crystallized from chloroform–hexane; liquids were purified by column chromatography. Yields and physical data are given for each compound.

2,3-Dimethyl-6-phenyl-4*H*-pyran-4-one (**17**) was obtained (62%) as tan needles: mp 103–105°; ir (KBr pellet) 1650, 1605, 1445, 1415, 1370 cm^{-1}; nmr ($CDCl_3$) δ 2.00 (3, s, 3-CH_3), 2.39 (3, s, 2-CH_3), 6.70 (1, s, 5-CH=), 7.3–7.9 ppm (5, m, 6-C_6H_5).

Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.17; H, 6.18.

2,5-Dimethyl-6-phenyl-4*H*-pyran-4-one (**18**) was obtained (87%) as a pale yellow oil: ir (neat) 1660, 1620, 1445, 1405 cm^{-1}; nmr ($CDCl_3$) δ 2.00 (3, s, 2-CH_3), 2.22 (3, s, 5-CH_3), 6.15 (1, s, 3-CH=), 7.3–7.7 ppm (5, m, 6-C_6H_5).

Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.75; H, 6.02.

2-Ethyl-3-methyl-6-phenyl-4*H*-pyran-4-one (**19**) was obtained (98%) as tan needles: mp 62–63°; ir (KBr pellet) 1640, 1600, 1450, 1410, 1370 cm^{-1}; nmr ($CDCl_3$) δ 1.34 (3, t, J = 7 Hz, 2-CH_3), 2.01 (3, s, 3-CH_3), 2.74 (2, q, J = 7 Hz, 2-CH_2), 6.70 (1, s, 5-CH=), 7.3–7.9 ppm (5, m, 6-C_6H_5).

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.45; H, 6.58.

2-Ethyl-5-methyl-6-phenyl-4*H*-pyran-4-one (**20**) was obtained (98%) as a pale yellow liquid: ir (neat) 1660, 1650, 1620, 1445, 1405, 1370 cm^{-1}; nmr ($CDCl_3$) δ 1.25 (3, t, J = 7 Hz, 2-CH_3), 2.06 (3, s, 5-CH_3), 2.57 (2, q, J = 7 Hz, 2-CH_2), 6.20 (1, s, 3-CH=), 7.51 ppm (5, s, 6-C_6H_5).

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.26; H, 6.69.

2,3,5-Trimethyl-6-phenyl-4-(1*H*)-pyridone (**25**).—Liquid ammonia (10 ml) was added to a solution of triketone **7** (1.0 g, 0.0045 mol) in absolute ethanol (300 ml) and the mixture was warmed gently for 10 min and then boiled to dryness on the steam bath. The remaining oil was triturated with acetone to form crude **25** (0.83 g, 86%) as a pale yellow solid. Recrystallization from acetone–absolute ethanol and then from chloroform gave colorless needles: mp 270°; ir (KBr pellet) 1614, 1598, 1490, 1371 cm^{-1}; nmr ($CDCl_3$) δ 2.33 (3, s, 2-CH_3), 2.45 (3, s, 5-CH_3), 2.75 (3, s, 3-CH_3), 7.3–7.7 (5, m, 6-C_6H_5), the 2- and 3-CH_3 signals are broadened by long-range coupling.

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.73; H, 6.99; N, 6.45.

Registry No.— **1**, 1469-95-0; **1c**, 37676-25-8; **2**, 37676-26-9; **3**, 37676-27-0; **4**, 37676-28-1; **5**, 37676-29-2; **6**, 37676-30-5; **7**, 37676-31-6; **11**, 815-57-6; **14**, 6668-24-2; **15**, 4220-52-4; **16**, 7424-54-6; **17**, 37676-33-8; **18**, 37676-34-9; **19**, 37735-76-5; **20**, 37676-35-0; **25**, 37676-36-1; **26**, 37676-37-2; **27**, 37735-77-6; methyl benzoate, 93-58-3; ethyl acetate, 141-78-6.

Synthesis of 1,4 and 1,5 Diketones from *N,N,N′,N′*-Tetramethyldiamides and Organolithium Reagents

DENNIS C. OWSLEY,* JANICE M. NELKE, AND JORDAN J. BLOOMFIELD

Corporate Research Department, Monsanto Company, St. Louis, Missouri 63166

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A new, one-step synthesis of 1,4 and 1,5 diketones from a variety of organolithium compounds and *N,N,N′,N′*-tetramethylsuccinamide and *N,N,N′,N′*-tetramethylglutaramide is described. Yields vary from 4 to 76%. Yields of 1,5 diketones are generally higher than those of 1,4 diketones. *N,N,N′,N′*-Tetraethylsuccinamide did not give 1,4 diketones with phenyllithium, 2-pyridyllithium, or 6-bromo-2-pyridyllithium.

