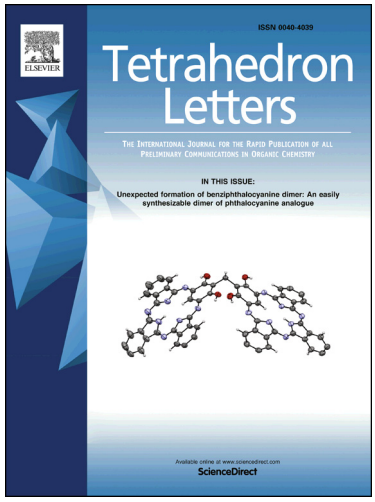

Convergent synthesis of 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines using Weinreb amide

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PII: S0040-4039(17)31200-5
DOI: https://doi.org/10.1016/j.tetlet.2017.09.064
Reference: TETL 49334

To appear in: *Tetrahedron Letters*

Received Date: 20 August 2017
Revised Date: 18 September 2017
Accepted Date: 21 September 2017

Please cite this article as: Nishimura, Y., Kubo, T., Okamoto, Y., Cho, H., Convergent synthesis of 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines using Weinreb amide, *Tetrahedron Letters* (2017), doi: https://doi.org/10.1016/j.tetlet.2017.09.064

Tetrahedron Letters
journal homepage: www.elsevier.com

Convergent synthesis of 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines using Weinreb amide

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

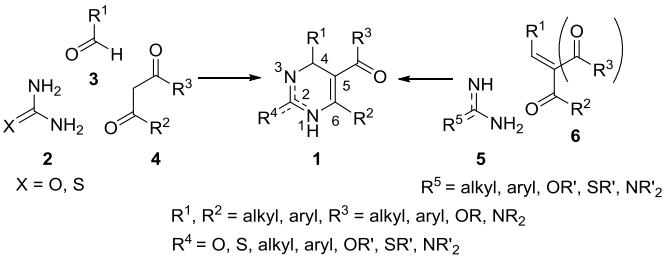
Keywords:
dihydropyrimidine
heterocycles
Staudinger reaction
Aza-Wittig reaction
Weinreb amide

ABSTRACT

A method of convergent synthesis of novel 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines **7** is developed. The synthetic intermediate of **7**, 4,6-unsubstituted 2-aminodihydropyrimidines **9** having a Weinreb amide at the 5-position, is prepared by the sequential Staudinger/aza-Wittig/cyclization reactions of (*E*)-*tert*-butyl {3-azido-2-[methoxy(methyl)carbamoyl]allyl}carbamate (*E*)-**10**. The transformation of the Weinreb amide of **9** to an acyl group proceeds smoothly by a substitution reaction using aryllithiums or alkyllithiums in the presence of a catalytic amount of BF_3 etherate, affording **7** in good to high yield. The N-protecting group of **7** can be easily removed to obtain N-unsubstituted 2-amino-5-acyldihydropyrimidines **8**, and the derivatives are observed as a single isomer in ^{1}H NMR spectroscopy. All dihydropyrimidines in this study were hitherto unavailable and difficult to synthesize by conventional methods.

Dihydropyrimidines have received much attention from synthetic and medicinal chemists owing to their biological activities and unique physical and chemical characteristics.[1] They exhibit a wide range of activities for medicinal applications, such as antiviral, antitumor, antibacterial, and anti-inflammatory activities. In addition, they are regarded as calcium channel antagonists,[2] Rho-associated kinase isoform 1 (ROCK1) inhibitors for cardiovascular diseases,[3] or pharmaceutical agents for anti-hepatitis B virus replication.[4] Their anticancer potential has also been explored recently.[5] Therefore, the development of versatile synthetic methods for dihydropyrimidines and the expansion of the structural diversity of these compounds are important and will contribute to advances in medicinal chemistry.

