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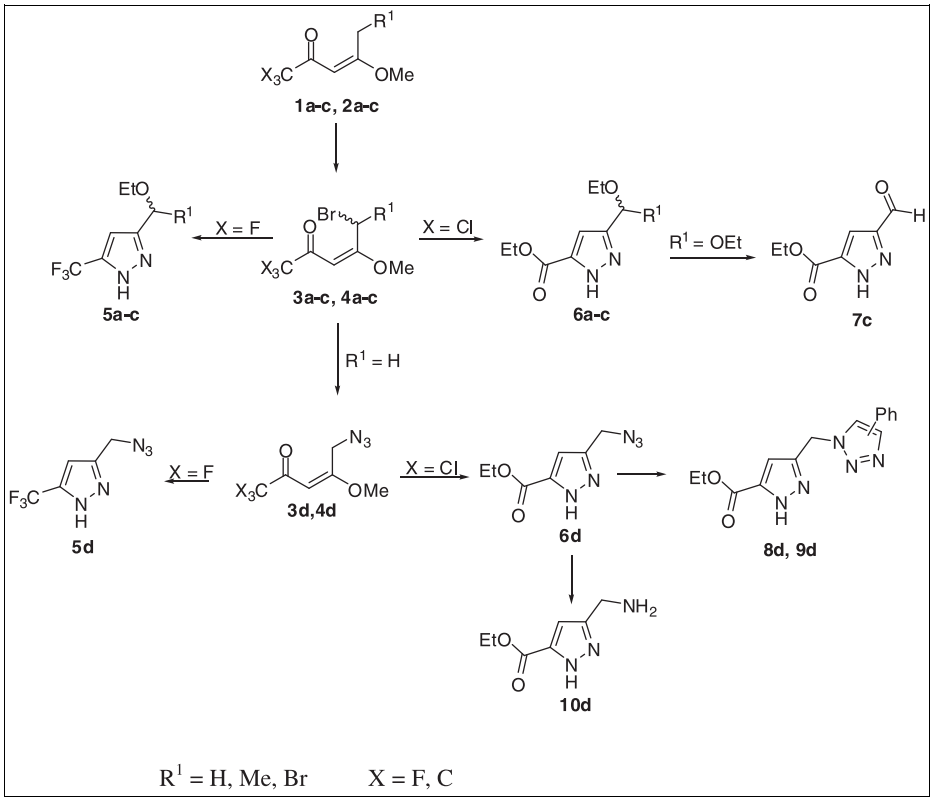

5-Bromo[5,5-dibromo]-1,1,1-trihalo-4-methoxy-3-penten[hexen]-2-ones are explored as precursors to the synthesis of 3-ethoxymethyl-5-trifluoromethyl-1*H*-pyrazoles from a cyclocondensation reaction with hydrazine monohydrate in ethanol. 3-Ethoxymethyl-carboxyethyl ester pyrazoles were formed as a result of a substitution reaction of bromine and chlorine by ethanol. The dibrominated precursor furnished 3-acetal-pyrazole that was easily hydrolyzed to formyl group. In addition, brominated precursors were used in a nucleophilic substitution reaction with sodium azide to synthesize the 3-azidomethyl-5-ethoxycarbonyl-1*H*-pyrazole from the reaction with hydrazine monohydrate. These products were submitted to a cycloaddition reaction with phenyl acetylene furnishing the 3-[4(5)-phenyl-1,2,3-triazolyl]5- ethoxycarbonyl-1*H*-pyrazoles and to reduction conditions resulting in 3-aminomethyl-1*H*-pyrazole-5-carboxyethyl ester. The products were obtained by a simple methodology and in moderate to good yields.

