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Synthesis of α-functionalized trichloromethylcarbinols

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A new series of α-functionalized trichloromethylcarbinols have been synthesized from corresponding α-halomethyl ketones, ester and amides in 48-78% overall yields. Reactivity of nitrates obtained in the first step was dependent on the electron-withdrawing nature of the functional groups, and increases with increasing electron deficiency. Synthetic applications of such trichloromethylcarbinols for the preparation of chloromethyl-α-diketones, trichloromethylated dihydrofurans and enol acetates of α-functionalized acid chlorides have been demonstrated. The reaction of these compounds in the Jocic-Reeve reaction was also demonstrated.

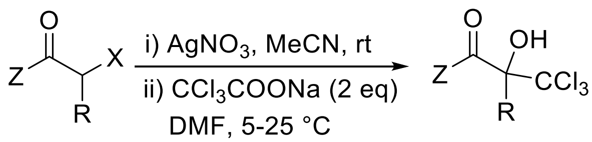
Trichloromethylcarbinols have been widely appreciated over their use in several useful transformations.[1] The formation of α-amino acids,[2] α-substituted carboxylic acids/amides,[3] heterocycles[4] and substituted enoic acids[5] was realized owing to their tendency to form a *gem*-dichloroepoxide intermediate in the presence of a strong base followed by the ring opening by a nucleophile (such as amines,[2a,2g,4c,4f] azide,[2b-f,4d-e] hydroxide,[3a-b] alcohols,[3e,5] phenols,[3c] thiols,[5] fluoride,[3e] cyanide,[3e] cyanate,[3e] hydride,[3f] selenide,[3f,3h] pyrroles,[3g] thiourea[4b]). Trichloromethylcarbinols can be converted into epoxides,[6] vinyl dichlorides,[7] alkynes,[8] chloromethyl ketones,[8a,9] 2-haloalk-2(Z)-en-1-ols and 1-chloro-1(Z)-alkenes,[10] and ring-expanded ketones by the reaction of cyclic trichloromethylcarbinols with aldehydes.[11] The synthesis of trichloromethylcarbinols has been realized by the reaction of various simple aldehydes and ketones with chloroform in the presence of a base,[12] such as sodium or potassium hydroxide,[12a-d,12g] amidines[12h] and lithium dicyclohexylamide.[12e-f] Electroreduction of CCl_4 in the presence of carbonyl compounds has also been studied.[13] Additionally, milder methods involving CCl_3COOH,[14] CCl_3COOH/CCl_3COONa[15] have been developed. However, trimethylsilyl-protected trichloromethylcarbinols were prepared from either trimethyl(trichloromethyl)silane ($TMSCCl_3$) in the presence of a catalyst,[16] such as TBAF,[16a] TASF[16b] and sodium formate,[16c] thermally[17] or trimethylsilyl trichloroacetate with K_2CO_3[18] and KF.[19] Due to the volatility and sublimation of $TMSCCl_3$, methods were developed using $TMSCl/CCl_4/Mg/HMPT$[20] or $TMSCl/CHCl_3/LiHMDS/Bu_4NOAc$,[21] where it was *in situ* formed. One-pot synthesis of trichloromethylcarbinols from primary alcohols has also been reported,[22] where Dess−Martin periodinane (DMP) was used as an oxidant and $CHCl_3/TBD$ for the transformation of resulting aldehydes into trichloromethylcarbinols. Recently, an improved method for the preparation of trichloromethylcarbinols from enolizable ketones using $CHCl_3$/TiCl(O*i*-Pr)$_3$/BuLi has been developed.[23] Decarboxylative trichloromethylation of aromatic aldehydes and its application in continuous flow have also been explored.[24]

However, there is no report for the synthesis of α-functionalized trichloromethylcarbinols i.e. 3,3,3-trichloro-2-hydroxy ketones, esters or amides using trichloromethyl anion as a nucleophile. The aldehyde precursors for these molecules immediately convert into hydrate in the presence of moisture[25] and prone to oxidation and polymerization.[25b] Also, selective addition to one carbonyl is doubtful for dicarbonyl compounds. Moreover, the construction of such molecules using other methods has not been much explored.[26] Methods for the synthesis of such molecules include (i) the reaction of chloral with HCN to form adduct which is further hydrolyzed to give β,β,β-trichlorolactic acid and esterified to give β,β,β-trichlorolactates[26e] otherwise β,β,β-trichlorolactamide derivatives[26b] by controlled hydrolysis or by direct reaction of this adduct with phenol in presence of $AlCl_3$ derivatives to give aryl β,β,β-trichlorolactates[26b,26d] (ii) Passerini reaction for the synthesis of trichlorolactamides by reaction of isocynides with chloral hydrate[26a,26c,26g] (iii) from isocynides with trichloroacetic acid anhydride[26f] to produce hydrates of trichloropyruvamides. Toxicity of CN^- ion is the major drawback of the first method whereas difficult preparation and purification[27] and extremely distressing odour[27a] of isocynides bring insignificance to last two methods. *O*-Methyl protected methyl trichlorolactate was also prepared by the reaction of ketene silyl acetals with carbon tetrachloride.[28] In one report, *N*-(methoxymethyl)-*N*,1,1,1-tetramethylsilanecarboxamide was reacted with chloral to provide corresponding *O*-trimethylsilyl protected or unprotected trichlorolacamide.[29] The electrolysis of 9,10-phenanthrenequinone in the presence of benzenediazonium tetrafluoroborate in chloroform provided 10-hydroxy-10-(trichloromethyl)phenanthren-9(10*H*)-one in low yield.[30] Such compounds are found to be biologically active as β,β,β-trichlorolactamide is effective against plant growth both pre- (mustard: dicot) and post-germinative (celery, tomatoes, coleus: dicots),[26b] while isopropyl β,β,β-trichlorolactate was active against cereal grains (monocots).[26b] However, due to the limited accessibility such compounds have not been comprehensively studied.

