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Note

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Rearrangement of Benzylic Trichloroacetimidates to Benzylic Trichloroacetamides

*Arijit A. Adhikari, Tamie Suzuki, Reesheda J. Gilbert, Matthew R. Linaburg and John D. Chisholm**

Department of Chemistry, 1-014 Center for Science and Technology, Syracuse University, Syracuse, NY 13244

jdchisho@syr.edu

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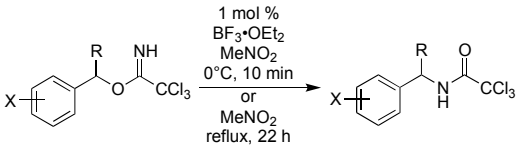


Abstract

The rearrangement of allylic trichloroacetimidates is a well-known transformation, but the corresponding rearrangement of benzylic trichloroacetimidates has not been explored as a method for the synthesis of benzylic amines. Conditions that provide the trichloroacetamide product from a benzylic trichloroacetimidate in high yield have been developed. Methods were also investigated to transform the trichloroacetamide product directly into the corresponding

amine, carbamate and urea. A cationic mechanism for the rearrangement is implicated by the available data.

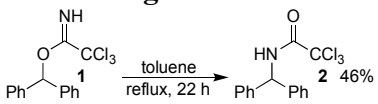
Benzylic amines are commonly encountered in the structures of pharmaceuticals, biologically active natural products, insecticides, and food additives.[1] Due to their prominent position in the pantheon of functional groups, a variety of techniques have been explored for the preparation of benzylic amines. Common precursors include benzylic alcohols, which are commonly converted to the corresponding amine using the Gabriel amine synthesis,[2] the Mitsunobu reaction[3] and "borrowing hydrogen" methodology.[4] While these methods are effective, they all require either transition metal catalysts or generate significant waste streams.

The rearrangement of allylic trichloroacetimidates to trichloroacetamides is often employed in the synthesis of allylic amines.[5] The related benzylic transformation has received little attention, but potentially could provide rapid entry to benzylic trichloroacetamides that may be elaborated into benzylic amines or their protected variants. Cramer first reported that some alkyl and benzylic trichloroacetimidates rearranged to the corresponding trichloroacetamides when exposed to a Lewis acid.[6] Later Schmidt and co-workers observed that some glycosidic trichloroacetimidates provided small amounts of the corresponding acetamide product.[7] A number of other examples have been reported with glycosidic trichloroacetimidates,[8] and these results have recently been reviewed.[9] More recently Motawia and co-workers described conditions for promoting the rearrangement of glycosyl trichloroacetimidates to glycosyl trichloroacetamides utilizing catalytic TMSOTf.[10] Nguyen and co-workers have also developed a transition metal-catalyzed rearrangement of glycosyl trichloroacetimidates to the corresponding acetamides, which are utilized in the synthesis of glycosyl ureas.[11] Some specific

trichloroacetimidate systems (such as α-methylene-β-trichloroacetimidate alkanoates,[12] α-diazo-β-trichloroacetimidate carbonyl compounds[13] and "doubly activated" imidates, being both benzylic and propargylic[14]) rapidly rearrange to the trichloroacetamide, which may preclude isolation of the imidate.

During some recent studies on alkylations utilizing trichloroacetimidates as electrophiles without the addition of an exogenous catalyst,[15] it was observed that the rearrangement of trichloroacetimidate **1** to acetamide **2** was rapid and could be effected simply by heating (Scheme 1).[15a,15c] In order to evaluate the possibility of utilizing this transformation in the synthesis of protected benzylic amines, a study was undertaken to determine if the yield and rate of the reaction could be improved.

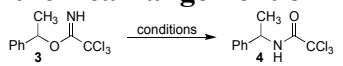
Scheme 1. Rearrangement of DPM Imidate 1



Initially some concern was expressed that the rearrangement of imidate **1** may be a special case, as imidate **1** is a precursor to the especially stable diphenyl methyl cation. Should cation formation be critical, this would limit the scope of the transformation. Furthermore, imidate **1** cannot undergo elimination, which has been observed to be a competing side reaction in other substrates.[14] Therefore a less biased system, the phenethyl trichloroacetimidate **3**, was utilized for optimization (Table 1). Initially thermal conditions were explored by heating imidate **3** without an added catalyst. Nonpolar aromatic solvents like toluene and *m*-xylene gave mainly decomposition under these thermal conditions (entries 1 and 2). Alternatively, only starting material was observed with 2-methyl-2-butanol (entry 3). Some conversion was achieved with 1,4-dioxane and propionitrile (entries 4 and 5), but nitromethane gave significantly improved results, providing an 80% isolated yield. While trace amounts (3-4%) of elimination could be

observed in the crude ^{1}H NMR when 1,4-dioxane and propionitrile were used, no elimination byproduct was observed with nitromethane. Previously nitromethane was shown to enhance the reactivity of *tert*-butyl trichloroacetimidate towards substitution in the alkylation of anilines.[16] This was attributed to the ability of nitromethane to facilitate cation formation without elimination, which may also explain the excellent yield in the thermal rearrangement. One limitation of the thermal reaction was the long reaction time. To increase the rate of the transformation, Brønsted and Lewis acid catalysts were evaluated (Table 1, entries 7-16). Most Brønsted acid catalysts resulted in slow reactions at room temperature (entries 7 and 8), but triflic acid provided complete rearrangement in only 10 min (entry 9). While promising, the use of strong Brønsted acids like triflic acid may limit functional group compatibility, and therefore a number of Lewis acids were evaluated. Mild Lewis acids like $CuBr_2$ and $CuCl_2$ (entries 10 and 11) led to slow reactions, while stronger Lewis acids like $ZnCl_2$, $FeCl_3$ and BF_3•OEt_2 (entries 12-14) gave rapid rearrangement and excellent conversion. In the case of BF_3•OEt_2, the catalyst loading could be lowered to 1 mol % without a significant drop in reaction rate, providing 93% isolated yield in just 10 min. Two sets of conditions from Table 1 seemed worth exploring, the catalyst free thermal transformation (entry 6) and the BF_3•OEt_2 catalyzed conditions (entry 15), as some substrates that may not be stable to one set of conditions may rearrange under the alternate conditions, and so both conditions were evaluated further.

Table 1. Optimization of the Rearrangement of Imidate 3 to Acetamide 4.



