Promoter Free Allylation of Trichloroacetimidates with Allyltributylstannanes Under Thermal Conditions to Access the Common 1,1'-Diarylbutyl Pharmacophore

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PAPER

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1,1'-Diarylbutyl groups are a common pharmacophore found in many biologically active small molecules. To access these systems under mild conditions, the reaction of diarylmethyl trichloroacetimidates with allyltributylstannanes was explored. Simply heating allyltributylstannane with the trichloroacetimidate resulted in substitution of the imidate with an allyl group. Unlike other methods used to access these systems, no strong base, transition metal catalyst, Brønsted acid or Lewis acid promoter was required to affect the transformation. Conversions are best with electron rich benzylic trichloroacetimidate systems, where excellent yields are achieved just by refluxing the reactants together in nitromethane.

Introduction

The 1,1'-diarylbutyl group is a common structural motif in medicinal chemistry.[1] The particular placement of the two aryl groups at the terminus of the alkyl chain, usually with a basic amine or heterocycle on the other end of the linker, has been used to great effect in engineering potent biologically active small molecules. Compounds with this substructure have a wide range of pharmacological properties (Figure 1), and have been used in the development of anticancer agents (like the naphthol **1**[2]), treatments for psychoses (like pimozide **2**[3]), aromatase inhibitors (like MPV-1489 **3**[4]) and histamine-H1 receptor agonists (like histaprodifen **4**[5]).

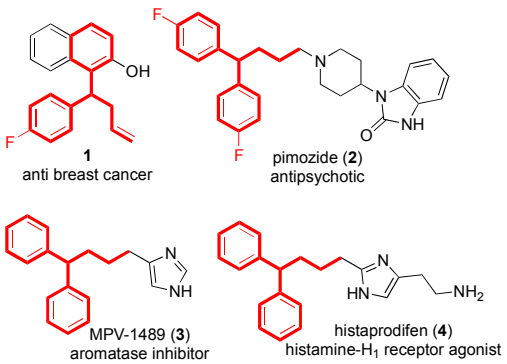

Figure 1 Biologically active 1,1'-diarylbutane containing structures.

Given the potent biological activity found in these systems significant effort has been expended in the synthesis of the 1,1-diarylbutyl architecture. The most common methods to synthesize these systems are summarized in Figure 2. The direct carbon-carbon bond forming transformations utilized to synthesize 1,1'-diarylbutyl systems typically require the use of either stoichiometric strong base (to completely deprotonate a diarylmethane, as in the case of nucleophilic substitution of halides (and pseudohalides) like **7** with anions (like **6**) derived from diarylmethanes[6]) or the use of strong Lewis acid promoters to generate diarylmethyl electrophiles that can then be trapped by less reactive allylmetal reagents, usually allylsilanes.[7] These pharmacophores have also been accessed by the hydrogenation of 1,1'-diarylalkenes,[1b] arylation at benzylic positions,[8] and by several other methods.[9]

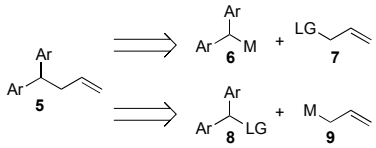

Figure 2 Common C-C bond forming disconnections for the synthesis of 1,1'-diarylbutyl pharmacophore.

Recently our group has been exploring new methods to leverage the chemistry of trichloroacetimidates in substitution reactions. Trichloroacetimidates are often used to activate alcohols as leaving groups, and are easily synthesized in high yields from trichloroacetonitrile, the corresponding alcohol utilizing a catalytic amount of base. The displacement of trichloroacetimidates by heteroatom nucleophiles like alcohols,[10] carboxylic acids,[11] thiols[12] and amines[13] is commonly promoted by Lewis acids or transition metal catalysts. This chemistry is perhaps most associated with the synthesis of carbohydrates,[14] where it is used to great effect,

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although it has also been investigated for applications in diversity oriented synthesis.[15] In many cases we have found that substitution reactions with heteroatom nucleophiles and benzylic trichloroacetimidates proceed without the addition of a Brønsted or Lewis acid catalyst. These transformation typically involve the use of protic heteroatom nucleophiles which have been shown to undergo alkylation under promoter free conditions.[10d,11a-d,13d] Usually a proton transfer from the nucleophile is thought to activate the imidate prior to displacement. When more basic nucleophiles are used (like anilines), an acid[13f] or transition metal catalyst[13a-c] is still required, as the more basic amine cannot function as a proton donor unless it is first protonated. The side product from the trichloroacetimidate displacement is the acetamide, which is a weak acid that is easily removed by aqueous washing and rarely interacts with acid sensitive functional groups.