During the course of some studies on the synthesis and properties of a number of heterocyclic systems, we needed a series of 1,4 and 1,5 diketones as intermediates. In the case of a bis-2-pyridyl diketone, no ready one-step synthesis of these compounds was available. The pyridine substitution pattern dictated the use of a 2-pyridyl Grignard reagent or 2-pyridyllithium compound.

Both aldehydes and ketones have been prepared from *N,N*-dialkylamides and either Grignard reagents[1] or organolithium compounds.[2] Furthermore, it has been reported that diketones are produced in low yield by the reaction of 2 equiv of a Grignard reagent with an *N,N,N′,N′*-tetraalkyldiamide.[3] Repeated failures to prepare any ketone from the Grignard reagent of 2,6-dibromopyridine led us to investigate the organolithium compound.[4] Owing to our initial success, we decided to study the scope of the reaction. To our knowledge, no reaction of 2 equiv of an organolithium compound with *N,N,N′,N′*-tetraalkyldiamides has been reported.

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(2) (a) J. Sicé, *J. Amer. Chem. Soc.*, **75**, 3697 (1953); (b) J. Sicé, *J. Org. Chem.*, **19**, 70 (1954); (c) E. A. Evans, *J. Chem. Soc.*, 4691 (1956); (d) E. A. Braude and E. A. Evans, *ibid.*, 3334 (1955); (e) E. Jones and I. M. Moodie, *J. Chem. Soc. C*, 1195 (1967).

(3) (a) E. E. Blaise, *C. R. Acad. Sci.*, **173**, 313 (1921); (b) E. E. Blaise and M. Montague, *ibid.*, **180**, 1345 (1925).

(4) J. E. Parks, B. E. Wagner, and R. H. Holm, *Inorg. Chem.*, **10**, 2477 (1971).

Results and Discussion

The results of our study of the reaction of a variety of organolithium reagents with either *N,N,N′,N′*-tetramethylsuccinamide or *N,N,N′,N′*-tetramethylglutaramide are summarized in Table I. With the exception of 2-thienyllithium, no attempts were made to optimize yields. Butyllithium gave a very complex mixture with *N,N,N′,N′*-tetramethylsuccinamide. In general, the yields of 1,5 diketones were higher than those of the 1,4 diketones.

TABLE I

YIELDS OF PRODUCTS FROM THE REACTION

$$2RLi + Me_2NCO(CH_2)_nCONMe_2 \xrightarrow{-78^\circ} RCO(CH_2)_nCOR$$

R	n	Yield,[a] %	Solvent	Reaction time, hr
Phenyl	2	4	Ether	24
6-Bromo-2-pyridyl	2	71	Ether	3
2-Pyridyl	2	20	Ether	3–4
2-Thienyl[b]	2	33	THF	24
Phenyl	3	50	Ether	24
6-Bromo-2-pyridyl	3	76	Ether	3
2-Pyridyl	3	20	Ether	3–4
2-Thienyl[b]	3	24	THF	24
n-Butyl	3	19	Ether	2

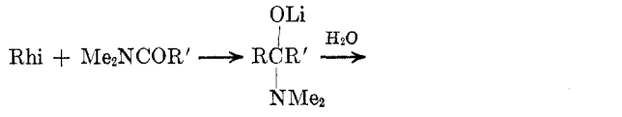
[a] Yields based on purified product. [b] Run with 4 equiv of 2-thienyllithium.

The reactions were monitored by glc. Immediately after mixing of the organolithium reagent with amide, glc showed that all of the starting amide had disappeared and was replaced by diketone and another component which had a shorter retention time. As the reactions proceeded, the shorter retention time peak slowly disappeared as more diketone was formed. In all reactions, this intermediate compound was never completely consumed. The nmr spectra of the crude products showed that an amide was present.

Apparently the short retention time by-products of the reactions are keto amides. These materials were oils which were difficult to purify and were not characterized further. The ease of separation of diketone from these by-products is one of the advantages of the synthetic method.