Dihydropyrimidines **1** have generally been synthesized by the reactions of (thio)urea **2** with aldehydes **3** and 1,3-dicarbonyl compounds **4**, or the reactions of amidines, guanidines, and *O*(*S*)-alkyliso(thio)urea derivatives **5** with α,β-unsaturated carbonyl compounds **6** (Scheme 1).[1a,6] Therefore, the R^1 and R^2 substituents at the C-4 and C-6 positions of **1** are typically alkyl or aryl groups, whereas the COR^3 substituent at the 5-position is an acyl, alkoxycarbonyl, or amide group. Multisubstituted dihydropyrimidines **1** are comparatively easy to synthesize, whereas the synthesis of less substituted dihydropyrimidines is problematic. Some reasons for this are as follows: it is difficult to control the high reactivity of formaldehyde (**3**; R^1= H), and



Scheme 1. Synthesis of dihydropyrimidines by condensation reactions

β-oxoaldehyde (**4**; R^2 = H) is not easily available. To overcome these difficulties during the course of our continuous research on dihydropyrimidines,[7] we previously developed a novel method of synthesis of 4,6-unsubstituted 2-phenyldihydropyrimidines having an acyl group at the 5-position, in which a Weinreb amide was used as an acyl precursor.[7h,8] Although this method is useful for the synthesis of hitherto unavailable 4,6-unsubstituted 5-acyldihydropyrimidines, the substituent at the 2-position was limited to only a phenyl group. On the other hand, we previously developed sequential Staudinger/aza-Wittig/cyclization reactions for the synthesis of 4,6-unsubstituted 2-aminodihydropyrimidine-5-carboxylates.[7g] Using the sequential reactions, we herein describe a method of convergent synthesis of 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines **7** and N-unsubstituted **8** from dihydropyrimidines **9** (Scheme 2). Namely, the sequential

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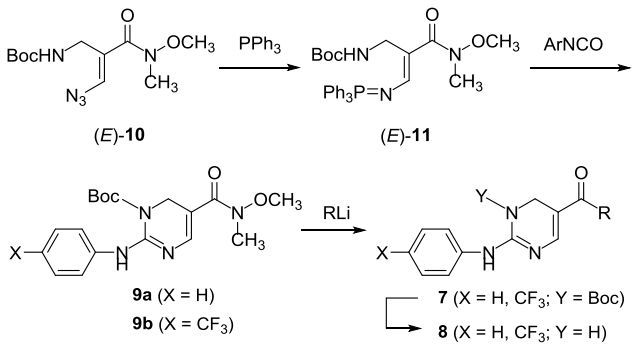


Scheme 2. Synthetic strategy for 5-acyl-2-aminodihydropyrimidines **7** and **8**

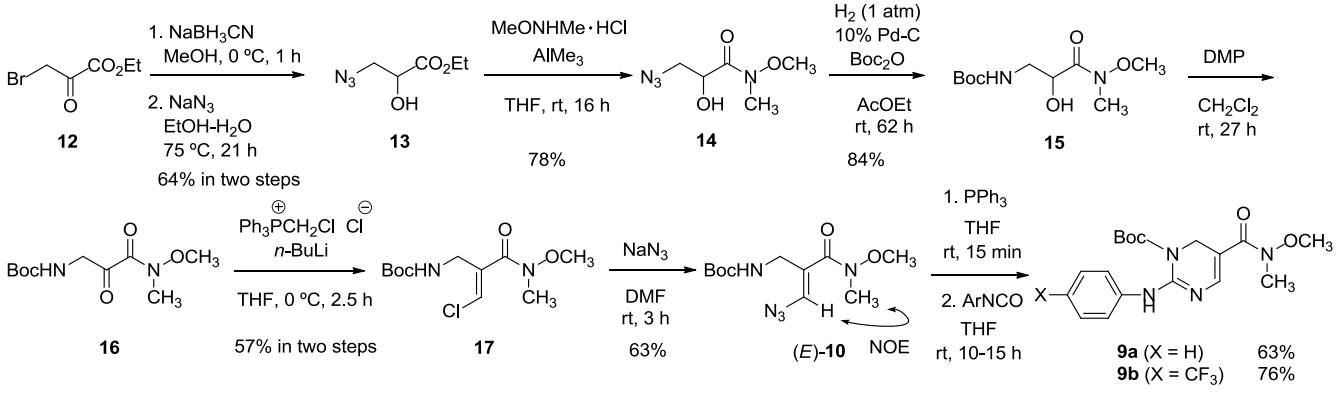
reactions of alkenyl azide (*E*)-**10** having Weinreb amide provide **9** via iminophosphorane intermediate (*E*)-**11**. Subsequently, the substitution reaction of the Weinreb amide of **9** by organolithium reagents gives **7**. It is difficult to synthesize **7** and **8** by conventional methods. In fact, the general formulae of **7** and **8** have not as yet been reported. Therefore, our novel method enables to introduce various 2-amino and 5-acyl groups to the dihydropyrimidine scaffold.