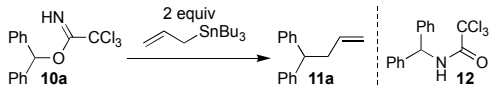
Extension of this promoter free direct displacement chemistry into the formation of carbon-carbon bonds is now being investigated. While imidates are best known for their reactivity with oxygen nucleophiles to form ethers, carbon-carbon bond forming reactions with these systems have been explored in several contexts. Trichloroacetimidates have been utilized in Friedel-Crafts type alkylation reactions with Lewis acid promoters previously,[16] and have shown exceptional reactivity by undergoing alkylation even with electron poor imidates.[17] More recently the first displacement of an imidate with an alkylmetal reagent (trimethylaluminum) was reported, although in most cases this also required a Lewis acid promoter to achieve good yields.[18] In this study the direct C-C bond formation of benzylic trichloroacetimidates with a stable carbon nucleophile (allyltributylstannanes) is investigated, with the premise that it will lead to a new method to access 1,1'-diarylbutyl groups under mild conditions.

Results and discussion

Allyltributylstannane was chosen as the initial nucleophilic partner for evaluation, as this reagent is known to be an excellent allyl anion equivalent[19] and even reacts with aldehydes under thermal conditions.[20] In addition, this reagent does not bear an acidic proton to activate the trichloroacetimidate, so the reactivity may be significantly different than the other systems that have previously been studied. The less reactive allyltrimethylsilane has been reported to displace some trichloroacetimidates previously,[16c,21] but these substitution reactions have always been promoted or catalyzed by a Lewis acid, typically $BF_3{\bullet}OEt_2$ or TMSOTf.

Initially the reaction of diphenylmethyl trichloroacetimidate **10a** with allyltributylstannane was evaluated (Table 1). Imidate **10a** was selected as it cannot undergo competing elimination and has been shown to be highly reactive previously.[10d] Toluene was employed because of the high boiling point of the solvent and its success in other imidate alkylations with alcohols.[10d] Heating imidate **10a** and one equivalent of allyltributylstannane together in refluxing toluene only gave trace amounts of the allylation product **11a** in the crude ^{1}H NMR, with the balance of the material being unreacted imidate **10a**. Increasing the amount of allyltributyltin to two equivalents significantly increased the yield of the transformation to ~30%. Other nonpolar solvents like 1,2-DCE, DCM and α,α,α-trifluorotoluene also did not provide significant amounts of the allylation product. Employment of 1,4-dioxane showed some promise, providing 32% yield of the desired product after 48 h. Significantly better results were observed in more polar solvents like DMF; the reaction was more rapid with the same yield being obtained in 24 h. Nitromethane proved to be the optimal solvent, however, providing a significantly higher yield of alkene **11a**. Nitromethane has been previously shown to be an excellent solvent for the rearrangement of imidate **10a** to acetamide **12**,[22] and also improves the yield of ether formation when *tert*-butyl trichloroacetimidate is employed to synthesize *tert*-butyl ethers.[13e] These increases in efficiency have been attributed to the high dielectric constant combined with the weak Lewis bascicity of nitromethane, which make it an excellent solvent for stabilizing polar intermediates.[23]

Table 1 Etherification with imidate **1** under Thermal Conditions

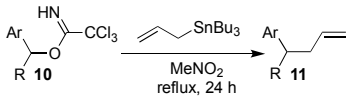


Entry	Solvent	Conditions	Yield
1	toluene	reflux, 24 h	trace[a,b]
2	toluene	reflux, 16 h	31
3	1,2-DCE	reflux, 24 h	32[b]
4	DCM	rt, 24 h	0[b]
5	CF_3Ph	reflux, 48 h	trace[b]
6	1,4-dioxane	reflux, 48 h	32
7	DMF	100 °C, 24 h	32
8	MeCN	reflux, 24 h	8
9	$MeNO_2$	reflux, 16 h	71
10	$MeNO_2$	reflux, 24 h	30[a]

[a]One equiv of allyltributyltin was used. [b]Starting material was also recovered from the reaction.