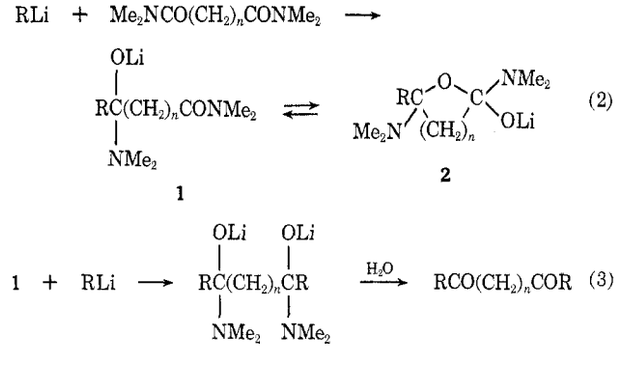
A monoadduct of organolithium compound and an *N,N,N',N'*-tetraalkyldiamide is implicated as an intermediate in these reactions on the basis of the glc data and in the reaction of 6-bromo-2-pyridyllithium with *N,N,N',N'*-tetramethylglutaramide. This reaction gives only a 21% yield of diketone when it is hydrolyzed after 5-min reaction time (all of the starting amide was completely consumed in this time). After 3 hr, a 76% yield of diketone was obtained. In our studies, glc also indicated that very little polyalkylation occurred except in the reactions of *n*-butyllithium. The violence of some of the hydrolyses indicated that organolithium reagent remained in some of the reactions.

It is thought that the intermediate formed in the reaction of an organolithium reagent with an *N,N*-dialkylamide does not lose amine until hydrolysis (eq 1).[2d,e] Thus, this appears to be the reason why very



$$\text{Rhi} + \text{Me}_2\text{NCOR}' \longrightarrow \text{RC(OLi)(NMe}_2\text{)R}' \xrightarrow{\text{H}_2\text{O}} \text{RCOR}' + \text{Me}_2\text{NH} + \text{LiOH} \quad (1)$$

little polyalkylation is observed. However, this does not explain why the intermediate (**1**) which leads to keto amide reacts so slowly with additional organolithium reagent. We believe that our data indicate an interaction between the amide and alkoxide groups in **1** (**2**, eq 2, 3). The possibility of an interaction such as in



$$\text{RLi} + \text{Me}_2\text{NCO(CH}_2\text{)}_n\text{CONMe}_2 \longrightarrow$$

$$\underset{\textbf{1}}{\text{RC(OLi)(NMe}_2\text{)(CH}_2\text{)}_n\text{CONMe}_2} \rightleftharpoons \underset{\textbf{2}}{\text{RC(OLi)(NMe}_2\text{)O(CH}_2\text{)}_n\text{NMe}_2} \quad (2)$$

$$\textbf{1} + \text{RLi} \longrightarrow \text{RC(OLi)(NMe}_2\text{)(CH}_2\text{)}_n\text{CR(OLi)(NMe}_2\text{)} \xrightarrow{\text{H}_2\text{O}} \text{RCO(CH}_2\text{)}_n\text{COR} \quad (3)$$

2 stabilizing **1** toward the attack of additional organolithium reagent is most markedly seen in the reaction of 2-thienyllithium with either *N,N,N',N'*-tetramethylsuccinamide or *N,N,N',N'*-tetramethylglutaramide. These reactions, which were the only ones in which product optimization studies were carried out, gave the best yields of 1,4 and 1,5 diketones when 4 equiv of 2-thienyllithium was utilized. In some attempts to hinder the possible formation of **2** sterically, 2-pyridyllithium, 6-bromo-2-pyridyllithium, and phenyllithium were treated with *N,N,N',N'*-tetraethylsuccinamide. These reactions failed to produce any 1,4 diketone. An attempt to trap **1** or **2** with chlorotrimethylsilane also failed.

We believe that our data indicate that it may be possible to prepare any 1,*n* diketone (where $n = 2, 3, 4 \ldots$) from *N,N,N',N'*-tetraalkyldiamides and organolithium reagents (except in the case of acidic amides such as malondiamides or monoalkylmalondiamides). If **2** is a factor which inhibits the formation of diketones from **1**, then the yields of diketones from diamides should increase with increasing chain length because of decreased intramolecular interactions as the ring size of **2** is increased.