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INTRODUCTION

The introduction of halogens and halogenated groups into organic molecules often confers significant and useful changes in their chemical and physical properties. Therefore, methods for the synthesis of halogenated compounds have received considerable interest [1]. The most convenient method to construct halogenated compounds is to use halogen-containing building blocks as starting material [2]. During the last 20 years, we have developed a general synthesis of 4-alkoxy-1,1,1-trihalo-3-alken-2-ones [3,4], an important halogen-containing building block, and

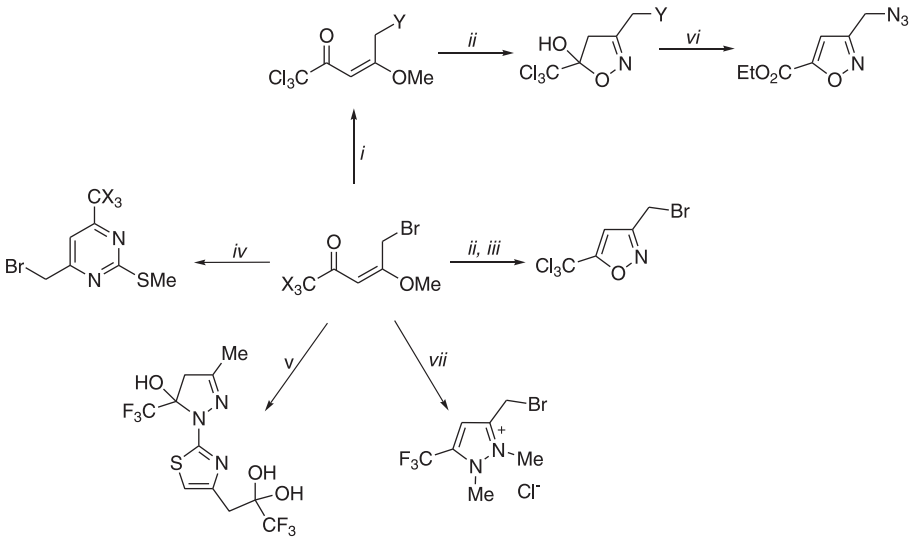
demonstrated its usefulness in heterocyclic preparations, for example, isoxazoles [3,5,6], pyrazoles[7], pyrazolium chlorides [8], pyrrolidinones [9], pyrimidines [10], pyridines [11], thiazines [12], and diazepines[13].

Despite extensive studies on applications of 4-alkoxy-1,1,1-trihalo-3-alken-2-ones in heterocyclic chemistry [4,6–15], 5-heteroalkyl substituted 4-alkoxy-1,1,1-trihalo-3-alken-2-ones and their usefulness in the synthesis of heterocycles have been less explored. These compounds are highly functionalized intermediates, which may be useful for further synthetic conversions. In a previous work [6], we reported the synthesis of 5-bromo-1,1,1-trichloro-4-methoxy-3-penten[hexen]-2-ones, in high purity, from the reaction of 1,1,1-trichloro-4-methoxy-3-penten[hexen]-2-ones with bromine in the presence of pyridine. The use of these important 1,3,4-trielectrophiles in the synthesis of other 1,1,1-trichloro-5-heteroalkyl-4-methoxy-3-penten[hexen]-2-ones by nucleophilic substitution of bromine and their application in the synthesis of isoxazole heterocyclic systems was also reported [6] (Scheme 1). In another work, we reported a general and efficient synthetic approach for the preparation of a series of 5-bromo[5,5-dibromo]-1,1,1-trihalo-4-methoxy-3-alken-2-ones in high purity and good yields and the use of 5-bromo-1,1,1-trichloro-4-methoxy-3-penten[hexen]-2-ones in the synthesis of several heterocycles, such as pyrazolium [8], 4,5-dihydropyrazoles [6], isoxazoles[6], and tiopyrimidines [6] (Scheme 1). Herein, we report the use of mono- and dibrominated 5-bromo [5,5-dibromo]-1,1,1-trihalo-4-methoxy-3-alken-2-ones as building blocks in the synthesis of 3(5)-ethoxymethyl-5 (3)trihalomethyl-1*H*-pyrazoles from cyclocondensation reactions of these brominated precursors with hydrazine monohydrate and with subsequent easy acetalhydrolyzation leading to the formyl group. We also demonstrate the synthesis of 3-triazolemethyl-5-halomethyl[ethoxycarbonyl]-1*H*-pyrazoles by a set of reactions of the brominated precursors with sodium azide, followed by a cyclocondensation reaction with hydrazine monohydrate and then a cycloaddition reaction with phenyl acetylene. Finally, we show a reduction reaction where the azide group present in the compound 3-azidomethyl-1*H*-pyrazole-5-ethoxycarbonyl ester is reduced to amine.