In general, multisubstituted 2-aminodihydopyrimidines have been synthesized by three-component condensation using guanidines, aldehydes, and β-dicarbonyl compounds,[9] by cyclization of guanidines with α,β-unsaturated carbonyl compounds,[6f,10] or by the nucleophilic substitution reactions of 2-alkylthio[7a,11a] or 2-alkoxydihydropyrimidines[11b] with amines. For the synthesis of less substituted 2-aminodihydropyrimidines, several methods that provide 5,6-unsubstituted 2-amino-4-oxo-dihydropyrimidines[12] and a few reduction reactions of pyrimidines have been reported thus far.[13]

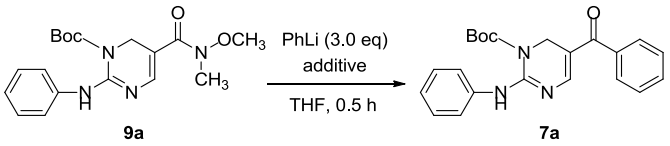
First, the precursor of **9**, alkenyl azide (*E*)-**10** with a Weinreb amide, was prepared from ethyl bromopyruvate **12** in seven steps, as shown in Scheme 3. The reduction of **12** using sodium cyanoborohydride and the subsequent substitution reaction with sodium azide afforded ethyl 3-azido-2-hydroxypropanoate **13** in two steps in 64% yield.[7g,14] Subsequently, **13** was reacted with N,O-dimethylhydroxylamine hydrochloride in the presence of trimethylaluminum at room temperature (rt) to give the Weinreb amide **14** in 78% yield.[15] Next, the one-pot reduction of the azide group to a primary amine and protection of the amine by *t*-butoxycarbonyl (Boc) group gave the carbamate **15** in 84% yield. Although the oxidation reaction of **15** was examined under several conditions using pyridinium dichromate (PDC), sulfur trioxide pyridine complex, or 2-iodoxybenzoic acid (IBX), the reactions resulted in a low yield (<30%) of **16**. Eventually the optimal conditions were the same as before, and the reaction using freshly prepared Dess–Martin periodinane (DMP) worked well and gave the desired α-keto ester in high yield.[7g] When the crude α-keto ester was subjected to the Wittig reaction using chloromethyltriphenylphosphonium chloride and *n*-butyllithium, chloroalkene **17** was obtained as a single stereoisomer in two steps in 57% yield. The treatment of **17** with sodium azide afforded azidoalkene (*E*)-**10** as a single stereoisomer in 63% yield. The olefin geometries of **17** and **10** were different from those in our previous report on the synthesis of azidoalkene bearing an ethyl ester,[7g] probably because the bulky Weinreb amide group prevented the production of (*Z*)-isomers of **17** and **10**. The structure of (*E*)-**10** was determined by NOE experiments: a significant NOE was observed between the methyl protons of the Weinreb amide and the alkene proton. Therefore, the structure was determined to be (*E*)-**10** (see Supplementary Material). After obtaining (*E*)-**10**, the sequential reactions for the synthesis of **9** were attempted. The Staudinger reaction of (*E*)-**10** with triphenylphosphine proceeded smoothly with nitrogen generation to give the iminophosphorane intermediate (*E*)-**11** quantitatively (shown in Scheme 2), and the aza-Wittig reaction of (*E*)-**11** with phenylisocyanate following cyclization furnished the dihydropyrimidine **9a** in 63% yield.[16] 4-(Trifluoromethyl)phenylisocyanate was also successfully applied to the reaction to provide **9b** in 76% yield.