The generality of the substitution reaction with respect to the trichloroacetimidate reaction partner was next investigated (Table 2). Most of the simple electron rich diarylmethyl trichloroacetimidates (Table 2, entries 1-4) gave good yield of the allylated product. The incorporation of electron withdrawing substituents like a halogen was detrimental to the transformation and resulted in lower yields and slower reactions which needed longer reaction times to proceed to completion (entries 5-7). Stronger electron withdrawing groups like a nitro group completely shut down the transformation, providing only starting material (entry 8). The substitution of one of the phenyl groups with a benzothiophene (entry 9) was also successful, although the yield was more moderate.

Table 2 Allylation with Diarylmethyl Trichloroacetimidates



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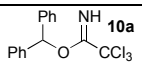
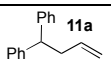
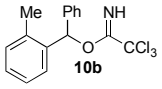
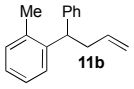
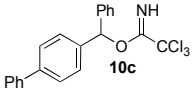
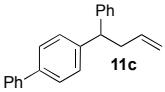
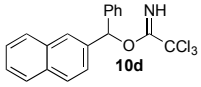
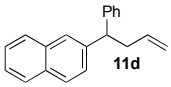
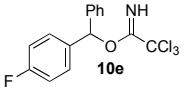
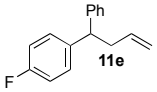
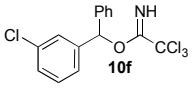
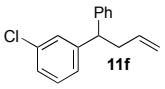
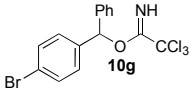
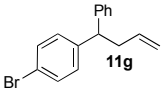
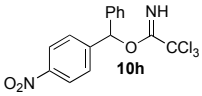
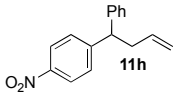
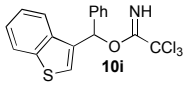
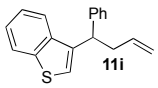
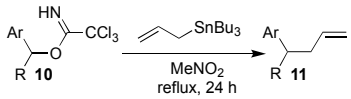
1	 10a	 11a	71
2	 10b	 11b	77
3	 10c	 11c	71
4	 10d	 11d	78
5	 10e	 11e	36
6	 10f	 11f	52[a,b]
7	 10g	 11g	64
8	 10h	 11h	0[b]
9	 10i	 11i	42

[a]Reaction was performed for 36 h [b]Some starting material was recovered.

In addition to diarylmethyl trichloroacetimidates, a number of simpler imidates were evaluated for their reactivity under these thermal displacement conditions (Table 3). Replacing one of the aryl groups with an alkyl group was detrimental to the transformation , and provided lower yields (entries 1-2). Given that trichloroacetimidates decorated with electron withdrawing groups gave lower yields (Table 2), simple benzylic trichloroacetimidates activated with electron donating groups were evaluated as they may have high enough reactivity to facilitate substitution. Congruent with this reasoning, benzylic trichloroacetimidates with methoxy groups (entries 3 and 4) gave significantly higher yields than benzylic trichloroacetimidates functionalized with methyl groups (entries 5 and 6). Benzyl trichloroacetimidate and 4-chlorobenzyl trichloroacetimidate only showed starting material or trace amounts of addition product (entries 7 and 8).