RESULTS AND DISCUSSION

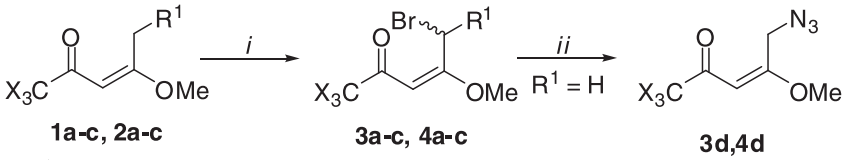
Firstly, the 4-alkoxy-1,1,1-trihalo-3-alken-2-ones, **1a–c**, **2a–c**, were obtained from the acylation reaction of enol ether or acetal with trifluoroacetic anhydride or trichloroacetic acid in accordance with the methodology developed in our laboratory [3]. Subsequently, the 5-bromo[5,5-dibromo]-1,1,1-trihalo-4-methoxy-3-penten[hexen]-2-ones, **3a–c**, **4a–c**, were synthesized from the reaction of 4-alkoxy-1,1,1-trihalo-3-alken-2-ones, **1a–c**, **2a–c**, with bromine in the presence of pyridine [6b]. The 5-bromo-1,1,1-trihalo-3-hexen-2-ones, **3a**, **4a**, were also submitted to the allylnucleophilic substitution of bromine by sodium azide

Scheme 1



X = Cl, F
i: (R^1 = H, Y = N_3, OPh, SCH_2CO_2Et, SPh, SCN, I), acetone or benzene, K_2CO_3 or Et_3N, 25 °C, 2–16 h
ii: (R^1 = H), NH_2OH•HCl (1.2 eq.), pyridine (1.2 eq.), MeOH, reflux, 16 h
iii: Conc. H2SO4, 30°C, 8 h
iv: (R^1 = H, Me), $NH_2C(SMe)$=NH, HCl, MeOH, reflux, 48 h
v: (R^1 = H), chloroform, 35°C, 24 h
vi: Y = N_3, conc. H2SO4, EtOH, reflux, 4 h
vii: (R^1 = H), MeNHNMe•2HCl, EtOH/HCl, reflux, 4–12 h

Scheme 2



R^1 = H, Me, Br; X = F, Cl
i: Br_2, CH_2Cl_2, 25°C, 1 h; pyridine, 0°C, 1 h
ii: NaN_3, acetone, 25°C, 2–96 h

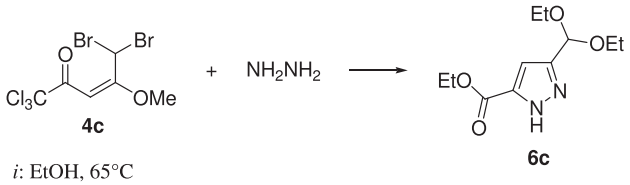
to synthesize 5-azido-1,1,1-trihalo-3-hexen-2-ones, **3d**, **4d**, using the reaction conditions previously determined by Martins *et al*. [6]. Scheme 2 shows the synthetic route to obtain the building block used in this work, which furnished the heterocyclic compounds.

We started our study from the cyclocondensation reaction of 5-bromo[5,5-dibromo]-1,1,1-trichloro-4-methoxy-3-penten-2-ones, **4c** (1 mmol), with hydrazine monohydrate (1.1 mmol), by evaluating the best reaction conditions for the formation of compound **6c**. The first test was performed in ethanol as solvent at 65°C for 4 h, on the basis of a work previously published by us [14]. However, the product was not identified using these reaction conditions. Therefore, the optimization of the reaction was carried out, varying the time and reaction conditions to obtain the desired product in high yields and purity. The optimization of this reaction is described in Scheme 3.

