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RESEARCH ARTICLE

Chemoselective Ketone Synthesis by the Strontium-mediated Alkylation or Arylation of *N*,*N*-Dimethylamides or Urea

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Abstract: Ketone synthesis via the addition of organometallic reagents to amides has long been investigated. In many cases, it is necessary to control the solvent, reaction temperature, and adhere to strict nucleophile stoichiometry for each combination of amide and organometallic reagent. Strontium, with an electronegativity comparable to lithium but a larger ionic radius, may display high reactivity with the characteristics of monoalkylation. Here, we show that the monoalkylation of various *N*,*N*-dimethylamide derivatives with alkyl iodides to afford the ketones proceeds smoothly under generally mild temperature conditions. By this method, not only aromatic amides but also α-proton-bearing aliphatic amides were suitable substrates for ketone synthesis. In addition, we found that tetramethylurea, typically a poor electrophile, also reacted to afford benzophenone in good yield with excellent selectivity.

Introduction

Ketones are valuable compounds found in a large number of biologically active molecules and serve as important synthetic building blocks for pharmaceuticals, agrochemicals, and functional materials.[1] The monoalkylation of carboxylic acid derivatives is a fundamental method for ketone synthesis. The classical method involves the addition reaction of an organocopper[2] or organochromium[3] reagent to an acid halide. However, this synthetic method is limited by the need for unstable and highly reactive acid halides as starting materials. In an attempt to use stable carboxylic acid derivatives as starting materials, Mukaiyama *et al.* reported a pioneering study using 2-thiopyridyl esters as substrates.[4] Thioesters are activated electrophiles that are also used for molecular conversion reactions *in vivo* and can be converted to ketones under mild conditions by treatment with organocopper reagents.[5]

Since amides are known to be readily available carboxylic acid derivatives, attempts at their monoalkylation have long been investigated (Figure 1).[6] Examples of ketone synthesis by the addition of alkyl lithiums to amides was reported by Evans *et al*. in 1956.[7] Almost 30 years later, Olah *et al.* reported the preparation of aldehydes and ketones from *N*,*N*-dimethylamides and Grignard or alkyl lithium reagents.[8] In many cases employing these reactions, it was necessary to strictly control the solvent, reaction temperature, and nucleophile stoichiometry for each amide and organometallic reagent combination. Otherwise, overreaction can occur with reactive nucleophiles to afford dialkylated tertiary alcohols, or reduction by β-hydride can proceed to give a secondary alcohol as a by-product (Figure 1A).[9]

To prevent such problems, a variety of approaches have been attempted. As mentioned, the first versatile method using 2-thiopyridyl esters was reported by Mukaiyama *et al*.[4] The prevention of overreaction by forming a chelated intermediate after monoalkylation can be achieved with Weinreb's particularly well-known *N*-methoxy-*N*-methyl amides (Figure 1B[1]);[10–12] commonly used 2-pyridylamide (Figure 1B[2])[13,14] and morpholineamide[15] function similarly. Also, a stereoselective version using chiral oxazolidinone derivatives[16] has been applied for the total synthesis of natural products.

Around the same time, it was found that stable tetrahedral intermediates were formed by the nucleophilic addition of organometallics to selected amides.[17] In the case of *N*-acylpyrrole substrates, protonated tertiary hemiaminals generated by the nucleophilic addition of the organometallic reagent could even be isolated (Figure 1B[3]).[18] Based on x-ray crystal structural analysis, Evans *et al*. reported stabilization of one such intermediate by a remarkable anomeric effect.[18a] Other stable tetrahedral intermediates have been generated by the reactions of "distorted" amides such as *N*-acylaziridine[19] or *N*-acylazetidine[20] (Figure 1B[4]).

In another approach, monoalkylation has been realized using organometallic reagents other than the frequently used lithium- and magnesium-based nucleophiles. [上野　雅晴1] When an organometallic reagent nucleophilic addition to an amide, the larger effective ionic radius of the metal ion would behave as "distorted" tetrahedral intermediates. Collins *et al*. reported the preparation of alkyl- and aryllanthanum triflates and their application in the monoalkylation of amides (Figure 1B[5]).[21] Recently, Knochel *et al.* reported the preparation of di(hetero)aryllanthanum reagents.[22] The electronegativity of lanthanum is close to those of lithium and magnesium on the Pauling scale (Li = 0.98, Mg = 1.31, La = 1.1),[23] and it has a larger

effective ionic radius (Li^+ = 76 pm, Mg^{2+} = 72 pm, La^{3+} =103 pm).[24] However, one of the technical drawbacks of these organic lanthanide reagents is that they must be prepared *in situ* from lithium reagents by halogen/lithium exchange with lanthanide salts.