Table 3 Allylation with Benzylic Trichloroacetimidates



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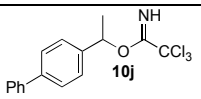
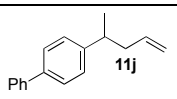
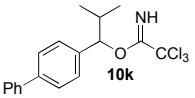
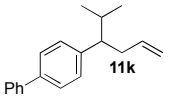
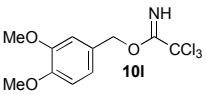
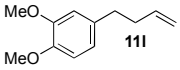
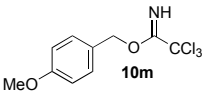
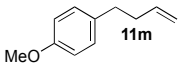
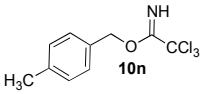
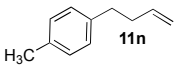
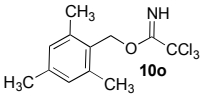
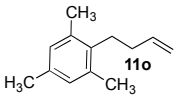
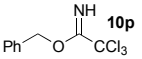
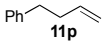
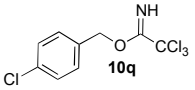
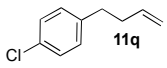
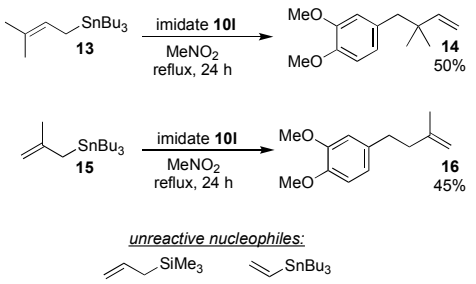
1	 10j	 11j	31
2	 10k	 11k	0[a]
3	 10l	 11l	61
4	 10m	 11m	43
5	 10n	 11n	0[a]
6	 10o	 11o	13
7	 10p	 11p	0[a]
8	 10q	 11q	trace

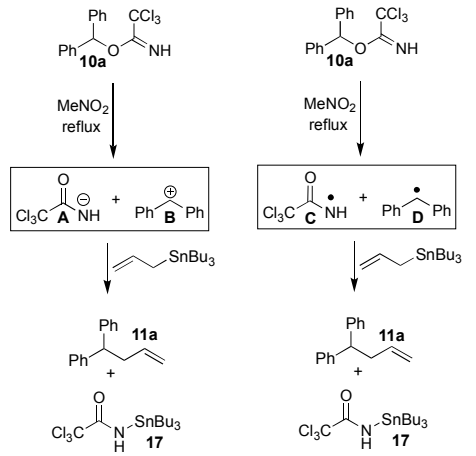
[a] Starting material was recovered.

Other allylstannanes were also effective nucleophiles in the thermal addition reaction (Scheme 1). Both prenyltributylstannane **13** and methallyltributylstannane **15** added to imidate **10l** to provide moderate yields of the allylated products. Attempts to execute similar transformations with allyltrimethylsilane or vinyltributylstannane proved fruitless, however, as under no conditions were these nucleophiles able to displace the imidate without the addition of a Lewis or Brønsted acid promoter. This included higher temperatures ($MeNO_2$, 100°C, sealed tube) and using an excess (5 equiv nucleophile, $MeNO_2$, reflux) of nucleophile. The lack or reactivity of allyltrimethylsilane is attributed to the lower reactivity of the allylsilanes in general, which has been measured to alkylate diphenylmethyl systems at more modest rates.[19a-b] In a similar fashion, the vinylmetal reagents have been reported to be significantly less reactive than their allyl counterparts, which explains the lack of reactivity observed in this system.[19c]



Scheme 1 Reactivity of Substituted Allyl Stannanes and Other Nucleophiles

Two possible mechanisms were considered for the allylation of trichloroacetimidates with allyltributylstannane: an ionic pathway and a radical pathway.(Scheme 2) At first, the substrate scope seemed to indicate that the ionic pathway was operative where the reaction proceeds through the ion pair **A** and **B**, with the presence of electron withdrawing groups significantly reducing the yield of the transformation. However we could not completely rule out a radical pathway where the stabilized diphenyl methyl radical **D** is formed, as allyltributylstannane has been shown to be highly reactive under radical conditions as well. We attempted to differentiate between the two pathways by adding the radical scavenger TEMPO to the reaction, which should trap any radical intermediates. The addition of 1 equiv of TEMPO to the reaction of **5a** with allyltributylstannane lowered the yield of **6a** to 30%, but did not completely stop the transformation. Given that the yield was lower but the transformation was not completely halted, both the radical and the cationic pathways may be operative in these systems with the imidate substrate influencing which pathway is dominant.