The best reaction condition to furnish product **6c** entailed the reaction time of 24 h under neat conditions, that is, without the presence of pyridine or HCl. Later, we focused our attention on the optimization of the reaction conditions of 3-[1(1-di)ethoxy]-5-trihalomethylpyrazoles, **5a–c**, **6a–c**. This reaction was performed between 5-bromo[5,5-dibromo]-1,1,1-trihalo-4-methoxy-3-penten[hexen]-2-ones, **3a–c**, **4a–c**, and hydrazine monohydrate, using EtOH as solvent at 65°C for 24 h. According to Scheme 4, the products **5a–c**, **6a–c**, were obtained in good yields 65–85%.

In the reaction of monobrominated enones, **3a–b**, **4a–b**, with hydrazine monohydrate, substitution of the bromine by ethanol took place, and products 3-[1-ethoxy]-5-trihalomethyl-1*H*-pyrazoles **5a–b**,**6a–b** were formed. Likewise, the reaction of dibrominated enones **3c**, **4c** with hydrazine monohydrate led to the disubstitution of both bromines by ethanol, resulting to acetal 3-[1-(diethoxy]-5-trifluoromethyl-1*H*-pyrazoles, **5c**, **6c**. The substitution of bromine by ethanol probably occurred by an S_N2 mechanism, where the solvent acted as nucleophile. Elucidation of the structure was carried out by assignments of ^1H and ^{13}C NMR and GC–MS analysis.

Scheme 3

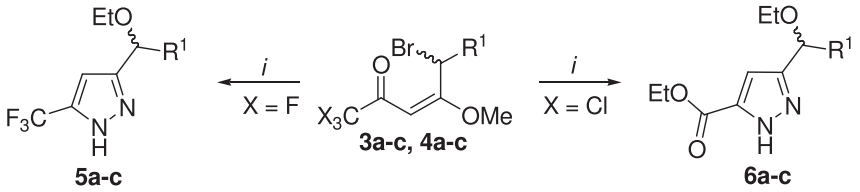


i: EtOH, 65°C

Reaction Conditions	Time (h)	Yield (%)[c]
pyridine	4	-[a]
pyridine	24	60[b]
HCl	24	75
-	24	80

[a]Product was not identified
[b]It was obtained as a mixture of product and reactant.
[c]Yield of isolated product.

Scheme 4



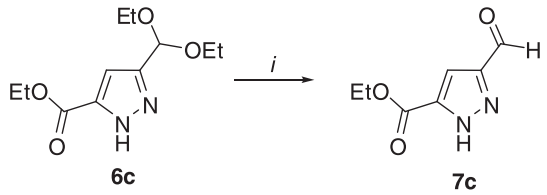
i: NH_2NH_2, EtOH, 65°C, 24 h (65-85%)

Reactant	R^1	Product	R^1	Yields (%)[a]
3a	H	**5a**	H	77
3b	Me	**5b**	Me	75
3c	Br	**5c**	OEt	65
4a	H	**6a**	H	85
4b	Me	**6b**	Me	83

[a]Yields of isolated mixture.

Although mild conditions were used, we believed that the conversion of group CCl_3 into CO_2Et can occur through a mechanism similar to those of neighboring assistance reported for the reaction of α-haloketones with alkoxide groups [16]. Through this mechanism, during ring closure, the carbonyl oxygen of the β-alkoxyvinyltrichloromethyl begins the chlorine substitutions with attack on the carbon atom of the trichloromethyl group.

Scheme 5



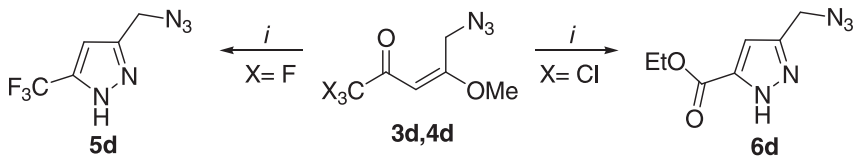
i: HCl (15%), 65°C, 6 h

It is interesting to mention that the acetal product **6c** can be hydrolyzed and easily forms the formyl group in the presence of the HCl (15%) under heating at 65°C for 6 h as shown in Scheme 5.