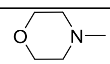
In view to the importance of trichloromethylcarbinols in the synthesis of a variety of building blocks as well as the utility of such structural unit in total synthesis, it was considered worthwhile to develop a general, efficient and practical method for the synthesis of α-functionalized trichloromethylcarbinols. It was expected that the easy access to such compounds would enhance the synthetic applications of trichloromethylcarbinols further. Herein, a facile synthesis of such trichloromethylcarbinols **2** by a direct two step-pathway starting from α-halomethyl ketones, esters and amides **1** has been reported. The method is quite general, which involves nucleophilic substitution of halo group (Br, I) by a nitrate group in acetonitrile at room temperature[25a,31] followed by its treatment with sodium trichloroacetate in DMF at 5−25 ˚C to give the desired products in moderate to high yields (**Table 1**). Resulting precipitate of silver halide in the first step was removed by filtration and the nitrates, obtained from the filtrate were used without further purification. Attempts were made to achieve one-pot synthesis of the **2a** by step-wise addition of the reagents $AgNO_3$ and

CCl_3COONa to a solution of **1a** in acetonitrile as well as in DMF at 20-25 ˚C. However, the reactions resulted in the formation of mixtures of unidentified products. The presence of AgBr thus formed during the reaction might have interfered in the next step. Additionally, the possible competition of trichloromethyl anion and nitrate particularly in DMF could be the reason for the complication. Almost all the products are solid (except **2h**) and stable under atmospheric conditions. These trichloromethylcarbinols were further investigated under some transformations in view to their importance.

Table 1. Synthesis of α-Functionalized Trichloromethylcarbinols 2a-*l*[a]



1 **2**

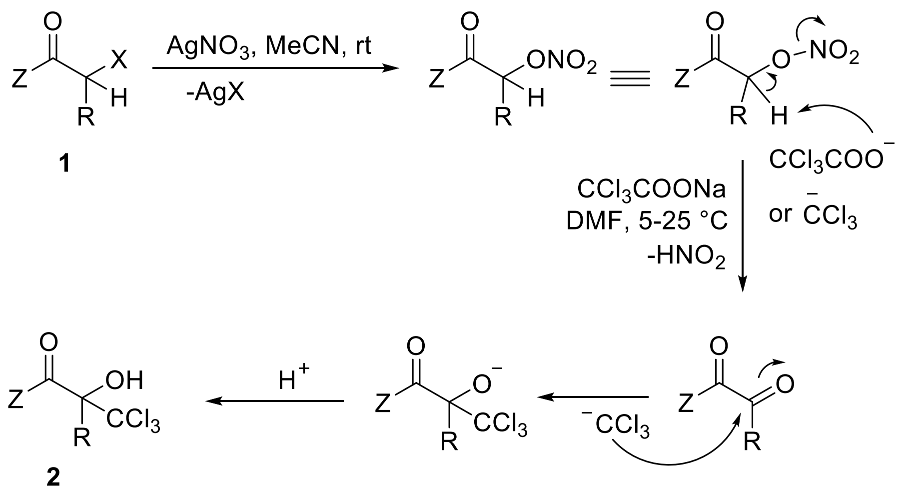
Entry	**1**	Z	R	X	time		yield (%) **2**
					step 1 (h)	step 2 (min)	
1	**a**	C_6H_5	H	Br	10	20	72
2	**b**	*p*-Me-C_6H_4	H	Br	10	30	78
3	**c**	*p*-MeO-C_6H_4	H	Br	10	30	74
4	**d**	*p*-Br-C_6H_4	H	Br	10	10[b]	64
5	**e**	*m*-O_2N-C_6H_4	H	Br	10	5[b]	60[c]
6	**f**	C_6H_5	Me	Br	10	60	60
7	**g**	2-furyl	H	I	10	10	60
8	**h**	*n*-hexyl	H	I	10	60	48
9	**i**	C_2H_5O	H	Br	12	60	75
10	**j**		H	Br	16	90	68
11	**k**	(*i*-Pr)$_2$N	H	Br	16	90	66
12	***l***	Ph(Me)N	H	Br	16	90	65

[a]All the reactions were performed by taking **1** (2 mmol), $AgNO_3$ (2 mmol), CCl_3COONa (4 mmol) at room temperature (20-25˚C). [b]The temperature was maintained at 0-5 ˚C. [c]3,3,3-Trichloro-2-hydroxy-2-(3-nitrophenyl)propyl nitrate **3** was also obtained in 18% isolated yield.

In all cases, reaction completion was confirmed by TLC. Relative observations revealed that the reactivity of nitrates increases as the electron-withdrawing nature of the substituted group increases (keto>ester>amide). Aromatic keto-nitrates were more reactive than aliphatic keto-nitrates, in which, electron donating groups like Me, OMe at aromatic ring (entry 2, 3) decreased the reactivity to some extent and required additional time for the completion of the reaction. On the other hand, electron withdrawing groups like Br, NO_2 (entry 4, 5) enough activated the substrate to react at 0-5 ˚C and the reaction was complete in 5-10 min. Interestingly, *m*-nitro group of **1e** also activated the keto group to react with trichloromethyl anion to give 3,3,3-trichloro-2-hydroxy-2-(4-nitrophenyl)propyl nitrate **3** along with the expected product **2e** in 18% isolated yield. Further reaction of the nitratomethyl group of