Next, we optimized the reaction conditions of nucleophilic substitution of **7** (Table 1). When **9a** was reacted with phenyllithium (3.0 eq) at 0 ºC, the desired 5-benzoyldihydropyrimidine **7a** was obtained in 55% yield with recovery of **9a** at 4% (entry 1). When 2.0 eq of phenyllithium was used, the reaction was not complete, as determined by TLC analysis. Therefore, excess phenyllithium was needed for consumption of **9a**, probably because 1.0 eq of phenyllithium was initially consumed to deprotonate the NH proton of the 2-phenylamino group of **9a**, and the coordination of other nitrogen atoms in the dihydropyrimidine ring of **9a** may deactivate phenyllithium. In entry 2, decreasing the reaction temperature (−40 ºC) increased the yield of **7a** to 68%. The reaction at −80 ºC was slow and gave **7a** in 61% yield, and unreacted **9a** (14%) was observed in the ^{1}H NMR spectrum of the crude reaction mixture (entry 3). Next, we tested the effect of additives on the yield of **7a**. Addition of $MgCl_2$ and $CeCl_3$ slightly increased the yields from 68% to 73% and 75%, respectively (entries 4, 5). When BF_3 etherate was added, **9a** was obtained in a good yield of 77% (entry 6). Further optimization revealed that the reaction in the presence of 0.2 eq of BF_3 etherate furnished **9a** in high yield of 81% (entry 7).

As reported previously,[7h] the reaction of 4,6-unsubstituted 2-phenyldihydropyrimidine **18** having a Weinreb amide at 5-position with RLi (*n*-C_4H_9Li or PhLi) gave 5-acyldihydropyrimidines **19** along with side products **20** by



Scheme 3. Preparation of dihydropyrimidine **9**.

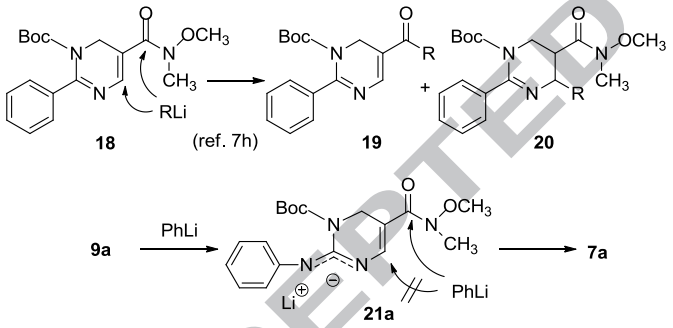


entry	additive	temp. (ºC)	Yield (%)[a]
1	none	0	55 (4)
2	none	–40	68 (4)
3	none	–80	61 (14)
4	$MgCl_2$ (0.5 eq)	–40	73 (2)
5	$CeCl_3$ (0.5 eq)	–40	75 (2)
6	BF_3•Et_2O (0.5 eq)	–40	77 (8)
7	BF_3•Et_2O (0.2 eq)	–40	81 (3)

a) The value in parentheses is unreacted **9a** (%) observed in ^{1}H NMR of crude reaction mixture.

Table 1. Optimization of reaction conditions for the synthesis of 5-benzoyldihydropyrimidine **7a**

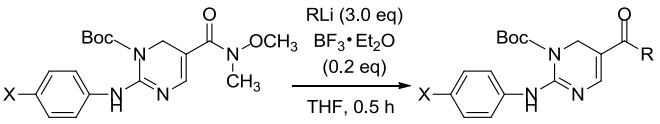
conjugate addition (Scheme 4). However, no such side product was observed in the reaction of **9a** shown in Table 1. In the reaction with **9a**, the initial deprotonation of the NH proton of the 2-phenylamino group by PhLi occurred prior to addition to the Weinreb amide, and conjugate addition of PhLi might not occur at a β-position that is close to the anionic character of nitrogen in **21a** (Scheme 4).



Scheme 4. Reaction of 2-phenyldihydropyrimidine **18** and **9a** with organolithium reagents

Under the optimized reaction conditions, various organolithium reagents were subjected to nucleophilic substitution reactions to form 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines **7**, and the results are summarized in Table 2.[17] In addition to phenyllithium (entry 1), alkyllithium such as butyllithium gave the 5-pentanoyl product **7b** in 59% yield at –80 ºC (entry 2) while the yield of **7b** in the reaction at –40 ºC was 51%. Although the reaction using (phenylethynyl)lithium at –40 ºC did not yield the desired product **7c** with the recovery of **9a** owing to the low reactivity of the ethynyl anion, the reaction at rt proceeded smoothly to afford **7c** in 80% yield (entry 3). Various aryllithiums, prepared from corresponding aryl bromides and *t*-butyllithium, reacted with **9a** to give 5-aryloyldihydropyrimidines **7d** and **7e** in good yields (entries 4 and 5). In entries 6 and 7, **9b** also exhibited good reactivity with aryllithiums, affording **7f** and **7g** in 60% and 59% yields, respectively.