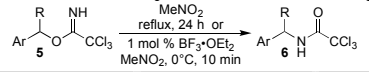
entry	reaction conditions	NMR yield[a]	yield[b]
1	toluene, reflux, 22 h	4	-
2	*m*-xylene, reflux, 16 h	0[c]	-
3	2-Me-2-butanol,reflux, 22 h	0[d]	-
4	1,4-dioxane, reflux, 16 h	18[e]	-
5	EtCN, reflux, 24 h	4[e]	-
6	$MeNO_2$, reflux, 22 h	80	80
7	10 mol % $(PhO)_2PO_2H$ $MeNO_2$, rt, 27 h	10	-
8	10 mol % CSA, $MeNO_2$, rt, 27 h	20	-
9	10 mol % TfOH, $MeNO_2$, rt, 10 min	85	80
10	10 mol % $CuBr_2$, $MeNO_2$, rt, 20 h	55	-
11	10 mol % $CuCl_2$, $MeNO_2$, rt, 20 h	74	-
12	10 mol % $ZnCl_2$, $MeNO_2$, rt, 1 h	90	-
13	10 mol % $FeCl_3$, $MeNO_2$, rt, 10 min	93	88
14	10 mol % BF_3•OEt_2 $MeNO_2$, rt, 10 min	91	90
15	1 mol % BF_3•OEt_2 $MeNO_2$, 0 °C, 10 min	94	94
16	1 mol % $FeCl_3$ $MeNO_2$, 0 °C-rt, 40 h	25	-

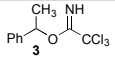
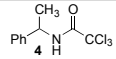
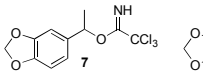
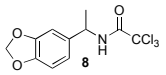
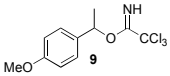
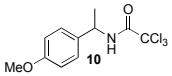
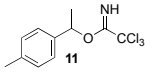
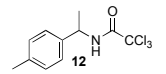
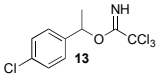
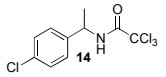
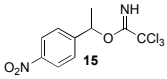
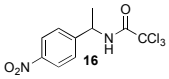
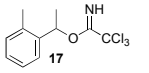
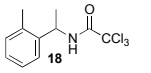
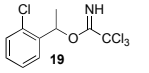
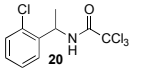
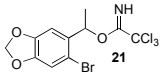
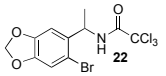
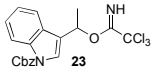
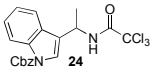
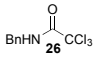
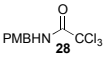
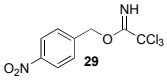
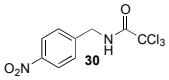
[a]Determined by ^{1}H NMR using mesitylene as an internal standard. [b]Isolated yield (%). [c]Starting material decomposed. [d]Starting material was recovered. [e]Trace amounts of styrene were detected in the ^{1}H NMR

A number of trichloroacetimidates were then subjected to both sets of rearrangement conditions (Table 2). Incorporation of electron-donating groups on the aromatic ring generally led to very good yields of the acetamide product under both thermal and Lewis acid catalyzed conditions (entries 2-4). Weak deactivating groups like chloride still gave an acceptable yield (entry 5), although the addition of a strongly deactivating nitro group was detrimental (entry 6). Indeed, trichloroacetimidate **15** was inert under the thermal conditions, and only gave rearrangement product in 32% yield under more vigorous Lewis acid catalyzed conditions (10 mol % BF_3•OEt_2, nitromethane, reflux, 24 h). Placing a halogen or methyl group at the ortho position of the aromatic ring lowered the isolated yields of the corresponding trichloroacetamide (entries 7-9), which was attributed to unfavorable steric factors. Replacing the benzene ring with an indole, as in the case of trichloroacetimidate **23**, (entry 10) provided the rearranged product with good yield (72%) under Lewis acid catalyzed conditions, however under thermal conditions

the imidate rapidly decomposed. This demonstrates the flexibility of having both thermal and Lewis acid catalyzed protocols available, as some substrates may not be compatible with both sets of conditions. Primary benzylic trichloroacetimidates (entry 11 and 12) provided lower yields than the secondary substrates. Strong electron withdrawing substituents on the adjacent aromatic ring were again detrimental, as shown with 4-nitrobenzyl imidate **29**.

Table 2. Rearrangement of Primary and Secondary Trichloroacetimidates



entry	imidate	acetamide	yield[a]	yield[b]
1			80	94
2			75	87
3			82	80
4			80	84
5			72[c]	67[d]
6			0	0 (32[e])
7			56	85
8			55[c]	59[f]
9			73	62
10			0[g]	72
11			25	15
12			47	13
13			0	0

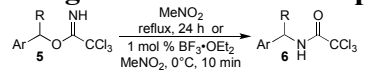
[a]Isolated yield (%) from thermal conditions (nitromethane, reflux, 24 h) [b]Isolated yield (%) from Lewis acid catalyzed conditions (1 mol % BF_3•OEt_2, nitromethane, 0 °C 10 min). [c]Reaction was performed for 72 h. [d]Reaction was performed for 24 h at rt. [e]10 mol % BF_3•OEt_2, nitromethane, reflux, 24 h. [f]Reaction was performed for 1 h at rt. [g]Starting material decomposed.

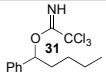
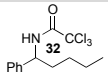
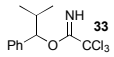
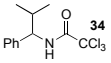
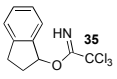
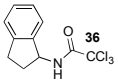
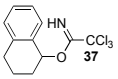
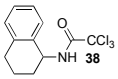
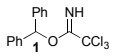
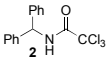
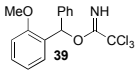
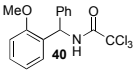
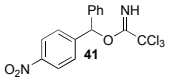
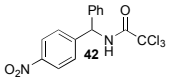
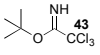
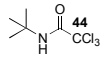
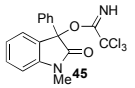
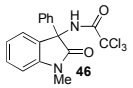
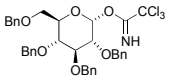
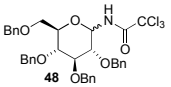
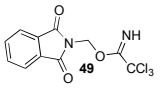
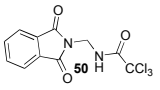
More complex substrates were also evaluated in the transformation (Table 3). A longer butyl chain next to the benzylic imidate (**31**) gave a lower yield, probably for steric reasons, with an

isopropyl substituent (**32**) reducing the isolated yield even further. Tethering the alkyl chain to the benzene ring, as in the case of imidate **35** and imidate **37**, provided reliable substrates for the rearrangement. Subjecting diphenylmethyl imidate **1** to either rearrangement conditions gave the trichloroacetamide product **2** in good yield. Adding a methoxy group at the ortho position in a similar diphenylmethyl system (imidate **39**) again gave lower yields, which may be attributed to sterics. Interestingly, addition of a *para*-nitro group to the DPM system (entry 7) did not slow the rearrangement, and excellent yields of trichloroacetamide **42** were obtained under both thermal and Lewis acid catalyzed conditions. Tertiary trichloroacetimidates were also briefly investigated. *tert*-Butyl trichloroacetimidate **43** gave very poor conversion under Lewis acid catalyzed conditions, and no product was isolated from the thermal conditions. This may be related to the high propensity of this imidate to eliminate.[16] In contrast, the tertiary imidate **45** (entry 9),[17] which cannot eliminate, provided a respectable yield of the rearranged product **46** but only under thermal conditions, with the starting material decomposing under the Lewis acid catalyzed conditions. Incorporation of a heteroatom next to the site of the imidate rearrangement was also explored. Rearrangement of a protected glucose with an anomeric trichloroacetimidate was successful, with imidate **47** undergoing rapid rearrangement under both thermal and Lewis acid catalyzed conditions. Little preference for either anomer of the product was observed, with the rearrangement providing a mixture of products in both cases. Incorporation of a nitrogen next to the site of rearrangement was also investigated with phthalimidomethyl trichloroacetimidate **49** (entry 11). Like other primary trichloroacetimidates, this substrate was found to be less reactive and had to be treated with 10% BF_3•OEt_2 at reflux for 48 hours to achieve rearrangement. More highly substituted imidates with a neighboring nitrogen are reported to be unstable, having to be prepared *in situ* and used immediately,[18] and so these substrates were not

pursued further. Rearrangement of ethyl trichloroacetimidate was also evaluated, but only trace amounts of rearrangement were observed.