In a continuation, herein, we present, for the first time, the application of 5-azido-1,1,1-trihalo-3-hexen-2-ones, **3d**, **4d**, as precursors in the synthesis of pyrazoles **5d**, **6d** by the cyclocondensation reaction with hydrazine monohydrate in EtOH at 65°C for 24 h as shown in Scheme 6. The reaction conditions were the same as those used in the synthesis of pyrazoles **5a–c**, **6a–c**. The products **5d** and **6d** were obtained in good yields (X = F, 68%; X = Cl, 73%).

Our research group has demonstrated the use of 5-azido-1,1,1-trichloro-3-hexen-2-ones as precursors to 4, 5-dihydroisoxazoles and their stability in dehydration reaction in acid media [6]. Therefore, it seemed that the azide function as a pyrazole substituent could be explored as a precursor to triazole synthesis. 1,2,3-Triazoles are

Scheme 6



i: NH_2NH_2, EtOH, 65°C, 24 h (68–73%)

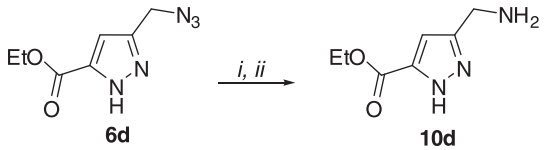
nitrogen heteroarenes that have a range of important applications in the pharmaceutical and agricultural industries [17]. The most widely used method for the synthesis of 1,2,3-triazoles, pioneered by Huisgen, involves the thermal 1,3-dipolar cycloaddition of organic azides with alkynes [18]. In connection with our ongoing investigation into the synthesis of trihalomethyl compounds, we were interested in exploring this cycloaddition reaction, where some of the key building blocks contained halomethyl groups. To the best of our knowledge, there is only one example of a 1,3-dipolar cycloaddition of heterocyclic methylene azides with alkynes [19].

Initially, we performed the reaction between compound **6d** and phenyl acetylene according to the literature [20] to obtain the 1,4-substituted 1,2,3-triazoles **8d** and 1,5-substituted **9d**. Then, we tested other reaction conditions to optimize the reaction as shown in Scheme 7. The best condition was obtained using toluene at 110°C for 24 h. The mixture of isomers was obtained in excellent yield (85%). The proportion of isomers was determinate by ^{1}H and ^{13}C NMR. Assignment of **8d** and **9d** isomers was possible by comparison of chemical shift of methylene group with the similar compounds in literature [19].

Another interesting point to mention here is the usefulness of compound **6d** as a precursor because the azide group can be reduced to amine. We started our study evaluating the best reaction conditions for products **10d**. We first used $LiAlH_4$ as a reducing agent; however, the product was not identified. In a second attempt, we used the method developed by Friguelli *et al*. [21], which uses $NaBH_4/CoCl_2.6H_2O$, and once again, we were unsuccessful. Finally, we used the technique developed by Zwierzaki [22], via the Staudinger reaction, which makes use of triethylphosphite and gaseous hydrochloric acid as reducing agents, and this method reduced the azide group to amine. The first step of the reaction was carried out using benzene as a solvent and the mixture of compound **6d** with triethylphosphite, in a molar ratio of 1:2, respectively, at room temperature for 12 h. In the second step, gaseous HCl was added, and the mixture was left under stirring for 12 h at room temperature. The product **10d** was obtained in moderate yield, 50% (Scheme 8).