In our laboratory, we have been investigating the synthetic applications of strontium compounds as alkaline-earth-based organometallic reagents.[25] However, apart from our work, few other studies on the preparation and reactivity of organostrontium compounds may be found in the literature.[26-29]

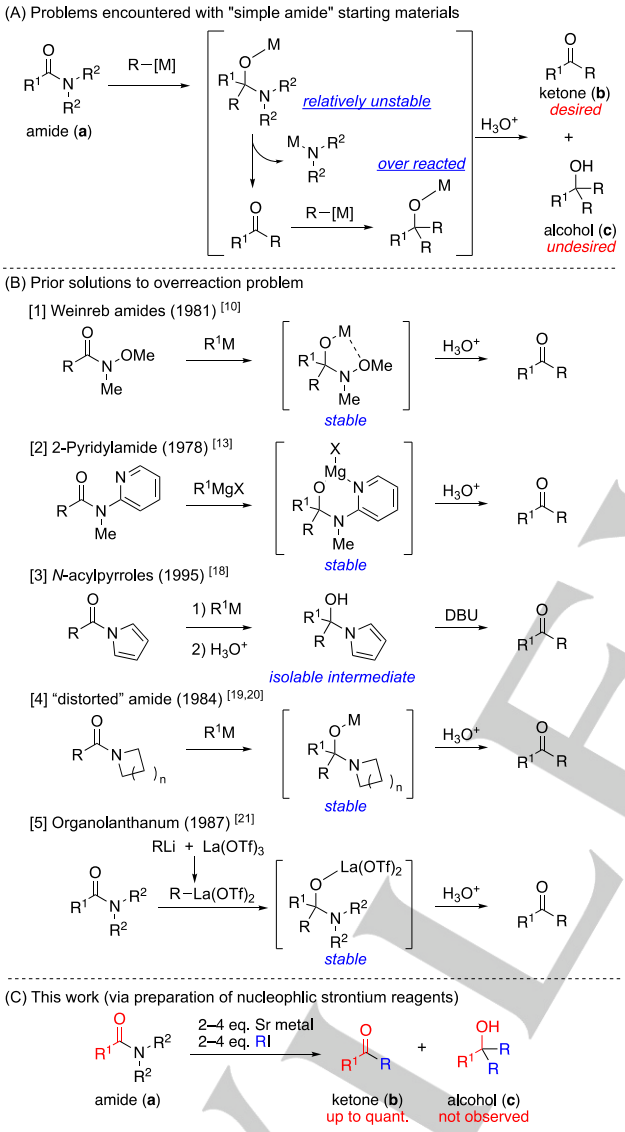
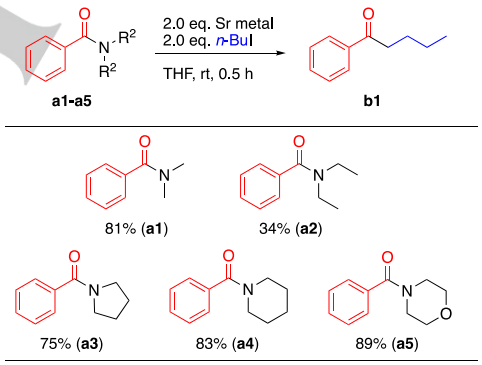


Figure 1. Synthesis of ketones from amides: prior solutions to overalkylation and our current work.

We previously reported that the alkylation of aldehydes or imines and the dialkylation of esters proceeded smoothly with the combination of metallic strontium and alkyl iodides under mild conditions.[30,31] The key feature of these transformations is that the organostrontium reagents can be readily prepared by the reaction of strontium metal and alkyl halides, in the same manner as organomagnesium reagents. Strontium has an electronegativity (0.95) comparable to lithium but with a larger ionic radius (Sr^{2+} = 118 pm) than lanthanum, suggesting that it may combine the high reactivity of organolithium species with the monoalkylation characteristics of organolanthanide reagents. Indeed, the expected monoalkylation of an *N*,*N*-dimethylamide substrate proceeded smoothly with an alkyl iodide in the presence of metallic strontium (Figure 1C). Herein, we report the details of the scope and limitations of ketone synthesis by the Sr(0)-mediated alkylation of *N*,*N*-dimethylamide derivatives.