Table 3. Rearrangement of More Complex Imidates

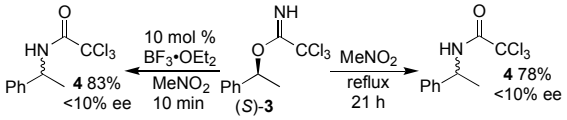


entry	imidate	acetamide	yield[a]	yield[b]
1			63	56
2			16	41
3			72	74
4			60	70
5			80	83
6			50	67
7			74	88
8			trace	8[c]
9			53	0
10			42[d]	67[e]
11			0	29[f]
12			0	0

[a]Isolated yield (%) from thermal conditions (nitromethane, reflux, 24 h) [b]Isolated yield (%) from Lewis acid catalyzed conditions (1 mol % BF_3•OEt_2, nitromethane, 0 °C 10 min). [c]10 mol % BF_3•OEt_2, nitromethane, reflux 24 h. [d]Isolated as a 44:54 (α:β) mixture of anomers [e]Isolated as a 58:42 (α:β) mixture of anomers. [f]10 mol % BF_3•OEt_2, nitromethane, reflux, 48 h.

The effect of the rearrangement on the stereochemistry of the substrate was also investigated by subjecting nonracemic phenethyl trichloroacetimidate (*S*)-**3** to the reaction conditions (Scheme 2). In both cases (thermal and Lewis acid catalyzed), nearly complete racemization was observed when the product of the reaction was analyzed by chiral HPLC.

Scheme 2. Rearrangement of (*S*)-3



Given the observed racemization during the rearrangement and the substrate scope, an analysis of the mechanism was undertaken. Two possibilities were considered: a concerted bimolecular pathway (path A) or an ionization recombination pathway (path B) (Figure 1). The poor yield with the ethyl imidate **51** and the success of the rearrangement of the hindered tertiary trichloroacetimidate **45** led us to favor the cationic pathway, path B. This pathway is also consistent with the observed racemization in Scheme 2, with the small deviation from completely racemic product being attributed to memory of chirality from ion pair interactions.[19] In the case of the nitro-substituted diphenylmethyl trichloroacetimidate **41**, the rearrangement may be rationalized as the extended resonance effects of the two aromatic rings combined with the inability to undergo elimination outweigh the electron withdrawing effect of the nitro group on cation formation.

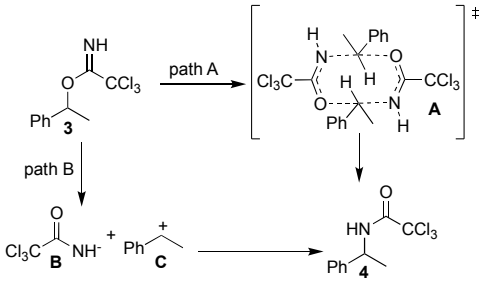
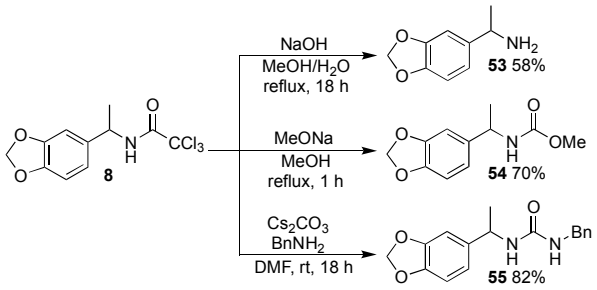


Figure 1. Possible Mechanisms for the Rearrangement

The benzylic trichloroacetamides provide ready access to both the corresponding benzylic amine as well as other amine-based functional groups such as carbamates and ureas. In addition, it should be noted that trichloroacetamides are valuable precursors to nitrogen containing heterocyclic systems via radical cyclizations.[20] The amine may be accessed directly by deprotection of the acetamide using sodium hydroxide,[21] as shown for the deprotection of

acetamide **8** below (Scheme 3). This provided the amine **53** in 58% yield. The trichloroacetamide may also be directly converted to the corresponding carbamate,[22] as heating acetamide **8** with sodium methoxide in methanol gave the corresponding methyl carbamate **54** in 70% yield. Additionally, the acetamide may be converted to the corresponding urea by the base promoted addition of an amine.[23] For example, subjecting acetamide **8** to Cs_2CO_3 and benzyl amine in DMF provided urea **55** in 82% yield.

Scheme 3. Further Transformations of Acetamide 8



In conclusion, conditions to facilitate the efficient rearrangement of benzylic trichloroacetimidates to their corresponding trichloroacetamides have been developed. Use of nitromethane as the reaction solvent is critical to achieve high conversion and avoid elimination. The rearrangement occurred under both thermal conditions (in refluxing nitromethane) or in the presence of Lewis acid catalysts like BF_3•OEt_2. Although some substrates decomposed under one set of these conditions, typically they still underwent rearrangement using the alternative protocol. Imidates that are precursors to stabilized carbocations gave the highest yields of the rearranged products. Primary imidates tended to provide lower yields of the reaction products, as the primary carbocation intermediate was more difficult to form. Increasing steric demands around the site of rearrangement was detrimental to the yield of the transformation. These O to N transpositions using trichloroacetimidates provide an entry to benzylic trichloroacetamides, which are useful intermediates to access amines and a number of amine based functional groups like carbamates and ureas.

Experimental Section

General: All anhydrous reactions were run under a positive pressure of argon or nitrogen. Dichloromethane and THF were dried by passage through an alumina column following the method of Grubbs.[24] Column chromatography was performed using silica gel 60 (230−400 mesh). Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$, with residual chloroform or TMS used as the internal reference. The trichloroacetimidates **1**,[25] **3**,[26] **11**,[27] **17**,[15e] **21**,[15e] **25**,[28] **27**,[29] **29**,[30] **37**,[15e] **45**,[17] **47**,[11b,31] and **49**[32] were prepared as previously described, while *tert*-butyl 2,2,2-trichloroacetimidate **43** and ethyl 2,2,2-trichloroacetimidate **51** were purchased from commercial sources and used without further purification. The synthesis and analysis of the enantiopurity of the chiral trichloroacetimidate (*S*)-**3** was performed as previously reported.[27]

General Procedure for Synthesis of Trichloroacetimidates.