Scheme 2 Proposed Mechanistic Pathways

Conclusion

This investigation reports the first promoter free displacement of a trichloroacetimidate with the stable allylmetal reagent allyltributylstannane. This technique provides a more mild alternative to other methods which depend on strong acids or strong base to form the C-C bond, which limits functional group compatibility. The displacement proceeds best with diarylmethyl trichloroacetimidates, although electron rich benzylic trichloroacetimidates also provide useful amounts of product. This transformation provides ready access to 1,1'-diarylbutyl structures, which are a common pharmacophore in medicinal chemistry and are present in a number of biologically active molecules.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (a) E. Teodori, E. Baldi, S. Dei, F. Gualtieri, M. N. Romanelli, S. Scapecchi, C. Bellucci, C. Ghelardini and R. Matucci, *J. Med. Chem.*, 2004, **47**, 6070; (b) G. Chen, H. Xia, Y. Cai, D. Ma, J. Yuan and C. Yuan, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 234; (c) R. Ghodsi and B. Hemmateenejad, *Med. Chem. Res.*, 2016, **25**, 834; (d) G. Chen, H. Xia, Y. Cai, D. Ma, J. Yuan and C. Yuan, *MedChemComm*, 2011, **2**, 315; (e) A. Cavalli, R. Buonfiglio, C. Ianni, M. Masetti, L. Ceccarini, R. Caves, M. W. Y. Chang, J. S. Mitcheson, M. Roberti and M. Recanatini, *J. Med. Chem.*, 2012, **55**, 4010.

2 B. Das, C. R. Reddy, J. Kashanna, S. K. Mamidyala and C. G. Kumar, *Med. Chem. Res.*, 2012, **21**, 3321.

3 R. Smyj, X.-P. Wang and F. Han, *Profiles Drug Subst., Excipients, Relat. Methodol.*, 2012, **37**, 287.

4 A. Karjalainen, A. Kalapudas, M. Sodervall, O. Pelkonen and R. Lammintausta, *Eur. J. Pharm. Sci.*, 2000, **11**, 109.

5 (a) S. Elz, K. Kramer, H. H. Pertz, H. Detert, A. M. Ter Laak, R. Kuehne and W. Schunack, *J. Med. Chem.*, 2000, **43**, 1071; (b) M. Govoni, R. A. Bakker, I. Van de Wetering, M. J. Smit, W. M. B. P. Menge, H. Timmerman, S. Elz, W. Schunack and R. Leurs, *J. Med. Chem.*, 2003, **46**, 5812.

6 (a) H. Sharma, S. Santra, J. Debnath, T. Antonio, M. Reith and A. Dutta, *Bioorg. Med. Chem.*, 2014, **22**, 311; (b) H. Kawashima, N. Ogawa, R. Saeki and Y. Kobayashi, *Chem. Commun.*, 2016, **52**, 4918; (c) S.-C. Sha, J. Zhang, P. J. Carroll and P. J. Walsh, *J. Am. Chem. Soc.*, 2013, **135**, 17602; (d) S.-C. Sha, H. Jiang, J. Mao, A. Bellomo, S. A. Jeong and P. J. Walsh, *Angew. Chem., Int. Ed.*, 2016, **55**, 1070.

7 (a) J. A. Cella, *J. Org. Chem.*, 1982, **47**, 2125; (b) G. Kaur, M. Kaushik and S. Trehan, *Tetrahedron Lett.*, 1997, **38**, 2521; (c) M. Yasuda, T. Saito, M. Ueba and A. Baba, *Angew. Chem., Int. Ed.*, 2004, **43**, 1414; (d) G. W. Kabalka, M.-L. Yao and S. Borella, *J. Am. Chem. Soc.*, 2006, **128**, 11320; (e) G. G. K. S. Narayana Kumar and K. K. Laali, *Org. Biomol. Chem.*, 2012, **10**, 7347; (f) A. Hassner and C. R. Bandi, *Synlett*, 2013, **24**, 1275; (g) M. Saito, N. Tsuji, Y. Kobayashi and Y. Takemoto, *Org. Lett.*, 2015, **17**, 3000; (h) I. Orizu and Y. Bolshan,

Tetrahedron Lett., 2016, **57**, 5798; (i) I. Solic, P. Seankongsuk, J. K. Loh, T. Vilaivan and R. W. Bates, *Org. Biomol. Chem.*, 2018, **16**, 119; (j) S. K. De and R. A. Gibbs, *Tetrahedron Lett.*, 2005, **46**, 8345; (k) T. Lebleu and J.-F. Paquin, *Tetrahedron Lett.*, 2017, **58**, 442; (l) S. J. Mahoney, T. Lou, G. Bondarenko and E. Fillion, *Org. Lett.*, 2012, **14**, 3474.