Results and Discussion

First, we examined the reaction of *N*,*N*-dimethylbenzamide (**a1**) with *n*-butyl iodide as the alkyl source (Scheme 1).[32] After screening several reaction conditions, the reaction of **a1** (1.0 eq.) with *n*-butyl iodide (2.0 eq.) was carried out to give *n*-butylphenylketone **b1** in 81% yield. Various amides were applied in the reaction, with the results shown in Scheme 1. Using diethylamide **a2**, the yield decreased drastically to 34%. In contrast, for cyclic amides **a3–a5**, the yields were very similar to that of **a1**. The reaction proceeded particularly smoothly with morpholinamide **a5** to afford the best yield of adduct **b1** (89%). However, since *N*,*N*-dimethylamide derivatives are the simplest, least expensive, and most abundant and easily accessible secondary amides, they were selected as the most useful substrates for ketone synthesis by monoalkylation using organic strontium reagents.



Scheme 1. [上野　雅晴2]Substrate screening for monoalkylation potential.

Next, we investigated the reactions of arene-functionalized *N*,*N*-dimethylbenzamide derivatives using metallic strontium and various alkyl iodides (Table 1). *N*,*N*-Dimethylbenzamide **a1** reacted smoothly with primary and secondary alkyl iodides (3.0 eq.) to give the monoalkylated products in good yield (entries 1–4). When using a highly reactive reagent such as methyl iodide, the reaction must be performed at low temperature (entry 4). Otherwise, the reactions proceed smoothly under mild conditions at room temperature. Substrate **a1** also reacted smoothly with aryl iodides having electron-donating or electron-withdrawing groups (entries 5–10). Derivatives of *N*,*N*-dimethylbenzamide having electron-donating or electron-withdrawing groups (**a6**–**a10**) afforded the corresponding monobutylated ketones in good yields ([上野　雅晴3] entries 11–15), although the reaction of *N*,*N*-dimethyl-*p*-nitrobenzamide did not proceed, and returned only starting material ([上野　雅晴4] entry 16). Notably, [上野　雅晴5] despite the two halogen groups in 1-chloro-4-

iodobenzene, *p*-chlorophenyl phenyl ketone **b9** was obtained chemoselectively (entry 9).

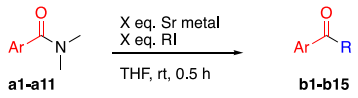


Table 1. Survey of reactant scope.

Entry	Ar	R	X (eq.)	Yield (%)
1	Ph (**a1**)	*n*-Bu	3.0	quant. (**b1**)
2	**a1**	iso-Bu	3.0	73 (**b2**)
3	**a1**	Et	3.0	82 (**b3**)
4	**a1**	Me	2.0	70[a] (**b4**)
5	**a1**	Ph	3.0	86 (**b5**)
6	**a1**	1-Naph	3.0	89[b] (**b6**)
7	**a1**	*p*-Me-C_6H_4	3.0	84 (**b7**)
8	**a1**	*p*-MeO-C_6H_4	3.0	78 (**b8**)
9	**a1**	*p*-Cl-C_6H_4	3.0	69[c] (**b9**)
10	**a1**	*m*-Cl-C_6H_4	3.0	62[c] (**b10**)
11	2-Naph (**a6**)	*n*-Bu	3.0	85 (**b11**)
12	*p*-Me-C_6H_4 (**a7**)	*n*-Bu	3.0	80 (**b12**)
13	*p*-MeO-C_6H_4 (**a8**)	*n*-Bu	2.0	78 (**b13**)
14	*p*-*t*-Bu-C_6H_4 (**a9**)	*n*-Bu	2.0	89 (**b14**)
15	*p*-CF_3-C_6H_4 (**a10**)	*n*-Bu	3.0	76 (**b15**)
16	*p*-NO_2-C_6H_4 (**a11**)	*n*-Bu	2.0	No reaction[d]

[a] The reaction was carried out at −78 °C, 24 h. [b] 0 °C, 4 h. [c] 0 °C, 1 h. [d] 84% of starting material **a11** was recovered.