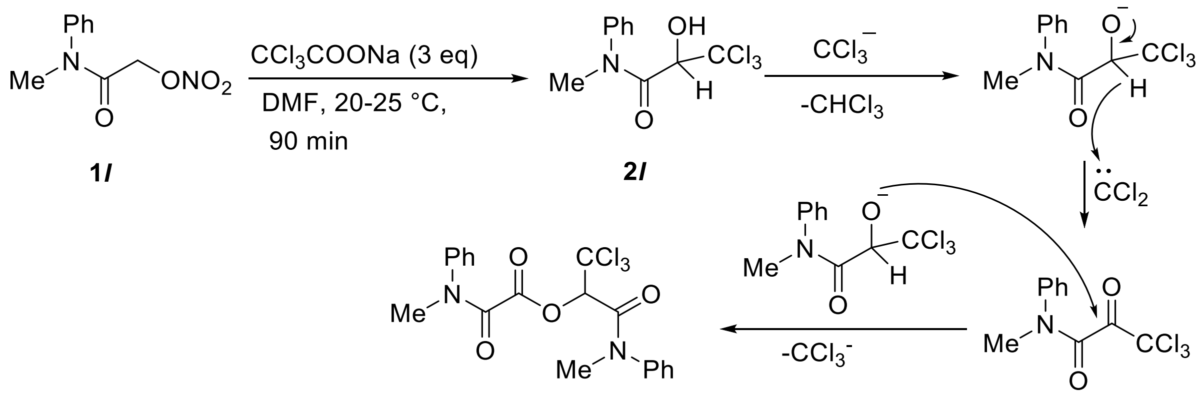
3 did not occur, probably due to its reduced reactivity towards base-promoted elimination reaction. A mechanism for the formation of trichloromethylcarbinols has been proposed (**Scheme 1**). The necessity of two equivalents of sodium trichloroacetate could be explained on the basis of possible consumption of one equivalent of sodium trichloroacetate during the elimination of HNO_2 in second step or slow decomposition of trichloromethyl anion. Remaining one equivalent was required for trichloromethylation of carbonyl group.

Scheme 1. Proposed Mechanism for the Formation of Trichloromethylcarbinols **2**



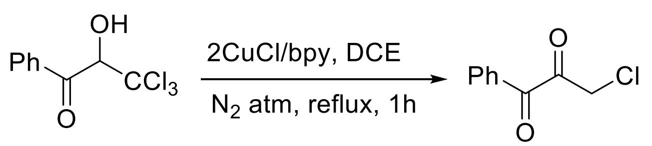
Incidentally, the reaction of the nitrate of **1*l*** with excess of sodium trichloroacetate (3 equiv) occurred vigorously with an increase in the reaction temperature and resulted in the formation of an interesting compound **4** (**Scheme 2**) in 54% isolated yield. It appeared that two molecules of the normal product **2*l***, initially formed were involved in its formation. A probable mechanism for its formation is proposed which involves oxidation of one molecule of **2*l*** with dichlorocarbene formed from excess sodium trichloroacetate (**Scheme 2**). The formation of dichlorocarbene might have been facilitated by considerable amount of heat generated during the exothermic decarboxylation of excess of the trichloroacetate. The intermediacy of **2*l*** was further supported by the reaction of **2*l*** with 2 equiv of sodium trichloroacetate in DMF under similar conditions which provided the same product **4** in 62% yield. With lower amount (1 or 1.5 equiv) of sodium trichloroacetate, the reaction of **2*l*** was not complete. Probably, an equivalent of CCl_3^- generated from the decarboxylation of the trichloroacetate was required to act as a base to facilitate the oxidation of **2*l*** with dichlorocarbene. The oxidation of alkoxides to aldehydes or ketones by hydride transfer to dichlorocarbene (generated from chloroform and NaOH) is reported in the literature.[32] The formation of the compound **4** was supported by IR, ^{1}H NMR, ^{13}C NMR spectroscopy HRMS data. The structure of **4** was also supported by single crystal X-ray diffraction data (see supporting information).

Scheme 2. Formation of **4** with Excess Sodium Trichloroacetate



α-Functionalized trichloromethylcarbinols obtained above are important synthetic intermediates. In order to demonstrate the synthetic importance of the trichloromethylcarbinols **2**, 3,3,3-trichloro-2-hydroxy-1-phenyl- propane-1-one **2a** as a representative member of **2** was treated with CuCl/bpy (2 equiv each) in refluxing DCE under nitrogen atmosphere for 1 h to give 3-chloro-1-phenylpropane-1,2-dione **5** in 65% isolated yield (**Scheme 3**). The reaction was considerably faster than that of simple trichloromethylcarbinols observed earlier, which required 3 h for completion.[9]

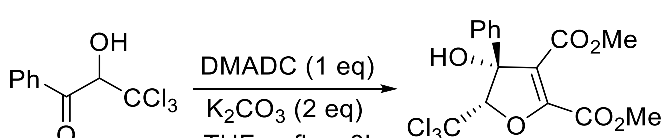
Scheme 3. Synthesis of 3-Chloro-1-phenylpropane-1,2-dione **5**



2a **5** (65%)

The formation of dihydrofuran by the reaction of 3-hydroxybutan-2-one with dimethyl acetylenedicarboxylate (DMAD) is reported in literature.[33] The application of the α-functionalized trichloromethylcarbinols **2** in the synthesis of highly substituted and functionalized dihydrofurans was demonstrated by the reaction of **2a** (**Scheme 4**) with DMADC in the presence of K_2CO_3 in refluxing tetrahydrofuran. This resulted in the formation of the 4,5-dihydrofuran derivative **6** containing a trichloromethyl group with complete diastereoselectivity in 72% isolated yield, where the bulky trichloromethyl group positioned itself *trans* to the phenyl group. An intramolecular Cl···H bonding might also be contributing to the selectivity. The structure of **6** was also supported by single crystal X-ray diffraction data (see supporting information).