The N-protecting group (Boc) was easily removed to produce N-unsubstituted dihydropyrimidines **8** (Scheme 5). When **7a** was treated with trifluoroacetic acid (TFA), **8a** was obtained in 73% yield after recrystallization. The deprotection of **7b** and **7c** also proceeded to give **8b** and **8c**, respectively. To analyze their

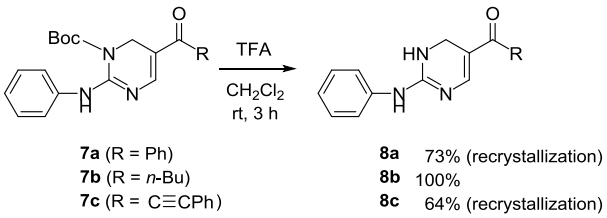


entry	X	R	temp. (ºC)	7	Yield (%)
1	H	Ph	–40	**7a**	81
2	H	*n*-C_4H_9	–80	**7b**	59
3[a]	H	PhC≡C	rt	**7c**	80
4[b]	H	4-$CH_3OC_6H_4$	–40	**7d**	74
5[b]	H	4-$CF_3C_6H_4$	–40	**7e**	50
6	CF_3	Ph	–40	**7f**	60
7[b]	CF_3	4-$CH_3OC_6H_4$	–40	**7g**	59

a) Phenylacetylene (4.0 eq) and butyllithium (4.0 eq) were used.
b) arylbromide (4.2 eq) and t-butyllithium (5.4 eq) were used.

Table 2. Synthesis of 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines **7**

tautomeric behavior, ^{1}H NMR spectra were measured in DMSO-d_6 at 25 ºC (0.01 M, 600 MHz). In all spectra, **8** was observed as a single isomer, the behavior of which was the same as that of 2-aminodihydropyrimidine-5-esters in our previous report.[7g] To compare the stability of dihydropyrimidine tautomers, theoretical calculation and detailed analysis of ^{1}H NMR measurements are in progress.[18]



Scheme 5. Synthesis of N-unsubstituted dihydropyrimidine **8**

In summary, it was demonstrated that 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines **7** and **8** were synthesized from **9** using the Weinreb amide as an acyl precursor. The substrates **9** were prepared from azidoalkene (*E*)-**10** by sequential Staudinger/aza-Wittig/cyclization reactions, and the transformation of the Weinreb amide of **9** to an acyl group proceeded smoothly in good to high yield by a substitution reaction using organolithium reagents in the presence of a catalytic amount of BF_3 etherate. Given that dihydropyrimidines **7** and **8** were previously unavailable and difficult to synthesize, the achievement in this study should contribute considerably to the expansion of dihydropyrimidine-based heterocyclic chemistry and pharmaceutical sciences for drug development.

Acknowledgments

This work was financially supported by JSPS KAKENHI Grant Number 16K01939 and 16K08335.

Supplementary Material

Supplementary Material (synthesis and characterization of compounds, spectroscopic data of IR, NMR, MS) associated with the article can be found, in the online version, at doi: ******/j.tetlet. *********.