As shown in entries 9 and 10 in Table 1, our method results in a strictly chemoselective reaction even for substrates with different halogen substituents. However, for a halogen-containing substrate, the organometallic reagent (as used in excess) can react not only with the starting material but also the halogenated product, causing side reactions such as dehalogenation and alkylation. In the conversion of *N*,*N*-dimethylamides to ketones reported by Olah,[8] a small excess of alkyl lithium reagent (1.05 eq.) was generally used. To explore the effects of stoichiometry on the selectivity of the reaction, we compared the differences between the two methods in detail for halogenated reactant **a12** (Table 2). In the case of *n*-butylation, when 1.05 eq. of the alkyl source was used, unreacted amide **a12** was observed for both methods, although more of the desired product was obtained under Olah's conditions (entry 1). However, upon adding excess *n*-butyl lithium (3.0 eq.) to drive the reaction to completion, the product distribution became more complex[33] and the yield of the target (**b16**) decreased. In contrast, by our method, the reaction did not become more complex even with the addition of excess reagent, with the yield of **b16** reaching 80% under these conditions (entry 2). Thus, the main feature of the strontium method is its high functional group selectivity, without a need to strictly control the reagent stoichiometry.

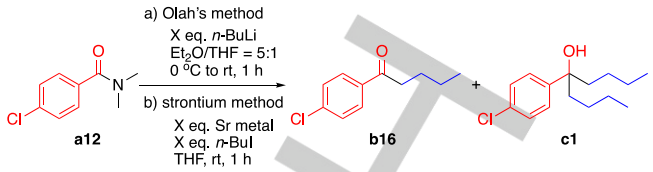
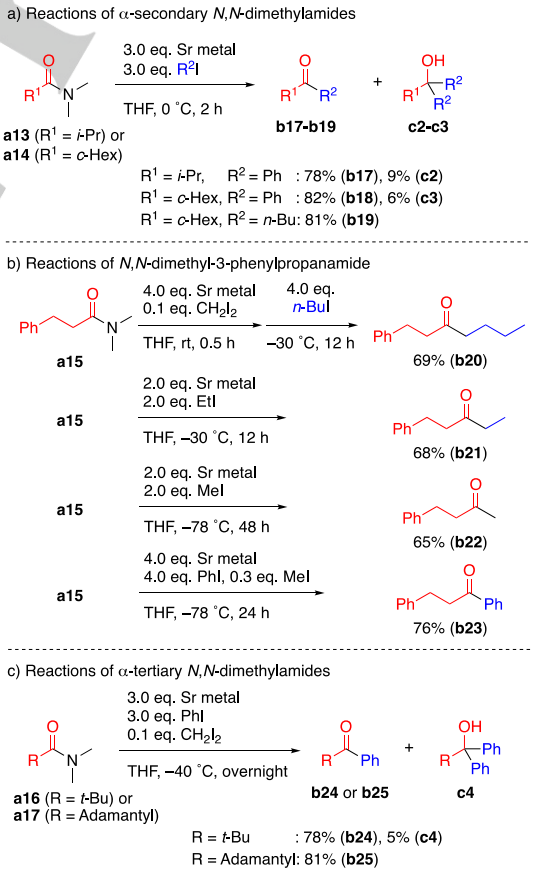


Table 2. Comparison of ketone syntheses for halogenated substrate **a12**.

		Olah's method			Strontium method		
Entry	X (eq.)	**a12**	**b16**	**c1**	**a12**	**b16**	**c1**
1	1.05	25	65	trace	46	40	-
2	3.0	-	47	21	-	80	-

Next, *N*,*N*-dimethylamides derived from aliphatic carboxylic acids were investigated, with similarly pleasing results (Scheme 2). Bulky α-secondary carboxylic amides **a13** and **a14** underwent the reaction to afford the corresponding mono-arylated or -alkylated ketones **b17–b19** in good yields at 0 °C (Scheme 2a). However, for these substrates, the reaction with phenyl iodide also gave small amounts of diarylated adducts **c2** and **c3**.



Scheme 2. Strontium-mediated alkylation or arylation of *N*,*N*-dimethylamides derived from aliphatic carboxylic acids.