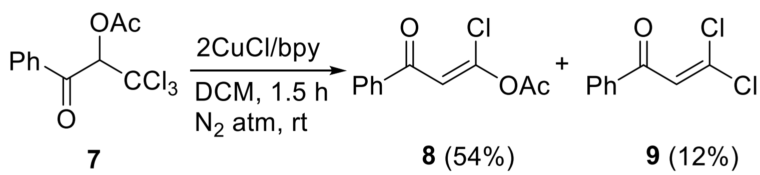
Scheme 4. Synthesis of Dihydrofuran **6** from **2a** and DMADC



2a **6** (72%)

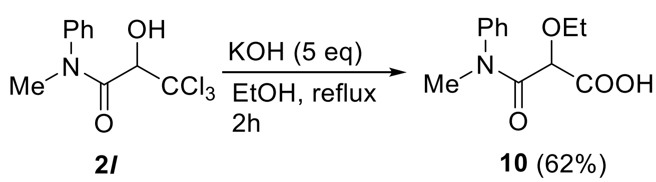
As reported by our laboratory[34] *O*-acetylated trichloromethylcarbinols undergo dechlorinative Surzur-Tanner rearrangement involving 1,2-acyloxy shift on treatment with CuCl/bpy to the diastereoselective formation of enol acetates of acid chlorides. The application of this reaction for stereoselective synthesis of such enol acetates was demonstrated by treating the acetylated trichloromethylcarbinol **7** (**Scheme 5**) with CuCl/bpy (2 equiv each) in DCM under a nitrogen atmosphere. As expected, the reaction occurred much faster than that of the simple trichloromethylcarbinol acetates observed earlier[34] and proceeded to completion in 1.5 h even at room temperature (20-25 ˚C). The acid chloride enol acetate **8** was isolated in 54% isolated yield. Formation of a small amount of 2,2-dichlorovinyl phenyl ketone **9** was also observed. The stereochemistry of **8** was presumed on the basis of our earlier observation.[35]

Scheme 5. Surzur-Tanner Rearrangement of **7**



Trichloromethylcarbinols are known to form dichloroepoxide in the presence of a base, which could be variously opened by nucleophiles.[1c] Therefore, the Jocic-Reeve reaction of the amide **2*l*** (**Scheme 6**) was performed with ethanolic KOH to furnish the tartronamic acid derivative **10** in 62% isolated yield.

Scheme 6. Synthesis of Tartronamic Acid Derivative **10** from **2*l***



In conclusion, we have developed a general, direct and efficient route to the synthesis of trichloromethylcarbinols having a keto, an ester or an amide functional group at the α-position from easily accessible α-halomethyl ketones, esters and amides, respectively, in moderate to high yields. The present method is fairly general as variously substituted trichloromethylcarbinols were successfully prepared. The applicability of the methodology for the synthesis of *tert*-trichloromethyl carbinols was also demonstrated. These compounds may possess some interesting biological activities. Nitrates can also be prepared directly from acetophenone derivatives.[36] The products are potential synthetic intermediates. Synthetic applications of such trichloromethylcarbinols for the preparation of chloromethyl-α-diketones, highly substituted trichloromethylated dihydrofurans and enol acetates of α-functionalized acid chlorides were demonstrated. The reaction of these compounds in the Jocic-Reeve reaction was also demonstrated.

Experimental Section

General remarks

IR spectra were recorded on FT-IR spectrometer by taking solid samples as KBr pellets and liquids as thin films on KBr discs. NMR spectra were recorded on a 300 MHz FT NMR spectrometer in $CDCl_3$ with TMS as internal standard. Multiplicities are indicated by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), sext (sextet), m (multiplet), dd (doublet doublet), dt (doublet triplet), td (triplet doublet). DEPT spectra were routinely recorded to identify different types of carbons. High-resolution mass spectra were recorded on a mass spectrometer (ESI-TOF) in positive ion mode. Melting points were determined on an electrically heated apparatus by taking the samples in a glass capillary sealed at one end and are uncorrected. The progress of the reaction was monitored by TLC. Iodine was used for visualizing the spots. Almost all the compounds were purified using column chromatography. Silica gel (60–120 mesh) was used as the stationary phase and *n*-hexane-EtOAc mixtures were used as the mobile phase. Solvents were evaporated on a rotary evaporator under reduced pressure using an aspirator. Starting materials **1a-f** were prepared by the bromination of the corresponding acetophenones.[37] 2-Iodoacetylfuran **1g** and 1-iodo-2-octanone **1h** were prepared from 2-chloroacetylfuran[38] and 1-chloro-2-octanone,[38] respectively. **1i** was commercially available and **1j-*l*** were prepared by the bromoacetylation of amines using bromoacetylbromide in DCM at 0-25 ˚C.[39]

Synthesis of trichloromethylcarbinols

***Typical procedure*:**

***3,3,3-Trichloro-2-hydroxy-1-phenylpropan-1-one* 2a:** To a solution of **1a** (2 mmol) in acetonitrile (10 mL) was added $AgNO_3$ (0.340 g, 2 mmol) and stirred for 10 h at room temperature. Completion of the reaction was confirmed by TLC. DCM (50 mL) was then added and stirred for additional 10 min. AgBr was precipitated out. The resulting solution was filtered and concentrated *in vacuo* to obtain the corresponding nitrate in quantitative yield. Nitrate was taken in dry DMF (10 mL) and CCl_3COONa (0.741 g, 4 mmol) was added in portion over 5 min while maintaining the temperature at 23–25 ˚C. TLC was performed, which showed the disappearance of **1a** after 30 min. The reaction mixture was diluted with EtOAc (80 mL) and washed with brine (2×50 mL). Organic layer was separated, dried ($NaSO_4$) and evaporated. The crude residue was purified by column chromatography (*n*-hexane–EtOAc, 9:1 v/v) to afford 3,3,3-trichloro-2-hydroxy-1-phenylpropan-1-one **2a** (0.381 g, 75%) as colorless flakes, mp 38 ˚C (*n*-hexane–EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J = 7.2 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 2H), 5.63 (d, J = 9.9 Hz, 2H), 4.55 (d, J = 9.9 Hz, 1H, D_2O exchangeable), ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 194.9 (C), 135.5 (C), 134.7 (CH), 129.6 (CH), 128.7 (CH), 98.0 (C), 79.5 (CH) ppm; IR (KBr): ν_{max} 3421(s), 3066(m), 1678(s), 1594(m), 1448(m), 1397(s), 1281(m), 1183(s), 1112(m), 965(s), 821(s), 787(s), 749(s), 696(m), 579(m) cm^{-1}; HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_9H_7Cl_3O_2Na$ 274.9404, found 274.9409.