8 (a) G. Islas-Gonzalez, J. Benet-Buchholz, M. A. Maestro, A. Riera and M. A. Pericas, *J. Org. Chem.*, 2006, **71**, 1537; (b) Y. Miyake, S. Uemura and Y. Nishibayashi, *ChemCatChem*, 2009, **1**, 342; (c) A. Lopez-Perez, J. Adrio and J. C. Carretero, *Org. Lett.*, 2009, **11**, 5514; (d) H.-Q. Do, E. R. R. Chandrashekar and G. C. Fu, *J. Am. Chem. Soc.*, 2013, **135**, 16288.

9 (a) Y.-M. Wang and S. L. Buchwald, *J. Am. Chem. Soc.*, 2016, **138**, 5024; (b) K. Feeney, G. Berionni, H. Mayr and V. K. Aggarwal, *Org. Lett.*, 2015, **17**, 2614; (c) J. Zhang, A. Bellomo, N. Trongsiriwat, T. Jia, P. J. Carroll, S. D. Dreher, M. T. Tudge, H. Yin, J. R. Robinson, E. J. Schelter and P. J. Walsh, *J. Am. Chem. Soc.*, 2014, **136**, 6276; (d) S. Roesner, J. M. Casatejada, T. G. Elford, R. P. Sonawane and V. K. Aggarwal, *Org. Lett.*, 2011, **13**, 5740; (e) A. Pinter, A. Sud, D. Sureshkumar and M. Klussmann, *Angew. Chem., Int. Ed.*, 2010, **49**, 5004; (f) Y.-L. Chen and D. Hoppe, *J. Org. Chem.*, 2009, **74**, 4188.

10 (a) T. Iversen and D. R. Bundle, *J. Chem. Soc., Chem. Commun.*, 1981, 1240; (b) H.-P. Wessel, T. Iversen and D. R. Bundle, *J. Chem. Soc. Pekin 1*, 1985, 2247; (c) I. A. I. Ali, E. S. H. El Ashry and R. R. Schmidt, *Eur. J. Org. Chem.*, 2003, 4121; (d) K. T. Howard, B. C. Duffy, M. R. Linaburg and J. D. Chisholm, *Org. Biomol. Chem.*, 2016, **14**, 1623; (e) M. Kurosu and K. Li, *Synthesis*, 2009, 3633; (f) S. F. Kirsch, L. E. Overman and N. S. White, *Org. Lett.*, 2007, **9**, 911.

11 (a) R. R. Schmidt and J. Michel, *J. Carbohydr. Chem.*, 1985, **4**, 141; (b) J. Thierry, C. Yue and P. Potier, *Tetrahedron Lett.*, 1998, **39**, 1557; (c) A. A. Adhikari, J. P. Shah, K. T. Howard, C. M. Russo, D. R. Wallach, M. R. Linaburg and J. D. Chisholm, *Synlett*, 2014, 283; (d) J. P. Shah, C. M. Russo, K. T. Howard and J. D. Chisholm, *Tetrahedron Lett.*, 2014, **55**, 1740; (e) A. Armstrong, I. Brackenridge, R. F. W. Jackson and J. M. Kirk, *Tetrahedron Lett.*, 1988, **29**, 2483; (f) M. Shoji, T. Uno, H. Kakeya, R. Onose, I. Shiina, H. Osada and Y. Hayashi, *J. Org. Chem.*, 2005, **70**, 9905; (g) S. F. Kirsch and L. E. Overman, *J. Am. Chem. Soc.*, 2005, **127**, 2866.

12 (a) R. R. Schmidt and M. Stumpp, *Liebigs Ann. Chem.*, 1983, 1249; (b) R. T. Dere, A. Kumar, V. Kumar, R. R. Schmidt and X. Zhu, *J. Org. Chem.*, 2011, **76**, 7539; (c) J. S. Andrews and B. M. Pinto, *Carbohydr. Res.*, 1995, **270**, 51; (d) M. Fridman, V. Belakhov, L. V. Lee, F.-S. Liang, C.-H. Wong and T. Baasov, *Angew. Chem. Int. Ed. Engl.*, 2005, **44**, 447 ; (e) E. Repetto, V. E. Manzano, M. L. Uhrig and O. Varela, *J. Org. Chem.*, 2012, **77**, 253 ; (f) I. A. I. Ali, X. Zhu, E. S. H. El Ashry and R. R. Schmidt, *ARKIVOC* 2012, 35; (g) B. C. Duffy, K. T. Howard and J. D. Chisholm, *Tetrahedron Lett.*, 2015, **56**, 3301 (h) L. E. Overman, S. W. Roberts and H. F. Sneddon, *Org. Lett.*, 2008, **10**, 1485.