The starting alcohol was dissolved in anhydrous DCM (0.25 M) under argon. DBU (10 mol %) was then added. The mixture was stirred at room temperature for 15 min and then cooled to 0 °C. Trichloroacetonitrile (1.2 equiv) was then added, and the reaction mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was then concentrated and the residue purified by silica gel chromatography (using the listed solvent system) to give the trichloroacetimidate.

General Procedures for Rearrangement of Trichloroacetimidates to Trichloroacetamides.

Method A: Thermal Conditions

The imidate was dissolved in anhydrous nitromethane (1.0 M) under an argon atmosphere. The resulting solution was heated to reflux for 24 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed *in vacuo*. The residue was purified by silica gel

chromatography (using the listed solvent system) to provide the corresponding trichloroacetamide product.

Method B: Lewis Acid Catalyzed Conditions

The imidate was dissolved in anhydrous nitromethane (0.25 M) under an argon atmosphere. The solution was cooled to 0 °C and BF_3•OEt_2 (1 mol %) was added. The resulting solution was then stirred at 0 °C for the listed amount of time. The mixture was then quenched by the addition of sat. aq. sodium bicarbonate. The resulting suspension was then extracted with DCM (3x). The combined extracts were dried (Na_2SO_4), filtered and concentrated. The residue was purified by silica gel chromatography (using the listed solvent system) to provide the pure trichloroacetamide product.

***N*-Benzhydryl-trichloroacetamide (2).**[15a] Prepared using method A (0.16 g, 80%) and method B (0.25 g, 83%), purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). White solid; mp = 121-123 °C; TLC R_f= 0.65 (10% ethyl acetate/90% hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.31 (m, 6H), 7.26-7.25 (m, 4H), 7.16 (d, *J* = 6.4 Hz, 1H), 6.18 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 139.8, 129.0, 128.2, 127.4, 92.7, 59.0.

2,2,2-Trichloro-*N*-(1-phenylethyl)acetamide (4).[26] Prepared using method A (0.12 g, 80%) and method B (0.24 g, 94%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 117-119 °C; TLC R_f = 0.33 (10% ethyl acetate/90% hexanes); IR (thin film) 3310, 3064, 2991, 1681, 1519 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 6.92 (br s, 1H), 5.07 (p, *J* = 7.2 Hz, 1H), 1.59 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 141.4, 129.0, 128.0, 126.1, 92.7, 51.1, 21.2. Chiral HPLC

analysis: Chiralcel OJ (heptane/*i*-PrOH = 50/50, 0.5 mL/min, 254 nm, 25 °C): t_1 = 11.1 min, t_2 = 12.7 min.

***N*-(1-(Benzo[*d*][1,3]dioxol-6-yl)ethyl)-2,2,2-trichloroacetimidate (7).** Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid (3.10 g, 75%); mp = 39-42 °C; TLC R_f = 0.69 (10% ethyl acetate/90% hexanes); IR (thin film) 3338, 2982, 2932, 2892, 1661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (br s, 1H), 6.93 (d, *J* = 1.2 Hz, 1H), 6.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.95 (s, 2H), 5.90 (q, *J* = 6.4 Hz, 1H), 1.61 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 147.8, 147.3, 135.2, 119.6, 108.2, 106.6, 101.1, 91.8, 77.0, 22.2. Anal. Calcd for $C_{11}H_{10}Cl_3NO_3$: C, 42.54; H, 3.25; N, 4.51; Found: C, 42.35; H, 3.17; N, 4.52.

***N*-(1-(Benzo[*d*][1,3]dioxol-6-yl)ethyl)-2,2,2-trichloroacetamide (8).** Prepared using method A (0.23 g, 75%) and method B (0.13 g, 87%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 112-115 °C; TLC R_f = 0.23 (10% ethyl acetate/90% hexanes); IR (thin film) 3307, 2997, 2957, 2897, 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.83-6.75 (m, 4H), 5.97 (s, 2H), 4.99 (p, *J* = 6.8 Hz, 1H), 1.57 (d, *J* = 6.8 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 148.1, 147.3, 135.2, 119.5, 108.5, 106.7, 101.3, 92.7, 51.0, 21.2; Anal. Calcd for $C_{11}H_{10}Cl_3NO_3$: C, 42.54; H, 3.25; N, 4.51; Found: C, 42.54; H, 3.25; N, 4.52.

2,2,2-Trichloro-*N*-(1-(4-methoxyphenyl)ethyl)acetimidate (9). Prepared using the general procedure for synthesis of trichloroacetimidates, purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid (1.14 g, 53%); mp = 59-68 °C; TLC R_f = 0.66 (10% ethyl acetate/90% hexanes); IR (thin film) 3337, 3059, 2986, 2934, 1685, 1660,

1513 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (br s, 1H), 7.36 (dd, *J* = 6.4, 1.6 Hz, 2H), 6.90-6.87 (m, 2H), 5.94 (q, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 1.63 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 159.3, 133.3, 127.3, 113.8, 91.8, 76.9, 55.2, 22.0; Anal. Calcd for $C_{11}H_{12}Cl_3NO_2$: C, 44.55; H, 4.08; N, 4.72; Found: C, 44.88; H, 4.13; N, 4.68.

2,2,2-Trichloro-*N*-(1-(4-methoxyphenyl)ethyl)acetamide (10). Prepared using method A (0.25 g, 82%) and method B (0.12 g, 80%), purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). White solid; mp = 89-91 °C; TLC R_f = 0.25 (10% ethyl acetate/90% hexanes); IR (thin film) 3329, 2977, 2934, 2836, 1660, 1585, 1513 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 6.92-6.90 (m, 2H), 6.75 (br s, 1H), 5.04 (p, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 1.59 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 159.3, 133.4, 127.4, 114.3, 92.8, 55.3, 50.6, 21.0; Anal. Calcd for $C_{11}H_{12}Cl_3NO_2$: C, 44.55; H, 4.08; N, 4.72; Found: C, 44.68; H, 4.24; N, 4.76.

2,2,2-Trichloro-*N*-(1-*p*-tolylethyl)acetamide (12). Prepared using method A (0.24 g, 82%, purified using silica gel chromatography with 2% ethyl acetate/98% toluene) and method B (0.084 g, 84%, purified using silica gel chromatography with 5% ethyl acetate/95% hexanes). Yellow solid; mp = 74-77 °C; TLC R_f = 0.44 (10% ethyl acetate/90% hexanes); IR (thin film) 3322, 3026, 2980, 2927, 2873, 1697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.18 (m, 4H), 6.78 (br s, 1H), 5.05 (p, *J* = 7.2 Hz, 1H), 2.35 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 138.5, 138.4, 137.7, 129.6, 126.1, 92.8, 51.0, 21.1; Anal. Calcd for $C_{11}H_{12}Cl_3NO$: C, 47.09; H, 4.31; N, 4.99; Found: C, 46.69; H, 4.38; N, 4.99.