***3,3,3-Trichloro-2-hydroxy-1-p-tolylpropan-1-one* 2b:** Colorless needles, mp 104 ˚C (*n*-hexane–EtOAc), 0.417 g, 78%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.61 (d, *J* = 9.9 Hz, 1H), 4.61 (d, *J* = 9.9 Hz, 1H, D_2O exchangeable), 2.45 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 194.2 (C), 146.1 (C), 132.8 (C), 129.8 (CH), 129.4 (CH), 98.1 (C), 79.2 (CH), 21.8 (CH_3) ppm; IR (KBr): ν_{max} 3440(m, br), 2974(m), 1671(s), 1599(m), 1513(m), 1462(m), 1315(s), 1270(m), 1177(s), 1110(m), 963(s), 821(s), 762(m), 686(m), 574(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{10}H_9Cl_3O_2Na$ 288.9560, found 288.9553.

***3,3,3-Trichloro-2-hydroxy-1-(4-methoxyphenyl)propan-1-one* 2c:** Colorless needles, mp 114 ˚C (*n*-hexane–EtOAc), 0.420 g, 74%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 5.58 (d, *J* = 9.9 Hz, 1H), 4.60 (d, *J* = 9.9 Hz, 1H, D_2O exchangeable), 2.45 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 192.6 (C), 164.9 (C), 132.3 (CH), 128.0 (C), 114.0 (CH), 98.4 (C), 79.0 (CH), 55.7 (CH_3) ppm; IR (KBr): ν_{max} 3310(m, br), 2970(m), 1669(s), 1602(m), 1424(m), 1288(s), 1225(m), 112(s), 1014(m), 818(s), 756(s), 719(s), 685(m), 584(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{10}H_9Cl_3O_3Na$ 304.9509, found 304.9513.

***1-(4-Bromophenyl)-3,3,3-trichloro-2-hydroxypropan-1-one* 2d:** Colorless flakes, mp 88 ˚C (*n*-hexane–EtOAc), 0.425 g, 64%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 5.57 (d, *J* = 9.9 Hz, 1H), 4.50 (d, *J* = 9.9 Hz, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 194.0 (C), 134.2 (C), 132.1 (CH), 130.9 (CH), 130.3 (C), 97.8 (C), 79.5 (CH) ppm; IR (KBr): ν_{max} 3337(m, br), 2984(m), 1679(s), 1583(m), 1420(m), 1287(m), 1229(m), 1119(s), 1070(m), 825(s), 772(m), 732(m), 682(m), 605(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_9H_6BrCl_3O_2Na$ 352.8509, found 352.8508.

***3,3,3-Trichloro-2-hydroxy-1-(3-nitrophenyl)propan-1-one* 2e:** Colorless cubes, mp 116 ˚C (*n*-hexane–EtOAc), 0.358 g, 60%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.53 (d, *J* = 8.1 Hz, 1H), 8.35 (d, *J* = 7.2 Hz, 1H), 7.78 (t, *J* = 8.1 Hz, 1H), 5.65 (d, *J* = 10.2 Hz, 1H), 4.45 (d, *J* = 10.2 Hz, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 193.3 (C), 148.3 (C), 136.8 (C), 134.8 (CH), 130.1 (CH), 128.6 (CH), 124.2 (CH), 97.4 (C), 80.0 (CH) ppm; IR (KBr): ν_{max} 3429(m, br), 1690(s), 1530(m), 1350(s), 1277(m), 1126(s), 1089(m), 812(s), 703(m), 719(s), 588(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_9H_6Cl_3NO_4Na$ 319.9255, found 319.9252.

***3,3,3-Trichloro-2-hydroxy-2-methyl-1-phenylpropan-1-one* 2f:** Colorless flakes, mp 60 ˚C (*n*-hexane–EtOAc), 0.321 g, 60%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.2 Hz, 1H), 4.71 (s, 1H, D_2O exchangeable), 2.10 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 199.1 (C), 136.8 (C), 132.7 (CH), 129.6 (CH), 128.2 (CH), 103.4 (C), 87.6 (C), 22.5 (CH_3) ppm; IR (KBr): ν_{max} 3425(m, br), 3060(m), 1679(s), 1593(m), 1446(m), 1386(s), 1251(m), 1170(s), 1096(m), 974(s), 826(s), 804(s), 778(s), 686(m), 619(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{10}H_9Cl_3O_2Na$ 288.9560, found 288.9552.

***3,3,3-Trichloro-1-(furan-2-yl)-2-hydroxypropan-1-one* 2g:** Colorless cubes, mp 108 ˚C (*n*-hexane–EtOAc), 0.292 g, 60%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.49 (d, *J* = 3.9 Hz, 1H), 6.68 (dd, *J* = 3.9, 1.5 Hz, 1H), 5.43 (d, *J* = 10.5 Hz, 1H), 4.30 (d, *J* = 10.5 Hz, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 182.0 (C), 150.9 (C), 148.5 (CH), 121.4 (CH), 113.4 (CH), 98.1 (C), 79.9 (CH) ppm; IR (KBr): ν_{max} 3397(m, br), 3130(m), 1660(s), 1561(m), 1460(m), 1401(m), 1280(m), 1248(m), 1123(s), 1036(m), 872(m), 818(m), 767(s), 714(m), 586(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_7H_5Cl_3O_3Na$ 264.9196, found 264.9201.

***1,1,1-Trichloro-2-hydroxynonan-3-one* 2h:** Colorless liquid, 0.251 g, 48%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.68 (d, *J* = 7.8 Hz, 1H), 4.51 (d, *J* = 7.8 Hz, 1H, D_2O exchangeable), 2.98 (dt, *J* = 15.0,7.8 Hz, 1H), 2.76 (dt, *J* = 15.0, 7.8 Hz, 1H), 1.69 (pent, *J* = 7.2 Hz, 2H), 1.37-1.26 (m, 6H), 0.89 (t, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 204.2 (C), 97.5 (C), 84.7 (CH), 42.5 (CH_2), 31.5 (CH_2), 28.6 (CH_2), 23.7 (CH_2), 22.4 (CH_2), 14.0 (CH_3) ppm; IR (KBr): ν_{max} 3435(m, br), 2929(s), 2863(m), 1720(s), 1648(m), 1461(m), 1391(s), 1280(m), 1118(m), 1061(m), 820(s), 625(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_9H_{15}Cl_3O_2Na$ 283.0030, found 283.0024.