13 (a) J. S. Arnold, E. T. Mwenda and H. M. Nguyen, *Angew. Chem., Int. Ed.*, 2014, **53**, 3688; (b) J. S. Arnold and H. M. Nguyen, *Synthesis*, 2013, **45**, 2101; (c) J. S. Arnold, R. F. Stone and H. M. Nguyen, *Org. Lett.*, 2010, **12**, 4580; (d) D. R. Wallach and J. D. Chisholm, *J. Org. Chem.*, 2016, **81**, 8035; (e) J. W. Cran, D. V. Vidhani and M. E. Krafft, *Synlett*, 2014, **25**, 1550; (f) D. R. Wallach, P. C. Stege, J. P. Shah and J. D. Chisholm, *J. Org. Chem.*, 2015, **80**, 1993; (g) L. Grigorjeva and A. Jirgensons, *Eur. J. Org. Chem.*, 2012, **2012**, 5307; (h) L. Grigorjeva and A. Jirgensons, *Eur. J. Org. Chem.*, 2011, 2421; (i) C. E. Anderson and L. E. Overman, *J. Am. Chem. Soc.*, 2003, **125**, 12412.

14 (a) R. R. Schmidt and K.-H. Jung, in *Preparative Carbohydrate Chemistry*, ed. S. Hanessian, CRC Press, 1997, pp. 283; (b) X. Zhu and R. R. Schmidt, in *Handbook of Chemical Glycosylation*, ed. A. V. Demchenko, Wiley-VCH, 2008, pp. 143.

15 (a) C. Piemontesi, Q. Wang and J. Zhu, *Org. Biomol. Chem.*, 2013, **11**, 1533; (b) A. A. Adhikari and J. D. Chisholm, *Org. Lett*, 2016, **18**, 4100; (c) A. Devineau, G. Pousse, C. Taillier, J. Blanchet, J. Rouden and V. Dalla, *Adv. Synth. Catal.*, 2010, **352**, 2881.

16 (a) R. R. Schmidt and M. Hoffmann, *Tetrahedron Lett.*, 1982, **23**, 409; (b) J.-A. Mahling and R. R. Schmidt, *Synthesis*, 1993, **1993**, 325; (c) I. A. I. Ali, E. S. H. El Ashry and R. R. Schmidt, *Tetrahedron*, 2004, **60**, 4773; (d) H. Tokuyama, K. Okano, H. Fujiwara, T. Noji and T. Fukuyama, *Chem. Asian J.*, 2011, **6**, 560.

17 (a) J. Zhang and R. R. Schmidt, *Synlett*, 2006, 1729; (b) A. A. Adhikari, L. Radal and J. D. Chisholm, *Synlett*, 2017, **28**, 2335.

18 N. S. Mahajani and J. D. Chisholm, *J. Org. Chem.*, 2018, **83**, 4131.

19 (a) J. Burfeindt, M. Patz, M. Mueller and H. Mayr, *J. Am. Chem. Soc.*, 1998, **120**, 3629; (b) B. W. Gung, *Org. React.*, 2004, **64**, 1; (c) J. C. Cochran and H. G. Kuivila, *Organometallics*, 1982, **1**, 97.

20 (a) C. Servens and M. Pereyre, *J. Organometal. Chem.*, 1972, **35**, C20; (b) S. E. Denmark and E. J. Weber, *J. Am. Chem. Soc.*, 1984, **106**, 7970; (c) K. König and W. P. Neumann, *Tetrahedron Lett.*, 1967, 495.

21 M. G. Hoffmann and R. R. Schmidt, *Liebigs Ann. Chem.*, 1985, 2403.

22 A. A. Adhikari, T. Suzuki, R. T. Gilbert, M. R. Linaburg and J. D. Chisholm, *J. Org. Chem.*, 2017, **82**, 3982.

23 J. F. Coetzee and T. H. Chang, *Pure Appl. Chem.*, 1986, **58**, 1541.

Promoter Free Allylation of Trichloroacetimidates with Allyltributylstannanes Under Thermal Conditions to Access the Common 1,1'-Diarylbutyl Pharmacophore

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