2,2,2-Trichloro-*N*-(1-(4-chlorophenyl)ethyl)acetimidate (13). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid (2.40 g, 79%); mp = 39-41 °C;

TLC R_f = 0.47 (10% ethyl acetate/90% hexanes); IR (thin film) 3341, 2983, 2933, 1663, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (br s, 1H), 7.37-7.32 (m, 4H), 5.95 (q, *J* = 6.8 Hz, 1H), 1.63 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 139.9, 133.7, 128.7, 127.3, 91.6, 76.4, 22.2; Anal. Calcd for $C_{10}H_9Cl_4NO$: C, 39.90; H, 3.01; N, 4.65; Found: C, 39.66; H, 3.31; N, 4.55.

2,2,2-Trichloro-*N*-(1-(4-chlorophenyl)ethyl)acetamide (14). Prepared using method A (0.22 g, 72%) and using a modified method B where the reaction was allowed to proceed for 1 h (0.10 g, 67%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 92-94 °C; TLC R_f = 0.33 (10% ethyl acetate/90% hexanes); IR (thin film) 3326, 3029, 2981, 2934, 1695, 1577 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 4H), 6.79 (br s, 1H), 5.05 (p, *J* = 6.8 Hz, 1H), 1.59 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 140.0, 133.7, 129.1, 127.5, 92.6, 50.6, 21.2; Anal. Calcd for $C_{10}H_9Cl_4NO$: C, 39.90; H, 3.01; N, 4.65; Found: C, 40.16; H, 3.25; N, 4.59.

2,2,2-Trichloro-*N*-(1-(4-nitrophenyl)ethyl)acetimidate (15). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (15% ethyl acetate/83% hexanes/2% triethylamine).White solid (1.80 g, 97%); mp = 56-59 °C; TLC R_f = 0.58 (30% ethyl acetate/70% hexanes); IR (thin film) 3340, 3083, 2987, 2936, 1666, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (br s, 1H), 8.24 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 6.05 (q, *J* = 6.8 Hz, 1H), 1.68 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 148.6, 147.5, 126.6, 123.9, 91.3, 75.9, 22.1; Anal. Calcd for $C_{10}H_9Cl_3N_2O_3$: C, 38.55; H, 2.91; N, 8.99; Found: C, 38.61; H, 2.92; N, 8.97.

2,2,2-Trichloro-*N*-(1-(4-nitrophenyl)ethyl)acetamide (16). Prepared using a modified method B (0.065g, 32%) where 10 mol % BF_3•OEt_2 was used and the reaction was heated to reflux for

24 h. Purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). White solid; mp = 118-126 °C; TLC R_f = 0.35 (30% ethyl acetate/ 70% hexanes); IR (thin film) 3341, 2983, 2931, 1699, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 4.4 Hz, 1H), 5.14 (p, *J* = 6.8 Hz, 1H), 1.65 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 148.8, 147.5, 126.9, 124.2, 92.3, 50.8, 21.5; Anal. Calcd for $C_{10}H_9Cl_3N_2O_3$: C, 38.55; H, 2.91; N, 8.99; Found: C, 38.57; H, 2.85; N, 9.25.

2,2,2-Trichloro-*N*-(1-*o*-tolylethyl)acetamide (18). Prepared using method A (0.15 g, 56%) and method B (0.085 g, 85%), purified using silica gel chromatography (10% ethyl acetate/90% hexanes). White solid; mp = 116-120 °C; TLC R_f = 0.42 (10% ethyl acetate/90% hexanes); IR (thin film) 3335, 3053, 3025, 2979, 2933, 2873, 1695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.19 (m, 4H), 6.79 (br s, 1H), 5.25 (p, *J* = 6.8 Hz, 1H), 2.39 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 139.2, 136.1, 131.0, 128.0, 126.6, 124.6, 92.7, 47.9, 20.4, 19.1. Anal. Calcd for $C_{11}H_{12}Cl_3NO$: C, 47.09; H, 4.31; N, 4.99; Found: C, 46.96; H, 4.22; N, 4.84.

2,2,2-Trichloro-*N*-(1-(2-chlorophenyl)ethyl)acetimidate (19). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). Colorless oil (1.04 g, 86%); TLC R_f = 0.63 (10% ethyl acetate/90% hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (br s, 1H), 7.57 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.31-7.21 (m, 2H), 6.31 (q, *J* = 6.4 Hz, 1H), 1.64 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 139.4, 131.7, 129.5, 128.9, 127.3, 126.2, 91.6, 74.1, 20.9; Anal. Calcd for $C_{10}H_9Cl_4NO$: C, 39.90; H, 3.01; N, 4.65; Found: C, 39.70; H, 2.95; N, 4.51.

2,2,2-Trichloro-*N*-(1-(2-chlorophenyl)ethyl)acetamide (20). Prepared using a modified method A where the reaction was refluxed for 72 h (0.11 g, 55%) and using a modified method B where the reaction was allowed to proceed for 1 h (0.080 g, 59%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 127-128 °C; TLC R_f = 0.32 (10% ethyl acetate/90% hexanes); IR (thin film) 3297, 3030, 2982, 2933, 1691, 1520 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.24 (m, 4H), 7.10 (br s, 1H), 5.35 (p, *J* = 6.8 Hz, 1H), 1.62 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 138.6, 132.9, 130.4, 129.1, 127.4, 127.2, 92.6, 49.6, 20.3; Anal. Calcd for $C_{10}H_9Cl_4NO$: C, 39.90; H, 3.01; N, 4.65; Found: C, 40.04; H, 3.01; N, 4.97.

***N*-(1-(5-Bromobenzo[*d*][1,3]dioxol-6-yl)ethyl)-2,2,2-trichloroacetamide (22).** Prepared using method A (0.15 g, 73%) and method B (0.16 g, 62%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 139-141 °C; TLC R_f = 0.62 (30% ethyl acetate/70% hexanes); IR (thin film) 3327, 2981, 2899, 1694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.92 (s, 1H), 6.82 (s, 1H), 5.99 (q, *J* = 1.2 Hz, 2H), 5.23 (p, *J* = 7.2 Hz, 1H), 1.56 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 148.0, 147.9, 133.4, 113.6, 113.4, 106.8, 102.0, 92.5, 51.3, 20.4; Anal. Calcd for $C_{11}H_9BrCl_3NO_3$: C, 33.92; H, 2.33; N, 3.60; Found: C, 33.67; H, 2.45; N, 3.83.

Benzyl 3-(1-(2,2,2-trichloroacetimido)ethyl)-1H-indole-1-carboxylate (23). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid (1.47 g, 76%); mp = 78-85 °C; IR (thin film) 3338, 3089, 3034, 2982, 2936, 1740, 1662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.18 (d, *J* = 5.6 Hz, 1H), 7.68-7.67 (m, 2H), 7.50-7.22 (m, 7H), 6.31 (q, *J* = 6.4 Hz, 1H), 5.44-5.37 (m, 2H), 1.77 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 161.8, 150.8, 135.9, 135.1, 128.9, 128.6, 128.4, 127.8, 125.1, 123.2, 123.0, 121.6, 120.2, 115.5, 91.9, 71.2, 68.9, 19.8; Anal. Calcd for $C_{20}H_{17}Cl_3N_2O_3$: C, 54.63; H, 3.90; N, 6.37; Found: C, 54.70; H, 3.92; N, 6.24.