***Ethyl 3,3,3-trichloro-2-hydroxypropanoate* 2i:** Colorless flakes, mp 64 °C (*n*-hexane–EtOAc), 0.332 g, 75%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.65 (d, *J* = 9.3 Hz, 1H), 4.34-4.43 (m, 2H), 4.13 (d, *J* = 9.3 Hz, 1H, D_2O exchangeable), 1.36 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 167.9 (C), 97.8 (C), 80.9 (CH), 63.4 (CH_2), 13.9 (CH_3) ppm; IR (KBr): ν_{max} 3374(m, br), 2994(m), 2938(m), 1735(s), 1472(m), 1393(s), 1302(s), 1217(s), 1128(m), 1014(s), 939(m), 862(s), 818(s), 720(s), 611(s) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$calcd for $C_5H_7Cl_3O_3Na$ 242.9353, found 242.9353.

***3,3,3-Trichloro-2-hydroxy-1-morpholinopropan-1-one* 2j:** Colorless cubes, mp 136 °C (*n*-hexane–EtOAc), 0.357 g, 68%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.96 (d, *J* = 10.2 Hz, 1H), 4.57 (d, *J* = 10.2 Hz, 1H, D_2O exchangeable), 3.63-3.80 (m, 4H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 165.8 (C), 99.2 (C), 75.7 (CH), 66.5 (CH_2), 66.1 (CH_2), 47.3 (CH_2), 43.6 (CH_2) ppm; IR (KBr): ν_{max} 3226(m, br), 2971(m), 2858(m), 1631(s), 1474(m), 1427(m), 1233(m), 1110(s), 1051(m), 873(s), 781(m), 719(s), 627(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_7H_{10}Cl_3NO_3Na$ 283.9618, found 283.9610.

***3,3,3-Trichloro-2-hydroxy-N,N-diisopropylpropanamide* 2k:** Colorless flakes, mp 74 °C (*n*-hexane–EtOAc), 0.365 g, 66%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.94 (d, *J* = 9.9 Hz, 1H), 4.71 (d, *J* = 9.9 Hz, 1H, D_2O exchangeable), 4.39 (sept, *J* = 6.6 Hz, 1H), 3.57 (sept, *J* = 6.6 Hz, 1H), 1.46 (d, *J* = 6.6 Hz, 3H), 1.41 (d, *J* = 6.6 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H), 1.26 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 165.7 (C), 99.4 (C), 76.4 (CH), 49.6 (CH), 47.1 (CH), 21.5 (CH_3), 20.2 (CH_3), 19.8 (CH_3), 19.7 (CH_3) ppm; IR (KBr): ν_{max} 3365(s), 3001(m), 2971(m), 2936(m), 1644(s), 1475(m), 1417(m), 1351(m), 1296(s), 1109(m), 1040(m), 761(m), 707(s), 633(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_9H_{16}Cl_3NO_2Na$ 298.0139, found 298.0145.

***3,3,3-Trichloro-2-hydroxy-N-methyl-N-phenylpropanamide* 2*l*:** Colorless needles, mp 126 °C (*n*-hexane–EtOAc), 0.367 g, 65%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 8.1, 6.6 Hz, 2H), 7.41 (t, *J* = 6.9 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 2H), 4.78 (s, 1H), 4.23 (s, 1H, D_2O exchangeable), 3.39 (s, 3H), ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 167.5 (C), 142.1 (C), 130.1 (CH), 128.5 (CH), 127.4 (CH), 99.0 (C), 76.2 (CH), 38.5 (CH_3) ppm; IR (KBr): ν_{max} 3304(s), 3057(m), 2928(m), 1666(s), 1592(m), 1494(m), 1384(s), 1290(m), 1101(s), 820(s), 770(m), 702(m), 648(m), 553(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{10}H_{10}Cl_3NO_2Na$ 303.9669, found 303.9674.

***3,3,3-Trichloro-2-hydroxy-2-(3-nitrophenyl)propyl nitrate* 3:** Colorless needles, mp 104 °C (*n*-hexane–EtOAc), 0.108 g, 18%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (t, *J* = 1.8 Hz, 1H), 8.30-8.34 (m, 1H), 8.10 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.63 (t, *J* = 8.1 Hz, 1H), 5.55 (d, *J* = 12.9 Hz, 1H), 5.39 (d, *J* = 12.9 Hz, 1H), 3.72 (s, 1H, D_2O exchangeable) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 147.9 (C), 136.3 (C), 134.5 (CH), 129.0 (CH), 124.5 (CH), 123.9 (CH), 103.2 (C), 83.3 (C), 72.6 (CH_2) ppm; IR (KBr): ν_{max} 3458(s), 3094(m), 2919(m), 1647(s), 1533(s), 1440(m), 1353(s), 1281(m), 1174(s), 1102(m), 1028(s), 834(s), 749(m), 672(s), 635(m), 587(m) cm-1; HRMS (ESI-TOF): *m/z* [M + Na]$^+$ calcd for $C_9H_7Cl_3N_2O_6Na$ 366.9262, found 366.9263.

1,1,1-Trichloro-3-(methyl(phenyl)amino)-3-oxopropan-2-yl 2-(methyl(phenyl)amino)-2-oxoacetate **4:** The reaction of *N*-methyl-*N*-phenylbromoacetamide **1*l*** (0.456 g, 2 mmol) with $AgNO_3$ (0.340 g, 2 mmol) in acetonitrile (10 mL) was stirred at room temperature (20-25 ˚C) for 16 h. Chloroform (50 mL) was then added and the suspension was stirred for additional 10 min. The silver bromide thus precipitated was filtered off and the filtrate was evaporated under reduced pressure to obtain the nitrate in quantitative yield.