We found that it was difficult to control the reaction of *N,N*-dimethyl-3-phenylpropanamide **a15**, with its α-protons, and it became necessary to independently study the conditions (temperature, stoichiometry, and/or activating agent) for each reactant as a nucleophile (Scheme 2b). Thereafter, ketones **b20–23** could be obtained from substrate **a15** in moderate to good yields under the optimized conditions. The reaction of *N,N*-dimethylpivalamide, which is very sterically hindered, was also difficult to control.[34] The best results were obtained for the overnight reaction with 3.0 equivalents phenyl iodide in the presence of 0.1 equivalents diiodomethane as an activator of metallic strontium at –40 °C. The reaction proceeded smoothly, producing monophenyl ketone **b24** in good yield (78%) while suppressing diarylated product **c4** to 5% (Scheme 2c). *N,N*-Dimethyladamantylcarboxamide also reacted cleanly, producing only the monophenyl adduct in 81% yield.

In Table 2, we presented the reactions of a special halogen-containing amide with excess organometallic reagents, and the differences in reactivity for each reagent were examined. Next, we compare the differences in reactivity of three organometallic reagents in excess, using aliphatic amide substrates (Table 3). With phenylmagnesium chloride, no reaction occurred with either *N,N*-dimethyl pivalamide **a16** or adamantylcarboxamide **a17**. Although the reaction of **a16** with phenyllithium did proceed, the yield greatly varied depending on the equivalents of organometallic reagent employed. The strontium metal/organohalide system worked nicely in both cases.

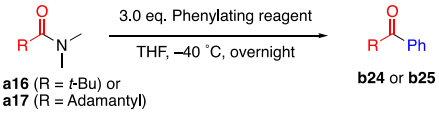
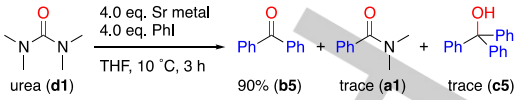


Table 3. Comparison of Sr(0)/RI with Grignard and organolithium reagents

Entry	R	Phenylating agent		
		Sr, PhI (%)[a]	PhMgCl (%)	PhLi (%)
1	*t*-Bu (**b24**)	78	no reaction	32[b] (66)[c]
2	Adamantyl (**b25**)	81	no reaction	-

[a] Activated with 0.1 eq. CH_2I_2 (see Scheme 2b). [b] Bis-arylated compound **c4** (38%) was also obtained. [c] 1.1 eq. PhLi was used.

Finally, we were interested in the reactivity of tetramethylurea as a derivative of dimethylamide. Carbon monoxide[35] and dithians[36] are well known as carbonyl synthons; however, due to their toxicity and difficulty in handling, it was hoped that urea **d1** could be used analogously. Several groups have reported the synthesis of unsymmetrical ketones by use of a special urea with a Weinreb amide-type structure.[37] Recently, Sarpong *et al.* reported that *N*-methoxy-*N*-methyl-1*H*-pyrrole-1-carboxamide could be used to synthesize unsymmetrical ketones with a relatively wide range of organometallic reagents applications, however, the reaction conditions must be individually tailored for each nucleophile.[37a] Compared to these specially prepared ureas, tetramethyl urea, a non-protic polar solvent, is available at low cost and has been used as a substitute for HMPA. Tetramethylurea reacted with reagents prepared from strontium metal and phenyl iodide to give mono-, di-, and triarylated adducts. After much investigation, the reaction of tetramethylurea **d1** with 4.0 equivalents phenyl iodide and metallic strontium was carried out at 10 °C for 3 h to afford predominantly the diarylated adduct, benzophenone **b5**, in 90% yield (Scheme 3[上野　雅晴9]).[34]



Scheme 3. Strontium-mediated arylation of *N,N,N',N'*-tetramethylurea as a carbonyl dication synthetic equivalent.

Conclusion

In summary, to demonstrate the usefulness of strontium-mediated monoalkylations, we investigated the scope and limitations of the reactions of *N,N*-dimethylamide derivatives with alkyl iodides and found them to proceed smoothly under suitable temperature conditions. Also, we revealed that, in the cases of aryl iodides with a second halogen substituent such as 1-chloro-4-iodobenzene, highly chemoselective monoalkylation was predominantly obtained to afforded the corresponding ketones. In addition, poorly reactive tetramethylurea also underwent the transformation to generate benzophenone in good yield with excellent selectivity.