Benzyl 3-(1-(2,2,2-trichloroacetamido)ethyl)-1H-indole-1-carboxylate (24). Prepared using method B (0.072 g, 72%), purified using silica gel chromatography (10% ethyl acetate/90% hexanes). White solid; mp = 126-128 °C; TLC R_f = 0.53 (25% ethyl acetate/75% hexanes); IR (thin film) 3333, 3065, 3031, 2979, 2936, 1734, 1703, 1608 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 6.8 Hz, 1H), 7.62 (s, 1H), 7.58-7.55 (m, 1H), 7.50-7.47 (m, 2H), 7.45-7.34 (m, 4H), 7.30-7.27 (m, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.50-5.34 (m, 3H), 1.71 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 150.7, 135.9, 134.9, 128.90, 128.85, 128.61, 128.56, 125.4, 123.5, 122.7, 121.9, 119.4, 115.5, 92.7, 69.0, 43.9, 19.4; Anal. Calcd for $C_{20}H_{17}Cl_3N_2O_3$: C, 54.63; H, 3.90; N, 6.37; Found: C, 54.67; H, 3.92; N, 6.50.

***N*-Benzyl-2,2,2-trichloroacetamide (26).**[33] Prepared using method A (0.050 g, 25%) and method B (0.015 g, 15%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 87-92 °C; TLC R_f = 0.50 (20% ethyl acetate/ 80% hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.30 (m, 5H), 7.00 (br s, 1H), 4.55 (d, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 136.3, 129.0, 128.2, 127.8, 92.6, 45.4.

***N*-(4-Methoxybenzyl)-2,2,2-trichloroacetamide (28).** Prepared using method A (0.070 g, 47%) and method B (0.013 g, 13%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 95-100 °C; TLC R_f = 0.18 (10% ethyl acetate/90% hexanes); IR (thin film) 3313, 3044, 3002, 2954, 1692, 1613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.24 (m, 2H), 6.92-6.84 (m, 3H), 4.49 (d, *J* = 5.6 Hz, 2H), 3.81 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 161.8, 159.5, 129.3, 128.4, 114.4, 92.6, 55.3, 44.9; Anal. Calcd for $C_{10}H_{10}Cl_3NO_2$: C, 42.51; H, 3.57; N, 4.96; Found: C, 42.72; H, 3.77; N, 5.22.

2,2,2-Trichloro-*N*-(1-phenylpentyl)acetimidate (31). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (8% ethyl acetate/90% hexanes/2% triethylamine). Yellow oil (1.69 g, 96%); TLC R_f = 0.71 (10% ethyl acetate/90% hexanes); IR (thin film) 3348, 3092, 3069, 3036, 2958, 2934, 2863, 1659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.41-7.27 (m, 5H), 5.81 (q, *J* = 5.6 Hz, 1H), 2.09-2.00 (m, 1H), 1.89-1.80 (m, 1H), 1.50-1.41 (m, 1H), 1.38-1.30 (m, 3H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 140.6, 128.4, 127.9, 126.2, 91.9, 81.0, 36.7, 27.7, 22.5, 14.1; Anal. Calcd for $C_{13}H_{16}Cl_3NO$: C, 50.59; H, 5.23; N, 4.54; Found: C, 50.32; H, 5.36; N, 4.42.

2,2,2-Trichloro-*N*-(1-phenylpentyl)acetamide (32). Prepared using method A (0.19 g, 63%) and method B (0.084 g, 56%), purified using silica gel chromatography (5% ethyl acetate/95% hexanes). White solid; mp = 57-61 °C; TLC R_f = 0.49 (10% ethyl acetate/90% hexanes); IR (thin film) 3431, 3067, 3033, 2957, 2931, 2861, 1698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.29 (m, 5H), 6.81 (br s, 1H), 4.90 (q, *J* = 7.6 Hz, 1H), 1.94-1.87 (m, 2H), 1.39-1.24 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 140.7, 128.9, 127.9, 126.5, 92.9, 55.8, 35.6, 28.3, 22.4, 14.0; Anal. Calcd for $C_{13}H_{16}Cl_3NO$: C, 50.59; H, 5.23; N, 4.54; Found: C, 50.49; H, 5.18; N, 4.79.

2,2,2-Trichloro-*N*-(2-methyl-1-phenylpropyl)acetimidate (33). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (5% ethyl acetate/93% hexanes/2% triethylamine). Colorless oil (3.01 g, 86%); TLC R_f = 0.63 (10% ethyl acetate/ 90% hexanes); IR (thin film) 3339, 3088, 3062, 3032, 2979, 2961, 2925,

2868, 1660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.41-7.28 (m, 5H), 5.57 (d, *J* = 7.2 Hz, 1H), 2.29-2.17 (m, 1H), 1.10 (d, *J* = 6.4 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 139.1, 128.2, 127.9, 126.9, 92.0, 85.8, 34.4, 19.0, 18.4; Anal. Calcd for $C_{12}H_{14}Cl_3NO$: C, 48.92; H, 4.79; N, 4.75; Found: C, 48.72; H, 4.42; N, 4.64.

2,2,2-Trichloro-*N*-(2-methyl-1-phenylpropyl)acetamide (34). Prepared using method A (0.049 g, 16%) and method B (0.062 g, 41%), purified using silica gel chromatography (1% ethyl acetate/99% toluene). White solid; mp = 78-82 °C; TLC R_f = 0.38 (10% ethyl acetate/ 90% hexanes); IR (thin film) 3338, 3066, 3033, 2963, 2934, 2873, 1693, 1515 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.34 (m, 2H), 7.31-7.24 (m, 3H), 6.96 (d, *J* = 6.8 Hz, 1H), 4.69 (t, *J* = 8.4 Hz, 1H), 2.23-2.11 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 139.7, 128.7, 127.8, 126.7, 93.0, 61.4, 33.6, 19.7, 18.5; Anal. Calcd for $C_{12}H_{14}Cl_3NO$: C, 48.92; H, 4.79; N, 4.75; Found: C, 48.96; H, 4.86; N, 4.87.

2,2,2-Trichloro-*N*-(2,3-dihydro-1H-inden-3-yl)acetimidate (35). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). Clear colorless oil (0.73 g, 86%); TLC R_f = 0.85 (10% ethyl acetate/90% hexanes); IR (thin film) 3340, 3028, 2943, 2852, 1660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.34-7.22 (m, 3H), 6.35 (q, *J* = 2.8 Hz, 1H), 3.19-3.11 (m, 1H), 2.96-2.89 (m, 1H), 2.67-2.58 (m, 1H), 2.27-2.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 144.5, 140.6, 129.2, 126.8, 125.7, 124.9, 91.9, 83.3, 32.0, 30.2; Anal. Calcd for $C_{11}H_{10}Cl_3NO$: C, 47.43; H, 3.62; N, 5.03; Found: C, 47.15; H, 3.95; N, 5.27.