Experimental Section

All nmr spectra were recorded on a Varian Associates T-60 nmr spectrometer. Ir spectra were obtained on a Beckman IR-8. Mass spectra were run on a Varian MAT CH-7 instrument. Gas chromatography was carried out on a Varian-Aerograph 1200 instrument using a 10 ft × 0.125 in. stainless steel 1% OV-17 on Chromosorb G column programmed from 70 to 260° at 10°/min. Microanalyses were obtained by Alfred Bernhardt Mikroanalytisches Laboratorium.

Materials.—*n*-Butyllithium (Foote Mineral Co.) in hexane was standardized before use.[5] 2,6-Dibromopyridine (Aldrich) was used without further purification. Thiophene (Fisher), bromobenzene (Baker and Adamson), and 2-bromopyridine (Eastman) were distilled from calcium hydride before use. Ether (Mallinckrodt Anhydrous Reagent) was used directly from the can. Tetrahydrofuran (THF) (Taylor Chemical) was distilled from benzophenone ketyl. Dimethylamine (Eastman) was used without further purification. 6-Bromo-2-pyridyllithium was prepared from 2,6-dibromopyridine and *n*-butyllithium.[4] 2-Pyridyllithium was prepared from 2-bromopyridine and *n*-butyllithium[6] at −78°. Phenyllithium[7] and 2-thienyllithium[8] were prepared according to "Organic Syntheses" procedures.

***N,N,N',N'*-Tetramethylsuccinamide.**—To a Parr 650-ml stainless steel split ring bomb equipped with magnetic stirrer was added 1 g of sodium methoxide and 174.2 g (1 mol) of diethyl succinate. To this mixture, cooled in an ice bath, was added 200 g (4.44 mol) of anhydrous dimethylamine. The sealed bomb was heated at 100° for 24 hr. The cooled reaction mixture, consisting of a solid and a liquid, was dissolved in THF and filtered. The filtrate was concentrated *in vacuo* to produce a solid which was recrystallized from THF–ether to yield 130 g (0.76 mol, 76%) of *N,N,N',N'*-tetramethylsuccinamide, mp 81–82° (lit.[9] mp 84.5–85.5°).

***N,N,N',N'*-Tetramethylglutaramide.**—Potassium *tert*-butoxide (1 g) and 240 g (1.5 mol) of dimethyl glutarate were placed in the 650 ml split ring bomb. The mixture was cooled and 250 g of anhydrous dimethylamine was added. The bomb was sealed and heated at 100° for 24 hr. At the end of this period some of the methanol which had formed was evaporated *in vacuo*. More dimethylamine (100 g) was added and the mixture was heated at 100° for 3 days. The cooled reaction mixture was filtered, concentrated *in vacuo*, and distilled at 117–120° (0.1 mm) to yield 215 g (1.16 mol, 77%) of *N,N,N',N'*-tetramethylglutaramide, mp 48–49° (lit.[10] 49–51°).

Preparation of Diketones.—The general procedure for the preparation of the diketones is illustrated for 1,5-diphenylpentane-1,5-dione and 1,4-bis(6-bromo-2-pyridyl)butane-1,4-dione.

(5) H. Gilman and F. K. Carteledge, *J. Organometal. Chem.*, **2**, 447 (1964).
(6) (a) D. W. Adamson and J. W. Billinghurst, *J. Chem. Soc.*, 1039 (1950); (b) H. Gilman and S. M. Spatz, *J. Org. Chem.*, **16**, 1485 (1951).
(7) L. A. Walters, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 757.
(8) E. Jones and I. M. Moodie, *Org. Syn.*, **50**, 104 (1970).
(9) J. K. Lawson, Jr., and J. T. Croom, *J. Org. Chem.*, **28**, 232 (1963).
(10) P. A. Meerburg, *Recl. Trav. Chim. Pays-Bas*, **18**, 365 (1899).

TABLE II[c]