The nitrate was dissolved in dry DMF (10 mL) and CCl_3COONa (1.112 g, 6 mmol) was added to the solution portion-wise over a 5 min duration with stirring at 20-25 ˚C. The reaction occurred vigorously with an increase in the temperature of the reaction mixture. The stirring was continued for 90 min. The reaction mixture was then diluted with EtOAc (80 mL) and washed with brine (2×50 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography (silica gel, *n*-hexane−EtOAc, 7:3 v/v) to afford 1,1,1-trichloro-3-{methyl(phenyl)amino}-3-oxopropan-2-yl 2-{methyl(phenyl)amino}-2-oxoacetate **4** (0.240 g, 54%) as colorless cubes, mp 146 ˚C (*n*-hexane−EtOAc). Colorless cubes, mp 146 ˚C (*n*-hexane−EtOAc), 0.240 g, 54%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.43 (m, 8H), 7.04 (s, 2H), 5.71 (s, 1H), 3.36 (s, 3H), 3.26 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 161.3, 159.7, 159.6, 141.3, 140.4, 129.9, 129.8, 128.8, 128.7, 127.8, 127.3, 94.4, 74.0, 38.4, 36.3 ppm; IR (KBr) νmax 3064(m), 2983(m), 2937(m), 1770(s), 1682(s), 1589(m), 1493(m), 1458 (m), 1424(m), 1392(m), 1265(m), 1193(m), 1102(m), 1042(m), 912(m), 823(m), 786(m), 746(m), 664(m), 625(m), 559(m) cm^{-1}. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{19}H_{17}Cl_3N_2O_4Na$ 465.0146, found 465.0145.

Reaction of 3,3,3-Trichloro-2-hydroxy-N-methyl-N-phenylpropanamide 2*l* with 2 equivalents of sodium trichloroacetate:

A solution of the trichloromethylcarbinol **2*l*** (0.565 g, 2 mmol) in dry DMF (10 mL) was added CCl_3COONa (0.741 g, 4 mmol) portion-wise over a 5 min duration with stirring at 20-25 ˚C. The reaction occurred vigorously with an increase in the temperature of the reaction mixture. The stirring was continued for 60 min. The reaction mixture was diluted with EtOAc (80 mL) and washed with brine (2×50 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography (silica gel, *n*-hexane−EtOAc, 7:3 v/v) to afford 1,1,1-trichloro-3-{methyl(phenyl)amino}-3-oxopropan-2-yl 2-{methyl(phenyl)amino}-2-oxoacetate **4** (0.275 g, 62%) as colorless cubes, mp 146 ˚C (*n*-hexane−EtOAc).

3-Chloro-1-phenylpropane-1,2-dione **5:** An atmosphere of nitrogen gas was created by Schlenk technique in a flame dried 50 mL two-neck round-bottomed flask equipped with a condenser, a rubber septum and a magnetic bar. Cuprous chloride (0.198 g, 2 mmol), bipyridine (0.312 g, 2 mmol) and dry degassed DCE (20 mL) were added to the flask. The flask was again evacuated and filled with dry nitrogen. The mixture was stirred for 15 min. While stirring, a solution of the ketocarbinol **2a** (0.253 g, 1 mmol) in dry degassed DCE (5 mL) was slowly injected into the mixture during a period of 5 min. The resulting mixture was then heated at reflux for 1 h. Monitoring the progress of the reaction by TLC indicated the disappearance of **2a** after this time. The reaction mixture was cooled to room temperature and *n*-hexane (25 mL) was added to it. The resulting mixture was stirred for 15 min under the open atmosphere and filtered. The filtrate was evaporated under reduced pressure. The crude product thus obtained was purified by flash column chromatography on a silica gel (60-120 mesh) column using *n*-hexane as the solvent for elution to obtain 3-chloro-1-phenylpropane-1,2-dione **5** (0.119 g, 65%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.5 Hz, 2H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 4.65 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 192.4 (C), 190.0 (C), 135.2 (C), 131.8 (CH), 130.4 (CH), 129.0 (CH), 45.6 (CH_2) ppm; IR (KBr): ν_{max} 3066(m), 2941(m), 1731(s), 1674(s), 1592(m), 1448(m), 1397(m), 1261(m), 1178(m), 1101(m), 951(m), 892(m), 761(m), 691(m), 642(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + K]^+$ calcd for $C_9H_7ClO_2K$ 220.9772, found 220.9754.

***Dimethyl 5-hydroxy-5-phenyl-4-(trichloromethyl)-4,5-dihydrofuran-2,3-dicarboxylate* 6:** A mixture of the ketocarbinol **2a** (0.507 g, 2 mmol), DMAD (0.284 g, 2 mmol) and K_2CO_3 (0.276 g, 2 mmol)in THF (30 mL)was heated at reflux with stirring. The progress of the reaction was monitored by TLC. After completion of the reaction (3 h), the volatiles were evaporated under reduced pressure. The residue thus obtained was taken up in diethyl ether (80 mL) and filtered. The filtrate was washed with brine (3×20mL), dried (Na_2SO_4), filtered and evaporated. The crude product thus obtained was recrystallized from a mixture of *n*-hexane and chloroform to obtain (*Z*)-dimethyl 5-hydroxy-5-phenyl-4-(trichloromethyl)-4,5-dihydrofuran-2,3-dicarboxylate **6** (0.570 g, 72%) as colorless needles, mp 118 ˚C (*n*-hexane–chloroform). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 6.9 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 5.10 (s, 1H), 3.98 (s, 3H), 3.74 (s, 1H, D_2O exchangeable), 3.65 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 162.9 (C), 159.4 (C), 153.8 (C), 143.5 (C), 128.8 (CH), 128.3 (CH), 125.0 (CH), 114.9 (C), 97.4 (CH), 94.1 (C), 84.7 (C), 53.3 (CH_3), 52.2 (CH_3) ppm; IR (KBr): ν_{max} 3466(s), 3067(m), 2955(m), 1730(s), 1671(s), 1444(m), 1360(s), 1324(m), 1283(s), 1215(s), 1182(s), 1126(s), 1032(s), 1016(s), 932(s), 829(s), 788(m), 745(m), 692(m), 665(m), 532(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{13}Cl_3O_6Na$ 416.9670, found 416.9681.