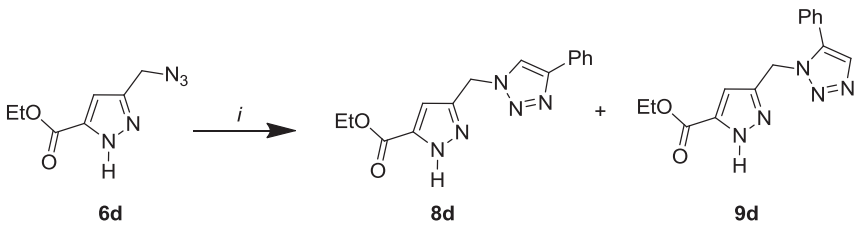
In summary, we have demonstrated the versatility of brominated trihalomethylated building blocks in the

Scheme 8



i: $P(OEt)_3$, benzeno, r.t., 12 h
ii: HCl(g), r.t., 12 h (50%)

Scheme 7



i: Toluene added after phenyl acetylene

Temperature (°C)	Time (h)	8d:9d ratio	Yield (%)[b]
80	9	-	-[a]
110	12	2:1	50
110	16	2:1	65
110	24	2:1	85

[a]Product was not identified.
[b]Yield of isolated product.

generation of both new precursors and heterocyclic compounds. In a set of reactions, we showed their synthetic potential, where it was demonstrated that 5-bromo-1,1,1-trihalo-4-methoxy-3-penten-2-one underwent a sequence of reactions including nucleophilic substitution, cyclocondensation, cycloaddition, and reducing reactions.

EXPERIMENTAL

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer (^{13}C at 100.61 MHz) and ^{1}H spectra were recorded on a Bruker DPX 200 spectrometer (^{1}H at 200.13 MHz) at 300 K, in $CDCl_3$ as solvent, containing TMS as internal standard. All spectra were acquired in a 5-mm tube at natural abundance. Mass spectra were registered in an HP 5973 MSD connected to an HP 6890 GC and interfaced by a Pentium PC. The GC was equipped with a split-splitless, injector, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas.

Typical procedure for the synthesis of compounds 5a–c, **6a–c**. The hydrazine monohydrate (1.1 mmol) was readily added to the 5-bromo-1,1,1-trihalo-4-methoxy-3-penten-2-ona (1 mmol) and dissolved in ethanol (3 mL). The reaction mixture was heated at 65°C for 24 h. Then, the solvent was evaporated at reduced pressure, and the residue was dissolved in dichloromethane (5 mL), washed with H_2O (2 × 5 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

Typical procedure for the synthesis of compound 7c. The aqueous HCl solution (15%) (3 mL) was added to the compounds **6c**, and the reaction mixture was heated at 65°C for 6 h. Then, the solvent was evaporated at reduced pressure, and the residue was dissolved in dichloromethane (5 mL), washed with H_2O (2 × 5 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

Typical procedure for the synthesis of compounds 5d, **6d**. The hydrazine (1.1 mmol) was readily added to the 5-azido-1,1,1-trihalo-4-methoxy-3-penten-2-one (1 mmol) and dissolved in ethanol (3 mL). The reaction mixture was heated at 65°C for 24 h. Then, the solvent was evaporated at reduced pressure, and the residue was dissolved in dichloromethane (5 mL), washed with H_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

Typical procedure for the synthesis of compounds 8d, **9d**. Phenylacetylene (1 mmol) was readily added to 3-azidomethyl-5-trichloromethyl-1*H*-pyrazoles (1 mmol) and dissolved in toluene (3 mL). The reaction mixture was heated at 110°C for 24 h. Then, the solvent was evaporated at reduced pressure and the residue was dissolved in dichloromethane (5 mL), washed with H_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

Typical procedure for the synthesis of compound 10d. 3-Azidomethyl-5-trichloromethyl-1*H*-pyrazoles (1 mmol) were readily added to triethylphosphite (2 mmol) and dissolved in benzene (2 mL). The reaction mixture was heated at room temperature for 12 h. Then, HCl gaseous was added, and the mixture was left under stirring for 12 h at room temperature. Subsequently, the solvent was evaporated at reduced pressure, and the residue was dissolved in dichloromethane (5 mL), washed with H_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

