (50 ml) is added dropwise with stirring. The mixture is stirred at −10° to +10° for 4 h and filtered to remove the triethylamine hydrochloride. The filtrate is then concentrated in vacuo to give the crude acyl carbonate **2** in quantitative yield as previously described[9]. Compound **2** is then used without any purification.

***N*,*N*-Dialkyl-3-oxoalkanamides 3; General Procedure:**

A solution of lithium diisopropylamide (0.1 mol) is prepared in the classical way from butyllithium (0.1 mol) in anhydrous diethyl ether (60 ml) and diisopropylamine (0.1 mol) in anhydrous tetrahydrofuran (20 ml). To this solution, the *N*,*N*-dialkylcarboxamide (0.1 mol) in tetrahydrofuran (20 ml) is added dropwise at 0°. Following the addition, the mixture is stirred for 2 h at 0°, then cooled to −40°, and the acyl carbonate **2** (0.1 mol) is added dropwise. The resultant solution is stirred at −20° for 1.5 h. After hydrolysis with dilute mineral, the organic layer is extracted with ether, washed with brine, and dried with magnesium sulfate. The *N*,*N*-dialkyl-3-oxoalkanamide **3** is then distilled or recrystallised from petroleum ether.

Compound **6b** is prepared by the same general procedure.

Received: April 30, 1979
(Revised form: June 11, 1979)

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[1] (a) G. E. Utzinger, *Angew. Chem.* **63**, 430 (1951).
(b) G. E. Utzinger, *Helv. Chim. Acta* **35**, 1359 (1952).
(c) G. E. Utzinger, A. Hoelle, *Helv. Chim. Acta* **35**, 1370 (1952).
(d) *British Patent* 709854 (1954); *C. A.* **48**, 11715 (1954).
(e) *U.S. Pat.* 2677705 (1954); *C. A.* **49**, 6303 (1955).
(f) *British Patent* 737951 (1955); *C. A.* **50**, 11600 (1956).

[2] (a) G. V. Chelintsev, O. D. Osetrova, *C. R. Acad. Sci. URSS* **4**, 419 (1936); *C. A.* **31**, 3467 (1937).
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[6] G. Stork, R. N. Guthikonda, *Tetrahedron Lett.* **1972**, 2755, and references therein.

[7] D. S. Tarbell, J. A. Price, *J. Org. Chem.* **22**, 245 (1957).

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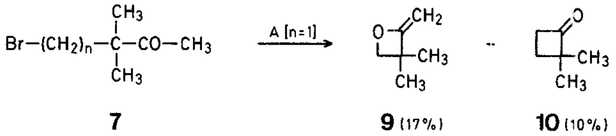
(b) R. Couffignal, J. L. Moreau, *J. Organometal. Chem.* **127**, C65 (1977).

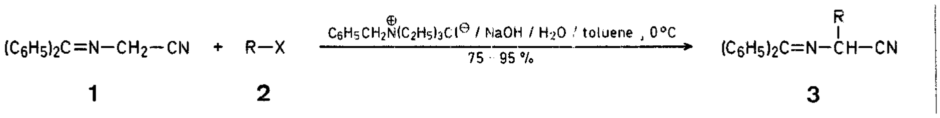
[9] R. Couffignal, J. L. Moreau, *Tetrahedron Lett.* **1978**, 3713.

[10] M. W. Rathke, J. Deith, *Tetrahedron Lett.* **1971**, 2953.