2,2,2-Trichloro-*N*-(2,3-dihydro-1H-inden-3-yl)acetamide (36). Prepared using method A (0.072 g, 72%) and method B (0.074 g, 74%), purified using silica gel chromatography (5% ethyl

acetate/94% hexanes/1% triethylamine). White solid; mp = 86-89 °C; TLC R_f = 0.51 (10% ethyl acetate/90% hexanes); IR (thin film) 3319, 3024, 2944, 2850, 1692, 1518 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.16 (m, 4H), 6.74 (s, 1H), 5.39 (q, *J* = 7.6 Hz, 1H), 3.02-2.95 (m, 1H), 2.91-2.83 (m, 1H), 2.66-2.58 (m, 1H), 1.91-1.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 143.5, 141.5, 128.7, 127.2, 125.1, 124.0, 92.7, 56.8, 33.4, 30.3; Anal. Calcd for $C_{11}H_{10}Cl_3NO$: C, 47.43; H, 3.62; N, 5.03; Found: C, 47.09; H, 3.90; N, 4.95.

2,2,2-Trichloro-*N*-(1,2,3,4-tetrahydronaphthalen-4-yl)acetamide (38). Prepared using method A (0.13 g, 60%) and method B (0.11 g, 70%), purified using silica gel chromatography (10% ethyl acetate/89% hexanes/1% triethylamine). White solid; mp = 129-130 °C; TLC R_f = 0.33 (10% ethyl acetate/90% hexanes); IR (thin film) 3285, 3057, 2920, 2864, 1691, 1536 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.14 (m, 4H), 6.80 (br s, 1H), 5.17-5.12 (m, 1H), 2.90-2.76 (m, 2H), 2.18-2.10 (m, 1H), 1.96-1.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 137.7, 134.9, 129.5, 128.5, 128.0, 126.7, 92.9, 49.9, 29.4, 29.1, 19.9; Anal. Calcd for $C_{12}H_{12}Cl_3NO$: C, 49.26; H, 4.13; N, 4.79; Found: C, 48.97; H, 4.13; N, 4.86.

2,2,2-Trichloro-*N*-((2-methoxyphenyl)(phenyl)methyl)acetimidate (39). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (5% ethyl acetate/94% hexanes/1% triethylamine). White solid (2.76 g, 81%); mp = 93-96 °C; IR (thin film) 3337, 3064, 3032, 3005, 2960, 2938, 1665, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.50-7.46 (m, 3H), 7.35-7.25 (m, 5H), 6.97 (td, *J* = 7.6, 0.8 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 156.4, 139.7, 129.1, 128.5, 128.3, 127.8, 127.0, 126.8, 120.7, 110.7, 91.7, 76.2, 55.6; Anal. Calcd for $C_{16}H_{14}Cl_3NO_2$: C, 53.58; H, 3.93; N, 3.91; Found: C, 53.54; H, 3.82; N, 3.97.

2,2,2-Trichloro-*N*-((2-methoxyphenyl)(phenyl)methyl)acetamide (40). Prepared using method A (0.072 g, 50%) and method B (0.100 g, 67%), purified using silica gel chromatography (5% ethyl acetate/95% hexanes). White solid; mp = 109-112 °C; TLC R_f = 0.34 (10% ethyl acetate/90% hexanes); IR (thin film) 3404, 3062, 3028, 2936, 2838, 1714, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.0 Hz, 1H), 7.37-7.20 (m, 7H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.28 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 157.1, 140.1, 129.8, 129.6, 128.5, 127.4, 127.1, 126.4, 121.2, 111.7, 93.1, 56.8, 55.6; Anal. Calcd for $C_{16}H_{14}Cl_3NO_2$: C, 53.58; H, 3.93; N, 3.91; Found: C, 53.86; H, 3.83; N, 3.83.

2,2,2-Trichloro-*N*-((4-nitrophenyl)(phenyl)methyl)acetimidate (41). Prepared using the general procedure for synthesis of trichloroacetimidates and purified using silica gel chromatography (10% hexanes/88% toluene/2% triethylamine). White solid (1.34 g, 86%); mp = 89-93 °C; TLC R_f = 0.62 (30% ethyl acetate/ 70% hexanes); IR (thin film) 3339, 3039, 1667, 1606, 1523 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 8.21 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.8 Hz, 2H), 7.43-7.32 (m, 5H), 7.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 147.6, 146.9, 138.3, 128.9, 128.7, 127.6, 127.1, 123.9, 91.2, 80.3; Anal. Calcd for $C_{15}H_{11}Cl_3N_2O_3$: C, 48.22; H, 2.97; N, 7.50; Found: C, 48.09; H, 2.97; N, 7.33.

2,2,2-Trichloro-*N*-((4-nitrophenyl)(phenyl)methyl)acetamide (42). Prepared using method A (0.149 g, 74%) and method B (0.088 g, 88%), purified using silica gel chromatography (10% ethyl acetate/90% hexanes). White solid; mp = 145-148 °C; TLC R_f = 0.29 (20% ethyl acetate/ 80% hexanes); IR (thin film) 3280, 3064, 1702, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.43-7.36 (m, 3H), 7.26-7.22 (m, 3H), 6.22 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 147.6, 146.9, 138.4, 129.5, 129.0, 127.9,

127.6, 124.2, 92.2, 58.7; Anal. Calcd for $C_{15}H_{11}Cl_3N_2O_3$: C, 48.22; H, 2.97; N, 7.50; Found: C, 48.23; H, 3.07; N, 7.49.

***N-tert*-Butyl-2,2,2-trichloroacetamide (44).**[34] Pink solid (0.012 g, 8%); TLC R_f = 0.40 (15% ethyl acetate/ 85% hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (br s, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 93.3, 53.0, 28.1.

2,2,2-Trichloro-*N*-(1-methyl-2-oxo-3-phenylindolin-3-yl)acetamide (46). Prepared using method A (0.047 g, 47%), purified using silica gel chromatography (20% ethyl acetate/88% hexanes/2% triethylamine). White solid; mp = 197-205 °C; TLC R_f = 0.21 (20% ethyl acetate/80% hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 8H), 7.11 (td, *J* = 7.6, 0.8 Hz, 1H), 6.87 (d, 7.6 Hz, 1H), 3.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 160.5, 144.6, 136.5, 130.2, 129.5, 129.3, 127.2, 126.7, 124.8, 123.2, 108.9, 91.8, 65.1, 27.0; Anal. Calcd for $C_{17}H_{13}Cl_3N_2O_2$: C, 53.22; H, 3.42; N, 7.30; Found: C, 53.40; H, 3.43; N, 7.28.

***N*-((2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-((benzyloxy)methyl)-tetrahydro-2H-pyran-2-yl)-2,2,2-trichloroacetamide (48a) and *N*-((2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-((benzyloxy)methyl)-tetrahydro-2H-pyran-2-yl)-2,2,2-trichloroacetamide (48b).** Rearrangement of imidate 47 using method A provided **48a** (0.040 g, 21%) and **48b** (0.040g, 21%) after purification with silica gel chromatography (10% ethyl acetate/90% hexanes). This rearrangement was also successful with method B, providing **48a** (0.047 g, 47%) and **48b** (0.020g, 20%) after purification with silica gel chromatography (10% ethyl acetate/90% hexanes).