3-(1-Ethoxyethyl)-5-trifluoromethyl-1H-pyrazole (5a). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.39 (s, 1H, H4), 4.52 (s, 2H, H6), 3.51 (q, 2H, H7), 1.16 (t, 3H, H8). ^{13}C NMR (400 MHz, $CDCl_3$) δ 142.3 (C3), 102.7 (C4), 142.5 (q, $^{2}J = 34$ Hz, C5), 66.5 (C6), 62.9 (C7), 14.6 (C8), 121.1(q, $^{1}J = 287$ Hz, CF_3). GC–MS (*m/z*, %) 194 (M^+, 4), 149 (100), 101 (23).

3-(1-Ethoxyethyl)-5-trifluoromethyl-1H-pyrazole (5b). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.06 (s, 1H, NH), 6.45 (s, 1H, H4), 4.70 (q, 1H, H6), 3.50 (q, 2H, H7), 1.20 (t, 3H, H8), 1.52 (d, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) δ 143.7 (C3), 101.3 (C4), 139.1 (q, $^{2}J = 34$ Hz, C5), 68.5 (C6), 65.3 (C7), 15.0 (C8), 120.5 (q, $^{1}J = 287$ Hz, CF_3), 20.6 (C10), 20.6 (CH_3). GC–MS (*m/z*, %) 208 (M^+, 2), 193 (67), 179 (3), 165 (100).

3-Diethoxymethyl-5-trifluoromethyl-1H-pyrazole (5c). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.60 (s, 1H, H4), 6.82 (s, 1H, H6), 3.86 (2q, 4H, H7, OCH_2), 1.22 (2t, 6H, H8, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) δ 137.7 (C3), 104.5 (C4), 143.7 (q, $^{2}J = 34$ Hz, C5), 80.3 (C6), 64.5 (C7, OCH_2), 14.6 (C8, CH_3), 120.6(q, $^{1}J = 287$ Hz, CF_3). GC–MS (*m/z*, %) 238 (M^+, 100).

3-Azidomethyl-5-trifluoromethyl-1H-pyrazole (5d). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.62 (s, 1H, H4), 4.45 (s, 2H, H6). ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.4 (C3), 103.4 (C4), 142.8 (q, $^{2}J = 38$ Hz, C5), 44.8 (C6), 120.9 (q, $^{1}J = 280$ Hz, CF_3). GC–MS (*m/z*, %) 191 (M^+, 50), 172 (25), 149 (100), 101 (80), 67 (100).

3-Ethoxymethyl-1H-pyrazole-5-carboxyethyl ester (6a). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 11.01 (s, 1H, NH), 6.79 (s, 1H, H4), 4.52 (s, 2H, H6), 3.45 (q, 2H, H7), 1.12 (t, 3H, H8), 4.28 (q, 2H, H10), 1.26 (q, 2H, H10); ^{13}C NMR (400 MHz, $CDCl_3$) δ 145.4 (C3), 107.3 (C4), 140.1 (C5), 65.8 (C6), 60.7 (C7), 14.8 (C8), 161.2 (C9), 61.1 (C10), 14.8 (C11); GC–MS (*m/z*, %) 198 (M^+, 2), 154 (70), 108 (100), 79 (40).

3-(1-Ethoxylethyl-1H-pyrazole-5-carboxyethyl ester (6b). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.51 (s, 1H, NH), 6.77 (s, 1H, H4), 4.65 (q, 1H, H6), 3.43 (q, 2H, H7), 1.19 (t, 3H, H8), 4.39 (q, 2H, H10), 1.27 (t, 3H, H10), 1.44 (d, 3H, CH_3); ^{13}C NMR (400 MHz, $CDCl_3$) δ 150.9 (C3), 105.6 (C4), 139.9 (C5), 70.4 (C6), 60.8 (C7), 14.1 (C8), 161.2 (C9), 64.1 (C10), 15.1 (C11), 21.6 (CH_3); GC–MS (*m/z*, %) 212 (M^+, 1), 197 (40), 168 (85), 123 (100), 65 (20).