PHYSICAL MEASUREMENTS ON DIKETONES

$$RC(CH_2)_nCR$$

Registry No.	R	Mp, °C	Recrystn solvent	Ir,[a] cm^{-1}	Nmr,[b] ppm
		$n = 2$			
	Phenyl	144–146° (lit.[d] 145–147°)	Petroleum ether–ether–benzene	1680	3.43 (s, 4 H) 7.53 (m, 6 H) 8.00 (m, 4 H)
37709-52-7	6-Bromo-2-pyridyl	200–201°	Ethanol–ethyl acetate	1700	3.63 (s, 4 H) 7.60–8.22 (2 m, 6 H)
37709-53-8	2-Pyridyl	140–141°	Ethanol	1700	3.70 (s, 4 H) 7.2–8.8 (2 m, 6 H)
13669-05-1	2-Thienyl	131–132°	Chloroform–ethanol	1660	3.37 (s, 4 H) 7.13 (m, 2 H) 7.57 (dd, 2 H) 7.73 (dd, 2 H)
		$n = 3$			
	Phenyl	65–66° (lit.[e] 65°)	Petroleum ether–ether	1680	2.22 (q, 2 H) 3.13 (t, 4 H) 7.25 (m, 6 H) 7.98 (m, 4 H)
37709-55-0	6-Bromo-2-pyridyl	121–122°	Ethanol–water	1700	2.17 (q, 2 H) 3.32 (t, 4 H) 7.53–8.13 (2 m, 6 H)
37709-56-1	2-Pyridyl	79–81°	Ethanol	1700	2.20 (q, 2 H) 3.37 (t, 4 H) 7.27–8.17 (m, 6 H) 8.67 (d, 2 H)
37709-57-2	2-Thienyl	88–89°	Ethanol	1660	2.17 (q, 2 H) 3.03 (t, 4 H) 7.17 (m, 2 H) 7.57 (m, 4 H)
37709-58-3	*n*-Butyl	61–62°	Ethanol–water	1710	2.32[f] (t, 8 H) 0.66–2.02 (m, 16 H)

[a] $CHCl_3$ solution. [b] $CDCl_3$ solution, parts per million downfield from TMS internal standard. [c] Satisfactory analytical and molecular weight data were reported for all new compounds listed in the table. [d] P. S. Bailey and A. E. Lutz, *J. Amer. Chem. Soc.*, **70**, 2412 (1948). [e] L. A. Wiles and E. C. Baughan, *J. Chem. Soc.*, 933 (1953). [f] CCl_4 solution (TMS internal standard).

1,5-Diphenylpentane-1,5-dione.—A solution of 0.2 mol of phenyllithium[7] was prepared from lithium wire and bromobenzene under argon in 160 ml of ether in a 250-ml round-bottomed flask equipped with mechanical stirrer, addition funnel, condenser, and thermometer. The phenyllithium solution was cooled to −78° with a Dry Ice–acetone bath and 18.6 g (0.1 mol) of solid *N,N,N′,N′*-tetramethylglutaramide was added. The reaction was stirred for 24 hr at −78° and was then hydrolyzed with 75–150 ml of water. The hydrolysate was transferred to a separatory funnel, the layers were separated, and the aqueous layer was extracted twice more with 100 ml of ether. The ether was dried over sodium sulfate and concentrated *in vacuo* to yield a semisolid. Recrystallization from petroleum ether (bp 30–60°)–ether gave 12.1 g (0.05 mol, 50%) of 1,5-diphenylpentane-1,5-dione.

1,4-Bis(6-bromo-2-pyridyl)butane-1,4-dione.—To a 250-ml, three-necked, round-bottomed flask equipped with mechanical stirrer and addition funnel was added under argon 10.0 g (0.042 mol) of 2,6-dibromopyridine and 100 ml of ether. As soon as all of the dibromopyridine was dissolved, the reaction flask was quickly cooled with constant stirring to −78° with a Dry Ice–acetone bath. The suspension of microcrystalline solid[4] was stirred for a few minutes and 0.042 mol of *n*-butyllithium in hexane was added in one portion. The solid dissolved to give a pale yellow solution. As soon as the solid dissolved, 3.6 g (0.021 mol) of *N,N,N′,N′*-tetramethylsuccinamide was added. The mixture was stirred for 3 hr at −78°, allowed to warm to room temperature, hydrolyzed with 50 ml of water, and then concentrated *in vacuo* to give a solid which was recrystallized from ethanol–ethyl acetate or dichloromethane to yield 5.8 g (0.015 mol, 71%) of 1,4-bis(6-bromo-2-pyridyl)butane-1,4-dione.

Table II gives the pertinent physical data on all the compounds prepared in this study.

Registry No.—*N,N,N′,N′*-Tetramethylsuccinamide, 7334-51-2; *N,N,N′,N′*-tetramethylglutaramide, 13424-80-1; 6-bromo-2-pyridyllithium, 37709-60-7; 2-pyridyllithium, 17624-36-1; 2-thienyllithium, 2786-07-4; *n*-butyllithium, 109-72-8.