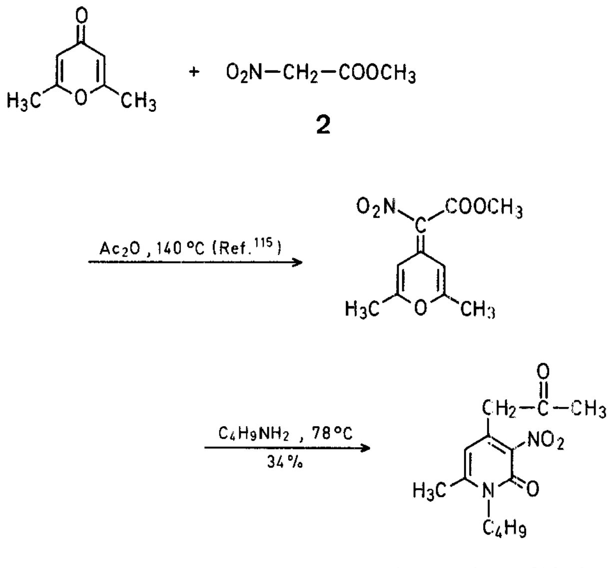
Abstract 5528, *Synthesis* **1979** (7), 554;
The formula scheme for the conversion **7**→**9**+**10** should be as follows:



Abstract 5556, *Synthesis* **1979** (8), 629;
The formula scheme for the conversion **1**+**2**→**3** should be as follows:



M. T. Shipchandler, *Synthesis* **1979** (9), 666-686;
The second reaction in Scheme **P** (p. 682) should be as follows:

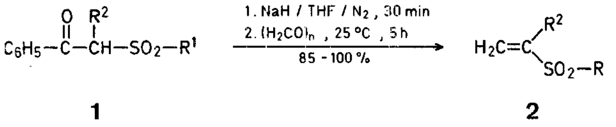


G. Sosnovsky, J. A. Krogh, S. G. Umhoefer, *Synthesis* **1979** (9), 722-724;
The heading for the third column of the Table (p. 723) should be as follows:

Solvent[c]
(Reaction
time[d] [h])

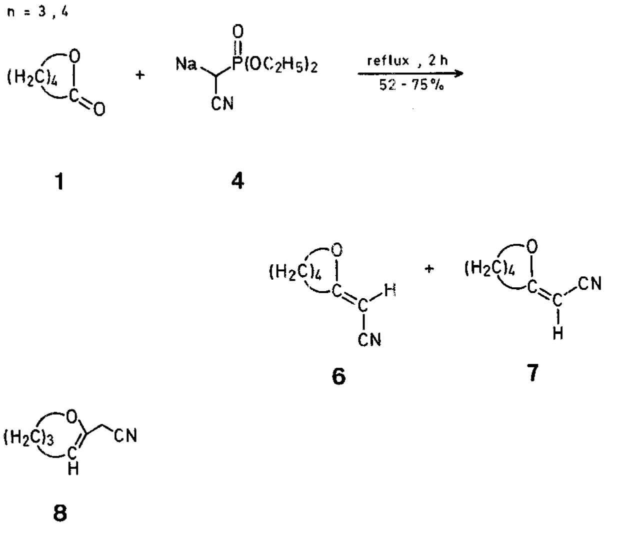
C. Venturello, R. D'Aloisio, *Synthesis* **1979** (10), 790-793;
The last two lines of the third paragraph of the right hand column on page 791 should read as follows:
drazines and of the not easily accessible 3-acetyl-5-methylisoxazole[4].

Abstract 5616, *Synthesis* **1979** (10), 840;
The formula scheme for the conversion **1**→**2** should be as follows:

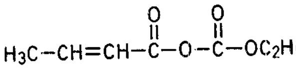


Abstract 5627, *Synthesis* **1979** (11), 917;
The title should be as follows:
[1,4]-Addition of 1,3-Dithianes to 2-Cycloalkenones.

Abstract 5637, *Synthesis* **1979** (11), 920;
The lower part of the formula scheme should be as follows:



C. Goasdoue, R. Couffignal, *Synthesis* **1979** (12), 954-955;
The structure of compound **5** (p. 955) should be as follows:



$$H_3C-CH=CH-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-OC_2H_5$$

5

P. Pollet, S. Gelin, *Synthesis* **1979** (12), 977-979;
The correct names for compounds **8** and **9** are 4-oxo-2-phenyl-2,6-dihydro-4*H*-furo[3,4-*d*]-1,2,3-triazoles and 4-oxo-4*H*,6*H*-furo[3,4-*c*][1,2,5]oxadiazoles, respectively.