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Keywords: dimethylamide • ketone • monoalkylation • strontium • synthetic method

[1] a) M. B. Smith, J. March, March's Advanced Organic Chemistry, 6th ed., Wiley, New Jersey, 2007. b) P. Vogel in Science of Synthesis, Vol. 26 (Ed.: J. Cossy), Thieme, New York, 2005, pp. 13–38.
[2] B. H. Lipshutz, S. Sengupta in Organic Reactions, Vol. 41 (Ed.: L. A. Paquette), Wiley, New York, 1992, pp. 135–631.
[3] K. Takai in Organic Reactions, Vol. 64 (Ed.: L. E. Overman), Wiley, New York, 2004, pp. 253–612.
[4] T. Mukaiyama, H. Araki, H. Takei, *J. Am. Chem. Soc.* **1973**, *95*, 4763–4765.
[5] a) N. Yoshikai, E. Nakamura, *Chem. Rev.* **2012**, *112*, 2339–2372; b) R. J. Anderson, C. A. Henrick, L. D. Rosenblum, *J. Am. Chem. Soc.* **1974**, *96*, 3654–3655.
[6] a) R. Luisi, V. Capriati, *Lithium Compounds in Organic Synthesis*, Wiley-VCH, Weinheim, **2014**; b) P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**; c) J. Clayden, *Organolithiums: Selectivity for Synthesis*; Pergamon Press, Oxford, **2002**; For a review on the addition reactions of organometallics to amides, see: d) V. Pace, W. Holzer, B. Olofsson, *Adv. Synth. Catal.* **2014**, *356*, 3697–3736; For the review on application for the total synthesis, see: e) T. Sato, M. Yoritake, H. Tajima, N. Chida, *Org. Biomol. Chem.* **2018**, *16*, 3864–3875.
[7] E. A. Evans, *J. Chem. Soc.* **1956**, 4691–4692.
[8] G. A. Olah, G. K. S. Prakash, M. Arvanaghi, *Synthesis* **1984**, 228–230.
[9] a) R. K. Dieter, *Tetrahedron* **1999**, *55*, 4177–4236; b) H. Maeda, J. Okamoto, H. Ohmori, *Tetrahedron Lett.* **1996**, *37*, 5381–5384.
[10] For the original report, see: a) S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815–3818; [上野　雅晴10] Quite recently, an efficient method for chemoselective synthesis of biaryl ketones by arylation of Weinreb amides with Grignard reagents, which prepared from Mg/halide exchange of *i*-PrMgCl·LiCl with aryl iodides was reported, see: b) G. Li, M. Szostak, *Org. Biomol. Chem.* **2020**, *18*, 3827–3831.
[11] For reviews, see: a) R. Senatore, L. Ielo, L. Castoldi, V. Pace, *Synthesis* **2019**, *51*, 2792–2808; b) V. K. Khlestkin, D. G. Mazhukin, *Curr. Org. Chem.* **2003**, *7*, 967–993; c) M. Mentzel, H. M. R. Hoffmann, *J. prakt. Chem.* **1997**, *339*, 517–524.
[12] For applications to total synthesis, see: a) S. Balasubramaniam, I. S.

Aidhen, *Synthesis* **2008**, 3707–3738; b) D. A. Evans, R. P. Polmiaszek, K. M. DeVries, D. E. Guinn, D. J. Mathre, *J. Am. Chem. Soc.* **1991**, *113*, 7613–7630.

[13] a) D. L. Comins, J. D. Brown, *Tetrahedron Lett.* **1984**, *25*, 3297–3300; b) A. I. Meyers, D. L. Comins, *Tetrahedron Lett*. **1978**, *19*, 5179–5182.

[14] Recently, the 2-pyridylamide group was used as a good leaving group for coupling reactions via the transition metal-mediated insertion of N–C cleavage, see: a) W.-P. Mai, Y. Liu, H.-D. Sui, Y.-M. Xiao, P. Mao, K. Lu, *Eur. J. Org. Chem*. **2019**, *2019*, 7814–7819; b) G. Meng, R. Lalancette, R. Szostak, M. Szostak, *Org. Lett*. **2017**, *19*, 4656–4659.

[15] a) N. Dittrich, E-K. Jung, S. J. Davidson, D. Barker, *Tetrahedron*, **2016**, *72*, 4676–4689; b) M. M. Jackson, C. Leverett, J. F. Toczko, J. Roberts, *J. Org. Chem*. **2002**, *67*, 5032–5035.

[16] For review, see: S. G. Davies, A. M. Fletcher, J. E. Thomson, *Chem. Commun*. **2013**, *49*, 8586–8598.

[17] For[上野　雅晴11] recent research examples, see: a) G. Li, M. Szostak, *Chem Eur. J.* **2020**, *26*, 611–615; b) L. Castoldi, W. Holzer, T. Langer, V. Pace, *Chem. Commun*. **2017**, *53*, 9498–9501; For review, see: c) M. Adler, S. Adler, G. Boche, *J. Phys. Org. Chem.* **2005**, *18*, 193–209.