References and notes

1. Recent reviews, see: (a) Cho, H. *Heterocycles* **2013**, *87*, 1441–1479; (b) Suresh; Sandhu, J. S. *ARKIVOC* **2012**, *i*, 66–133; (c) Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043–1052.
2. (a) Cho, H.; Ueda, M.; Shima, K.; Mizuno, A.; Hayashimatsu, M.; Ohnaka, Y.; Takeuchi, Y.; Hamaguchi, M.; Aisaka, K.; Hidaka, T.; Kawai, M.; Takeda, M.; Ishihara, T.; Funahashi, K.; Satoh, F.; Morita, M.; Noguchi, T. *J. Med. Chem.* **1989**, *32*, 2399–2406; (b) Atwal, K. S.; Rovnyak, G. C.; Kimball, S. D.; Floyd, D. M.; Moreland, S.; Swanson, B. N.; Gougoutas, J. Z.; Schwartz, J.; Smillie, K. M.; Malley, M. F. *J. Med. Chem.* **1990**, *33*, 2629–2635; (c) Rovnyak, G. C.; Atwal, K. S.; Hedberg, A.; Kimball, S. D.; Moreland, S.; Gougoutas, J. Z.; O'Reilly, B. C.; Schwartz, J.; Malley, M. F. *J. Med. Chem.* **1992**, *35*, 3254–3263.
3. Sehon, C. A.; Wang, G. A., Viet, A. Q.; Goodman, K. B.; Dowdell, S. E.; Elkins, P. A.; Semus, S. F.; Evans, C.; Jolivette, L. J.; Kirkpatrick, R. B.; Dul, E.; Khandekar, S. S.; Yi, T.; Wright, L. L.; Smith, G. K.; Behm, D. J.; Benthley, R.; Doe, C. P.; Hu, E.; Lee, D. *J. Med. Chem.* **2008**, *51*, 6631–6634.
4. Deres, K.; Schröder, C. H.; Paessens, A.; Goldmann, S.; Hacker, H. J.; Weber, O.; Krämer, T.; Niewöhner, U.; Pleiss, U.; Stoltefuss, J.; Graef, E.; Koletzki, D.; Masantschek, R. N. A.; Reimann, A.; Jaeger, R.; Groβ, R.; Beckermann, B.; Schlemmer, K.-H. Haebich, D.; Rübsamen-Waigmann, H. *Science* **2003**, *299*, 893–896.
5. (a) Mayer, T. U.; Kapoor, T. M.; Haggarty, S. J.; King, R. W.; Schreiber, S. L.; Mitchison, T. J. *Science* **1999**, *286*, 971–974. (b) Zhang, Y.; Xu, W. *Anticancer Agents Med. Chem.* **2008**, *8*, 698–704; (c) Jadhav, J.; Juvekar, A.; Kurane, R.; Khanapure, S.; Salunkhe, R.; Rashinkar, G. *Eur. J. Med. Chem.* **2013**, *65*, 232–239.
6. (a) Weis, A.; Frolow, F.; Zamir, D.; Bernstein, M. *Heterocycles* **1984**, *22*, 657–661; (b) Weis, A. *Synthesis* **1985**, 528–530; (c) Weis, A. L.; van der Plas, H. C. *Heterocycles* **1986**, *24*, 1433–1455; (d) Weis, A.; Zamir, D. *J. Org. Chem.* **1987**, *52*, 3421–3425; (e) Cho, H.; Iwashita, T.; Ueda, M.; Mizuno, A.; Mizukawa, K.; Hamaguchi, M. *J. Am. Chem. Soc.* **1988**, *110*, 4832–4834; (f) Cho, H.; Shima, K.; Hayashimatsu, M.; Ohnaka, Y.; Mizuno, A.; Takeuchi, Y. *J. Org. Chem.* **1985**, *50*, 4227–4230; (g) Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937–6963; (h) Kappe, C. O.; Stadler, A. *Org. React.* **2004**, *63*, 1–116.
7. (a) Cho, H.; Nishimura, Y.; Yasui, Y.; Kobayashi, S.; Yoshida, S.; Kwon, E.; Yamaguchi, M. *Tetrahedron* **2011**, *67*, 2661–2669.; (b) Cho, H.; Yasui, Y.; Kobayashi, S.; Kwon, E.; Arisawa, M.; Yamaguchi, M. *Heterocycles* **2011**, *83*, 1807–1818.; (c) Cho, H.; Kwon, E.; Yasui, Y.; Kobayashi, S.; Yoshida, S.; Nishimura, Y.; Yamaguchi, M. *Tetrahedron Lett.* **2011**, *52*, 7185–7188; (d) Cho, H.; Nishimura, Y.; Yasui, Y.; Yamaguchi, M. *Tetrahedron Lett.* **2012**, *53*, 1177–1179; (e) Nishimura, Y.; Yasui, Y.; Kobayashi, S.; Yamaguchi, M.; Cho, H. *Tetrahedron* **2012**, *68*, 3342–3350. (f) Nishimura, Y.; Cho, H. *Tetrahedron Lett.* **2014**, *55*, 411–414; (g) Nishimura, Y.; Cho, H. *Synlett* **2015**, *26*, 233–237. (h) Nishimura, Y.; Kubo, T.; Okamoto, Y.; Cho, H. *Tetrahedron Lett.* **2016**, *57*, 4492–4495.