48a.[11b] Colorless oil (0.04 g, 21%); TLC R_f = 0.38 (20% ethyl acetate/80% hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 19H), 7.15-7.12 (m, 2H), 5.60 (t, *J* = 5.6 Hz, 1H), 4.91 (d, *J* = 10.8 Hz, 1H), 4.79 (t, *J* = 11.2 Hz, 2H), 4.65-4.57 (m, 3H), 4.54-4.47 (m, 2H), 3.89-3.86 (m,

1H), 3.80-3.76 (m, 2H), 3.69-3.64 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 138.2, 137.9, 137.8, 136.9, 128.7, 128.51, 128.50, 128.43, 128.39, 128.2, 128.1, 128.04, 127.98, 127.9, 127.8, 92.4, 81.6, 77.0, 76.5, 75.5, 75.2, 73.6, 73.0, 71.9, 68.1.

48b.[11b] White solid (0.04 g, 21%); mp = 121-126 °C; TLC R_f = 0.32 (20% ethyl acetate/80% hexanes); IR (thin film) 3325, 3064, 3031, 2924, 2858, 1706, 1520 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.25 (m, 18H), 7.14-7.12 (m, 2H), 6.98 (d, *J* = 8.8 Hz, 1H), 5.08 (t, *J* = 9.2 Hz, 1H), 4.89 (s, 2H), 4.83-72 (m, 3H), 4.61 (d, *J* = 12.4 Hz, 1H), 4.51 (dd, *J* = 20.4, 10.8 Hz, 2H), 3.80-3.69 (m, 4H), 3.56-3.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 138.2, 137.9, 137.6, 137.4, 128.7, 128.52, 128.47, 128.46, 128.44, 128.2, 128.1, 127.90, 127.85, 92.2, 85.8, 81.0, 79.8, 77.3, 76.9, 75.7, 75.0, 74.8, 73.6, 67.9; Anal. Calcd for $C_{36}H_{36}Cl_3NO_6$: C, 63.12; H, 5.30; N, 2.04; Found: C, 63.19; H, 5.37; N, 2.06.

2,2,2-Trichloro-*N*-((1,3-dioxoisoindolin-2-yl)methyl)acetamide (50). Prepared using a modified method B (0.058 g, 29%) where the reaction was performed with 10 mol % BF_3•OEt_2 at rt for 48 h, purified using silica gel chromatography (1% ethyl acetate/99% dichloromethane). White solid; mp = 218-223 °C; TLC R_f = 0.71 (2% ethyl acetate/ 98% dichloromethane); IR (thin film) 3317, 3123, 1709, 1514 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.89 (m, 2H), 7.80-7.76 (m, 2H), 7.52 (br s, 1H), 5.31 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 161.6, 134.6, 131.7, 123.9, 92.0, 44.0; Anal. Calcd for $C_{11}H_7Cl_3N_2O_3$: C, 41.09; H, 2.19; N, 8.71; Found: C, 41.04; H, 2.21; N, 8.74.

1-(Benzo[*d*][1,3]dioxol-6-yl)ethanamine (53).[35] To the solution of amide **8** (0.10 g, 0.32 mmol) in 2.1 mL methanol, solution of sodium hydroxide (0.051 g in 0.5 mL water) was added and the reaction mixture was heated to reflux for 18 h. Then the mixture was cooled to room temperature and concentrated. The residue was partitioned between 10 mL water and 5 mL DCM. The

organic layer was separated and the aqueous layer was extracted with DCM twice (2 x 5 mL). The combined organic layers were dried over sodium sulfate and then filtered and concentrated to provide crude amine **53**. The crude residue was then purified by silica gel chromatography (1% triethylamine/ 2% methanol/ 97% dichloromethane) to provide the pure amine **53** (0.031 g, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, J = 1.6 Hz, 1H), 6.82-6.74 (m, 2H), 5.94 (s, 2H), 4.09 (q, J = 6.8 Hz, 1H), 2.86 (br s, 2H), 1.39 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 146.4, 141.1, 118.9, 108.1, 106.4, 100.9, 51.2, 25.3.

Methyl 1-(benzo[*d*][1,3]dioxol-6-yl)ethylcarbamate (54). To a solution of **8** (0.050 g, 0.16 mmol) in 0.5 mL methanol, sodium methoxide (0.086 g, 1.60 mmol) was added and the resulting mixture was stirred at reflux for 1 h. The mixture was then cooled to room temperature and was partitioned between dichloromethane and water (5 mL each). The organic layer was separated and the aqueous was extracted with dichloromethane (2 x 5 mL). The combined organic layers were dried over sodium sulfate and then filtered and concentrated to provide crude carbamate **54**. The crude residue was then purified by silica gel chromatography (5% ethyl acetate/ 95% dichloromethane) to provide the pure carbamate **54** (0.025 g, 70%) as a colorless oil. TLC R_f = 0.23 (20% ethyl acetate/80% hexanes); IR (thin film) 3324, 2974, 2897, 1703, 1504 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79-6.74 (m, 3H), 5.94 (s, 2H), 4.91 (br s, 1H), 4.74 (br s, 1H), 3.65 (s, 3H), 1.44 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 147.8, 146.7, 137.7, 119.1, 108.3, 106.6, 101.0, 52.1, 50.5, 22.5; Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27; Found: C, 59.10; H, 5.91; N, 6.35.

1-(1-(Benzo[*d*][1,3]dioxol-6-yl)ethyl)-3-benzylurea (55). To a solution of **8** (50.0 g, 0.16 mmol) in 0.6 mL DMF, Cs_2CO_3 (0.30 g, 0.96 mmol) and benzylamine (0.10 g, 0.96 mmol) were added and the resulting mixture was stirred at room temperature for 18 h. The mixture was then

diluted with saturated sodium bicarbonate solution and dichloromethane (5 mL each). The organic layer was separated and the aqueous was extracted with dichloromethane (2 x 5 mL). The combined organic layers were dried over sodium sulfate and then filtered and concentrated to provide crude urea **55**. The crude residue was then purified by silica gel chromatography (5% ethyl acetate/ 95% dichloromethane) to provide the pure urea **55** (0.079 g, 82%) as a white solid. mp = 143-147 °C; TLC R_f = 0.24 (40% ethyl acetate/60% toluene); IR (thin film) 3341, 3317, 3031, 2969, 2872, 1618, 1572 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.22 (m, 4H), 7.17 (d, *J* = 6.8 Hz, 2H), 6.78-6.74 (m, 3H), 5.93 (s, 2H), 4.68 (q, *J* = 6.8 Hz, 1H), 4.36-4.27 (m, 2H), 5.04-3.96 (br s, 1H), 1.40 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 148.1, 146.8, 138.9, 138.0, 128.6, 127.3, 119.0, 108.4, 106.4, 101.1, 77.2, 50.4, 44.5, 23.5; Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39; Found: C, 68.21; H, 5.88; N, 9.42.

Supporting Information Available

Copies of ^1H NMR and ^{13}C NMR spectra of new compounds and chiral HPLC data for compound **4**. This material is available free of charge via the Internet at http:// pubs.acs.org.

Author Information

Corresponding Author

*E-mail: jdchisho@syr.edu

Notes

The authors declare no competing financial interest.

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