[18] a) D. A. Evans, G. Borg, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2002**, *41*, 3188–3191; b) S. Brandänge, E. Holmgren, H. Leijonmarck, B. Rodriguez, *Acta Chem. Scand*. **1995**, *49*, 922–928.

[19] a) D. Schmidt, J. Conrad, I. Klaiber, U. Beifuss, *Chem. Commun*. **2006**, 4732–4734; b) S. Miwatashi, Y. Arikawa, K-i. Naruo, K. Igaki, Y. Watanabe, H. Kimura, T. Kawamoto, S. Ohkawa, *Chem. Pharm. Bull.* **2005**, *53*, 410–418; c) B. Lygo, *Tetrahedron* **1995**, *51*, 12859–12868; d) B. Lygo, *Tetrahedron Lett*. **1994**, *35*, 5073–5074; e) S. Wattanasin, F. G. Kathawala, *Tetrahedron Lett*. **1984**, *25*, 811–814.

[20] C. Liu, M. Achtenhagen, M. Szostak, *Org. Lett*. **2016**, *18*, 2375–2378.

[21] a) S. Collins, Y. Hong, G. J. Hoover, J. R. Veit, *J. Org. Chem.* **1990**, *55*, 3565–3568; b) S. Collins, Y. Hong, *Tetrahedron Lett.* **1987**, *28*, 4391–4394.

[22] A. D. Benischke, L. Anthore-Dalion, G. Berionni, P. Knochel, *Angew. Chem. Int. Ed*. **2017**, *56*, 16390–16394.

[23] L. C. Allen, *J. Am. Chem. Soc.* **1989**, *111*, 9003–9014.

[24] R. D. Shannon, *Acta. Cryst*. **1976**, *A32*, 751–767.

[25] For reviews, see: a) N. Miyoshi, in *Houben-Weyl: Methods of Molecular Transformation, Science of Synthesis*, Vol.7 (ed.: H. Yamamoto), Thieme, Stuttgart, **2004**, pp. 685–694; b) W. E. Lindsell, in *Comprehensive Organometallic Chemistry II*, Vol. 1 (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Pergamon Press, Oxford, **1995**, Chap. 3, pp57–127, and references cited therein.

[26] Lindsell et al. reported that in situ prepared methylstrontium iodide reacted with carbonyl compounds to afford the corresponding products. However, almost all cases in low yields except for the reaction with benzophenone.: a) G. Gowenlock, W. E. Lindsell, B. Singh, *J. Chem. Soc. Dalton* **1978**, 657–664; b) G. Gowenlock, W. E. Lindsell, B. Singh, *J. Organomet. Chem.* **1975**, *101*, C37–C39.

[27] a) M.S. Sell, R.D. Rieke, *Synth. Commun*. **1995**, *25*, 4107–4113; b) L. N. Cherkasov, V. N. Cherkasov, *Russ. J. Org. Chem*. **1995**, *31*, 298–299; c) L. N. Cherkasov, S. I. Radchenko, *Russ. J. Org. Chem*. **1994**, *30*, 456–457; d) L. N. Cherkasov, V. I. Panov, V. N. Cherkasov, *Russ. J. Org. Chem*. **1993**, *29*, 411–411.

[28] Yanagisawa *et al.* also reported the preparation of allyl strontium reagents and demonstrated a single example of the allylation of an azo compound; see: A. Yanagisawa, T[上野　雅晴12]. Jitsukawa, K. Yoshida, *Synlett* **2013**, *24*, 635–639.

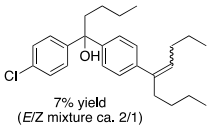
[29] Recently, several groups have reported the reaction mediated by strontium catalysts: a) B. Liu, T. Roisnel, J.-F. Carpentier, Y. Sarazin, *Angew. Chem. Int. Ed*. **2012**, *51*, 4943–4946; b) S. Datta, M. T. Gamer, P. W. Roesky, *Organometallics* **2008**, *27*, 1207–1213; c) A. G. M. Barrett, M. R. Crimmin, M. S. Hill, P. B. Hitch- cock, G. Kociok-Kçhn, P. A. Procopiou, *Inorg. Chem*. **2008**, *47*, 7366–7376; d) M. Agostinho, S. Kobayashi, *J. Am. Chem. Soc*. **2008**, *130*, 2430–2431.