3-Diethoxymethyl-1H-pyrazole-5-carboxyethyl ester (6c). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.88 (s, 1H, H4), 7.10 (s, 1H, H6), 4.40 (q, 2H, H7), 1.40 (t, 3H, H8), 4.18 (q, 2H, H10), 1.53 (t, 3H, H11); ^{13}C NMR (400 MHz, $CDCl_3$) δ 152.3 (C3), 107.1 (C4) (C4), 136.1 (C5), 66.7 (C6), 61.7 (C7), 13.5 (C8), 159.2 (C9), 64.1 (C10), 14.1 (C11); GC–MS (*m/z*, %) 199 ($M^{[-OEt]}$ 2), 169 (100), 153 (4), 137 (50), 123 (5).

3-Azidomethyl-1H-pyrazole-5-carboxyethyl ester (6d). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.82 (s, 1H, H4), 4.42 (s, 2H, H6), 4.28 (q, 2H, H8), 1.28 (t, 3H, H9); ^{13}C NMR (400 MHz, $CDCl_3$) δ 145.2 (C3), 107.7 (C4), 137.8 (C5), 46.2 (C6), 159.8 (C7), 60.7 (C8), 13.5 (C9); GC–MS (*m/z*, %) 195 (M^+, 8), 167 (6), 153 (100), 120 (22), 107(30).

3-Formyl-1H-pyrazole-5-carboxyethyl ester (7c). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.23 (s, 1H, H4), 9.99 (s, 2H, H6), 3.57 (q, 2H, H7), 1.12 (t, 3H, H8). ^{13}C NMR (400 MHz, $CDCl_3$) δ 152.5 (C3), 107.3 (C4), 137.0 (C5), 185.5 (C6), 159.9 (C9), 61.4 (C10), 14.4 (C11). GC– MS (*m/z*, %) 169 (M^+, 1), 154 (100), 121 (80), 67 (100).

1-[1H-Pyrazol-3-yl-5-carboxyethyl ester]-methyl-4-phenyl-1,2,3-triazole (8d). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.85(s, 1H, H4), 4.45 (s, 2H, H6), 5.64 (s, 1H, H10), 5.71 (s, 1H, H11), 4.37 (q, 2H, H13), 1.38 (q, 3H, H14), 7.33–7.88 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 145.2 (C3), 107.9 (C4), 138.2 (C5), 46.0 (C6), 130.1 (C10), 126.2 (C11), 160.3 (C12), 61.4 (C13), 14.0 (C14), 128–130 (Ph). GC–MS (*m/z*, %) 297 M^+ (22), 269 (15), 252 (9), 223 (23), 196(42), 153(100), 107 (25).

1-[1H-Pyrazole-3-yl-5-carboxyethyl ester]-methyl-5-phenyl-1,2,3-triazole (9d). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.7 (s, 1H, H4), 4.67 (s, 2H, H6), 5.64 (s, 1H, H10), 5.71 (s, 1H, H11), 4.37 (q, 2H, H13), 1.38 (q, 3H, H14), 7.33–7.88 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.0 (C3), 108.2(C4), 137.6(C5), 45.0 (C6), 132.8 (C10), 120.1 (C11), 160.0 (C12), 61.4 (C13), 14.0 (C14), 128–130 (Ph). GC–MS (*m/z*, %) 297 M^+ (13), 269 (16), 252 (25), 223 (100), 196 (22), 153 (40), 107 (70).

3-Aminomethyl-1H-pyrazole-5-carboxyethyl ester (10d). Oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ12.49 (s, NH_2), 6.87 (s, 1H, H4), 4.51 (s, 2H, H6), 4.39 (q, 2H, OCH_2), 1.43 (t, 3H, CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) δ 142.4 (C3), 108.5 (C4), 138.8 (C5), 36.0 (C6), 163.6 (C7), 61.4 (OCH_2), 12.4 (CH_3). GC–MS (*m/z*, %) 169 (M^+, 100), 170 (6%).

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