8. (a) Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, 4171–4174; (b) Nahm, S. Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815–3818; (c) Balasubramaniam, S.; Aidhen, I. S. *Synthesis* **2008**, 3707–3738.
9. Eynde, J. J. V.; Hecq, N.; Kataeva, O.; Kappe, C. O. *Tetrahedron* **2001**, *57*, 1785–1791.
10. Hamper, B. C.; Gan, K. Z.; Owen, T. J. *Tetrahedron Lett.* **1999**, *40*, 4973–4976.
11. (a) Matloobi, M.; Kappe, C. O. *J. Comb. Chem.* **2007**, *9*, 275–284; (b) Atwal, K. S.; Rovnyak, G. C.; O'Reilly, B. C.; Schwartz, J. *J. Org. Chem.* **1989**, *54*, 5898–5907.
12. (a) Li, J.; Kou, J.; Luo, X.; Fan, E. *Tetrahedron Lett.* **2008**, *49*, 2761–2763; (b) Kochubey, V. S.; Blochin, Ya. S.; Rodin, O. G.; Perevalov, V. P. *Chem. Heterocycl. Comp.* **2006**, *42*, 897–900.
13. Baskaran, S.; Hanan, E.; Byun, D.; Shen, W. *Tetrahedron Lett.* **2004**, *45*, 2107–2111.
14. McCort, G. A.; Pascal, J. C. *Tetrahedron Lett.* **1992**, *33*, 4443–4446.
15. Harikrishna, M.; Rakshit, A.; Aidhen, I. S. *Eur. J. Org. Chem.* **2013**, 4918–4932.
16. Under an argon atmosphere, to a solution of (*E*)-**10** (1.83 g, 6.41 mmol) in THF (60 mL) was added triphenylphosphine (2.01 g, 7.66 mmol). After the reaction mixture was stirred at rt for 15 min, phenylisocyanate (3.4 mL, 31.4 mmol) was added, and the stirring was kept at the temperature for 15 h. To the reaction mixture was added EtOAc (50 mL) followed by saturated $NaHCO_3$ aqueous solution (50 mL), and the stirring was kept for 30 min, and the organic layer was separated. The aqueous layer was extracted with EtOAc (50 mL), and the combined organic layers were washed with brine (20 mL x 2), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography [CH_2Cl_2-EtOAc (10:1 to 5:1)] to give **9a** (1.45 g, 4.02 mmol, 63%) as colorless crystals.
17. Under an argon atmosphere, to a solution of **9a** (54.0 mg, 0.150 mmol), trifluoroborane diethyl ether complex (4.00 μL, 0.0316 mmol) in THF (0.75 mL) was added phenyllithium (1.6 M in di*n*-butyl ether, 0.28 mL, 0.448 mmol) dropwise at –40 ºC, and the reaction mixture was stirred at –40 ºC for 0.5 h. To the reaction mixture were added saturated NH_4Cl aqueous solution (5 mL) and EtOAc (20 mL) at –40 ºC. The organic layer was separated, and the aqueous layer was extracted with EtOAc (10 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography [hexane-EtOAc-Et_3N (200:25:2 to 100:25:1)] to give **7a** (45.6 mg, 0.121 mmol, 81%) as a yellow amorphous.
18. Manuscript in preparation.

Highlights

- Novel 4,6-unsubstituted 5-acyl-2-aminodihydropyrimidines were synthesized.
- The Staudinger/aza-Wittig/cyclization reactions gave the synthetic intermediate.
- The transformation of the Weinreb amide to an acyl group proceeded smoothly.
- Tautomerization of N-unsubstituted dihydropyrimidines was analyzed by ^{1}H NMR.

Graphical Abstract

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