[30] a) S. D. Ohmura, Y. Miyazaki, D. Kanehiro, Y. Yamaguchi, S. Kitakata, S. Tateda, T. Nishizawa, R. Shimoda, G. Nagaoka, M. Ueno, N. Miyoshi, *Asian J. Org. Chem*. **2017**, *6*, 821–824; b) N. Miyoshi, T. Matsuo, M. Wada, *Eur. J. Org. Chem.* **2005**, *34*, 4253–4255; c) N. Miyoshi, D. Ikehara, T. Kohno, A. Matsui, M. Wada, *Chem. Lett.* **2005**, *34*, 760–761; d) N. Miyoshi, K. Kamimura, H. Oka, A. Kita, R. Kuwata, D. Ikehara, M. Wada, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 341–345.

[31] For the other reactions using strontium reagents that we have developed, see: a) S. D. Ohmura, M. Ueno, N. Miyoshi, *Tetrahedron Lett*. **2018**, *59*, 2268–2271; b) N. Miyoshi, M. Asaoka, Y. Miyazaki, T. Tajima, M. Kikuchi, M. Wada, *Chem. Lett.* **2012**, *41*, 35–36; c) N. Miyoshi, T. Matsuo, M. Mori, A. Matsui, M. Kikuchi, M. Wada, M. Hayashi, *Chem. Lett.* **2009**, *38*, 996–997; d) N. Miyoshi, T. Kohno, M. Wada, S. Matsunaga, I. Mizota, M. Shimizu, *Chem. Lett.* **2009**, *38*, 984–985; e) N. Miyoshi, T. Matsuo, M. Asaoka, A. Matsui, M. Wada, *Chem. Lett.* **2007**, *36*, 28–29.

[32] All experimental details and characterization data are provided in the Supporting Information.

[33] Another by-product was also isolated, as shown below:



7% yield
(*E*/*Z* mixture ca. 2/1)

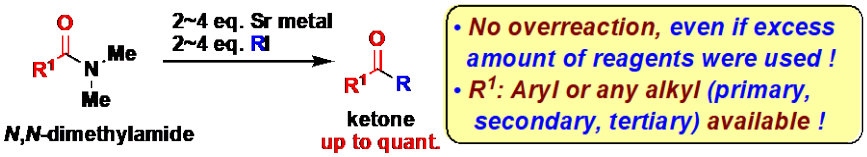
[34] A detailed discussion of the reaction conditions is provided in the Supporting Information.

[35] For a recent review of the field, see: X.-F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4986–5009. See also referenced therein.

[36] For overviews of this tactic, see: a) A. B. Smith III, S. M. Pitram, A. M. Boldi, M. J. Gaunt, C. Sfouggatakis, W. H. Moser, *J. Am. Chem. Soc*. **2003**, *125*, 14435–14445; b) M. Yus, C. Najera, F. Foubelo, *Tetrahedron* **2003**, *59*, 6147–6212; c) A. B. Smith III, S. M. Condon, J. A. McCauley, *Acc. Chem. Res*. **1998**, *31*, 35–46; d) A. B. Smith III, A. M. Boldi, *J. Am. Chem. Soc*. **1997**, *119*, 6925–6926; e) L. F. Tietze, H. Giessler, J. A. Gewert, U. Jakobi, *Synlett* **1994**, 511–512.

[37] a) S. T. Heller, J. N. Newton, T. Fu, R. Sarpong, *Angew. Chem. Int. Ed.* **2015**, *54*, 9839–9843; b) N. R. Lee, J. I. Lee, *Synth. Commun*. **1999**, *29*, 1249–1255; c) W. L. Whipple, H. J. Reich, *J. Org. Chem.* **1991**, *56*, 2911–2912; d) D. J. Hlasta, J. J. Court, *Tetrahedron Lett*. **1989**, *30*, 1773–1776.

Entry for the Table of Contents



We explore amide-to-ketone conversions by the action of organostrontium reagents. *N*,*N*-dimethylamides were monoalkylated with alkyl or aryl iodides in the presence of strontium metal, selectively affording ketones in good yields under mild conditions. Aromatic and aliphatic amides were suitable substrates. Even the poor electrophile, tetramethylurea, reacted with PhI/Sr(0) to afford benzophenone in good yield with excellent selectivity.