***1,1,1-Trichloro-3-oxo-3-phenylpropan-2-yl acetate* 7:** In a 50 mL two-neck round-bottomed flask equipped with a calcium chloride guard tube, a rubber septum and a magnetic bar were taken the ketocarbinol **2a** (0.507 g, 2 mmol), pyridine (0.17mL, 2 mmol) and dry DCM (25 mL). The solution was cooled to 0 ˚C and stirred for 15 min. A solution of AcCl (0.15mL, 2 mmol) in DCM (5 mL) was then slowly injected into the stirred solution over 5 min. The stirring was continued at 0-5 ˚C and the progress of the reaction was monitored by TLC, which indicated that the reaction was complete in 1 h. The solution was diluted with DCM (50 mL) and washed with brine (2×50 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated. The crude product thus obtained was purified by column chromatography on silica gel column using *n*-hexane–EtOAc (9:1 v/v), as the solvent for elution to obtain 1,1,1-trichloro-3-oxo-3-phenylpropan-2-yl acetate **7** (0.497 g, 84%) as a colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 6.61 (s, 1H), 2.25 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 190.1 (C), 169.3 (C), 136.4 (C), 134.1 (CH), 129.0 (CH), 128.8 (CH), 94.1 (C), 77.9 (CH), 20.3 (CH_3) ppm; IR (KBr): ν_{max} 3065(m), 1758(s), 1700(s), 1596(m), 1448(s), 1373(m), 1281(m), 1223(s), 1082(s), 1006(m), 956(m), 798(s), 754(s), 685(s), 582(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{11}H_9Cl_3O_3Na$ 316.9509, found 316.9516.

***Dechlorinative Suzur-Tanner Rearrangement: Synthesis of (Z)-1-Chloro-3-oxo-3-phenylprop-1-enyl acetate* 8 and *3,3-dichloro-1-phenylprop-2-en-1-one* 9:** A flame dried 50 mL two-neck round-bottomed flask having a magnetic bar equipped with a condenser and septum under nitrogen atmosphere purged with CuCl (0.198 g, 2 mmol) and bipyridine (0.312 g, 2 mmol) and dry DCM (20 mL) were taken and stirred for 15 min to ensure the complex formation. Then **7** (0.295 g, 1 mmol) in dry DCM (5 mL) was injected to this solution and stirred for 1.5 h. The reaction was completed as observed by TLC. *n*-Hexane (20 mL) was added and stirred for 15 min. Resulting solution was filtered and reduced *in vacuo*. The crude was eluted with *n*-hexane by column chromatography to obtain 1-chloro-3-oxo-3-phenylprop-1-enyl acetate **8** (0.122 g, 54%) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.2 Hz, 2H), 6.83(s, 1H), 2.32 (s, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.3, 167.6, 147.2, 136.0, 133.1, 129.3, 128.6, 124.7, 20.2 ppm; IR (KBr) ν_{max} 3093(s), 1771(s), 1670(m), 1607(m), 1444(s), 1372(m), 1320(m), 1253(m), 1194(s), 1140(m), 1015(m), 971(s), 847(s), 708(s), 657(m) cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_9ClO_3Na$ 247.0132, found 247.0129. Further elution gave 3,3-dichloro-1-phenylprop-2-en-1-one[40] **9** (0.024 g, 12%) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.2 Hz, 2H), 7.27 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 186.7, 136.9, 135.5, 133.7, 128.8, 128.5, 124.0 ppm; IR (KBr) ν_{max} 3059(m), 1671(s), 1568(s), 1449(m), 1265(m), 1221 (s), 1015(m), 938(m), 841(m), 788(m), 695(m), 628(m) cm^{-1}.

2-Ethoxy-3-(methyl(phenyl)amino)-3-oxopropanoic acid* 10:** A mixture of the trichloromethyl-hydroxyamide **2*l (0.282 g, 1 mmol) and KOH (0.280 g, 5 mmol) in ethanol (30 mL) was heated at reflux. The progress of the reaction was monitored by TLC, which indicated the completion of the reaction after 2 h. The reaction mixture was cooled to room temperature and the ethanol was removed under reduced pressure. The residual mass was taken up in EtOAc (50 mL) and washed successively with 2N HCl (50 mL) and brine (2×20 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated. The crude product thus obtained was purified by column chromatography on silica gel (60-120 mesh) column using *n*-hexane–EtOAc (1:1 v/v) as the solvent for elution to obtain 2-ethoxy-3-{methyl(phenyl)amino}-3-oxopropanoic acid **10** (0.147 g, 62%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (s, 1H, D_2O exchangeable), 7.41-7.21 (m, 5H), 4.36 (s, 1H), 3.33-3.44 (m, 1H), 3.25 (s, 3H), 3.10-3.21 (m, 1H), 1.03 (t, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 169.7 (C), 166.7 (C), 142.2 (C), 129.7 (CH), 128.5 (CH), 127.4 (CH), 75.8 (CH), 66.3 (CH_2), 38.0 (CH_3), 14.7 (CH_3) ppm; IR (KBr): ν_{max} 3469(m, br), 2979(m), 2932(m), 2590(m), 1750(s), 1656(s), 1594(m), 1493(m), 1394 (m), 1292(m), 1216(m), 1120(m), 1033(m), 897(m), 773(m), 700(m), 669(m) cm^{-1}; HRMS (ESI-TOF): *m/z* $[M + Na]^+$ calcd for $C_{12}H_{15}NO_4Na$ 260.0893, found 260.0893.

ASSOCIATED CONTENT

Supporting Information: Copies of ^{1}H NMR and ^{13}C NMR spectra of **2a-*l*, 3-10**; ORTEP diagrams and CIFs of **4** and **6**. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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