

Synthesis of Trifluoromethyl-Substituted Pyrazoles and 1,2,4-Triazines by Ring Transformation of Mesoionic 4-Trifluoroacetyl-1,3-oxazolium-5-olates with Phenylhydrazine

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Received August 29, 2007; accepted December 7, 2007; published online January 15, 2008

Mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates **1** were easily prepared by the cyclodehydration reaction of *N*-acyl-*N*-alkyl- α -amino acids with trifluoroacetic anhydride. Due to the presence of the trifluoromethyl ketone and the mesoionic five-membered oxazole, there are three reaction sites to be attacked by the nucleophiles at C-2, C-5 and the trifluoroacetyl group in **1**. Based on this model, three modes of regioselective attack by phenylhydrazine were found to provide three different products, *i.e.*, 6-trifluoromethyl-1,2,4-triazines **3**, 3-trifluoromethyl-5-pyrazolones **5** and 5-trifluoromethyl-3-hydroxypyrazoles **4**, in good yields, respectively, depending on the nature of the solvent and reaction temperature. These three types of different reactions may be explained by the polarity of the reaction solvent and the mesoionic oxazole-ketene tautomerism.

Key words 1,3-oxazolium-5-olate; trifluoromethyl; ring transformation; pyrazole; 1,2,4-triazine

Trifluoromethyl-substituted heterocyclic compounds have received much attention due to their potential biological activities and will continue to play a significant role in medicine and agricultural chemistry as well as in material science.^{1–4)} However, the facile introduction of the trifluoromethyl group into heterocyclic rings is limited, and the development of new practical methods remains a formidable task. Recently, such molecules have found outstanding applications in the pharmaceutical field, as illustrated by Celecoxib (antiarthritic) bearing a trifluoromethyl substituent on the pyrazole-ring, a recent drug used in the treatment of human diseases.⁵⁾ Therefore, much attention has been paid to the synthesis of trifluoromethyl-substituted pyrazoles due to their biological activities in the medicinal and agrochemical fields.^{6–13)} In contrast to the trifluoromethylated pyrazoles, the 1,2,4-triazines, which possess trifluoromethyl groups, seem to be less known in the literature, although some trifluoromethylated 1,2,4-triazines have been developed as agrochemicals.^{14,15)}

In previous papers, we reported that mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates **1** are useful synthons for the synthesis of trifluoromethyl substituted imidazoles by the reaction with amidines¹⁶⁾ or ammonia.¹⁷⁾ These reactions occur *via* the initial attack of the nucleophiles on the C-2 position of the ring. In line with this continuing interest,¹⁸⁾ we have undertaken an investigation of the reaction of **1** with the bis-nucleophile such as phenylhydrazine (PH). Regioselective attacks by PH on mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates **1** are found to be a function of the solvent and the reaction temperature. In principle, nucleophilic reagents can be expected to add to one of the three electrophilic centers at C-2, C-5 and COCF₃ in **1** (Chart 1). On this occasion, all three modes of attack leading to the addition products of type **2**, **3** or **4** were found (Chart 1). We now present a full account of the reactions of **1** with PH¹⁹⁾ and the efficient synthesis of new trifluoromethylated heterocycles in the 1,2,4-triazine, 3-pyrazolone and 5-pyrazolone.

Results and Discussion

The mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates **1** were generally obtained as colored (yellow) solids by the reaction of the *N*-acyl-*N*-alkyl- α -amino acids **2** with trifluoroacetic anhydride (Chart 2). Compounds **1** are the subject of a reaction with PH under a variety of reaction conditions.

Reaction of **1 with PH in *N,N*-dimethylformamide (DMF)** We examined the reaction of 4-trifluoroacetyl-1,3-oxazolium-5-olates **1a–f** with PH in DMF. The reaction was completed within 24 h at room temperature to afford the 6-trifluoromethyl-1,2,4-triazines **3** in good yields (Table 1).

In general, the terminal nitrogen (N-2) is more nucleophilic than the substituted nitrogen (N-1) in neutral media.²⁰⁾ Thus, PH would attack at the C-2 position of **1** to produce an adduct **8** followed by the decarboxylation. Subsequently, the intramolecular cyclization of **9** leads to the product **3**, as shown in Chart 3 (route A). The reaction appears to proceed *via* a mechanism similar to that described for the reaction of **1** and ammonia.¹⁷⁾ It is possible that in the highly polar DMF solvent, the mesoionic form of **1** is stabilized. This led to the attack mode by PH at C-2, which produced the product **3**. These data are consistent with the previous molecular orbital (MO) study that *N*-nucleophiles attack at C-2 in the mesoionic oxazole **1** on the basis of the Hard and

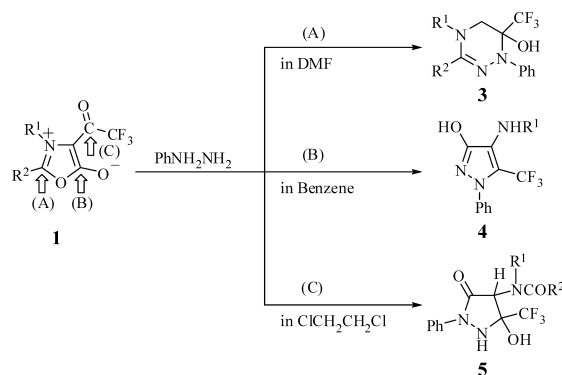


Chart 1

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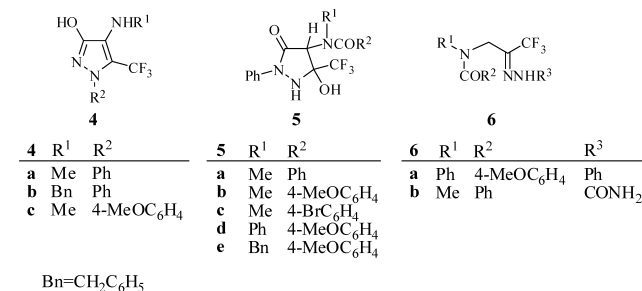
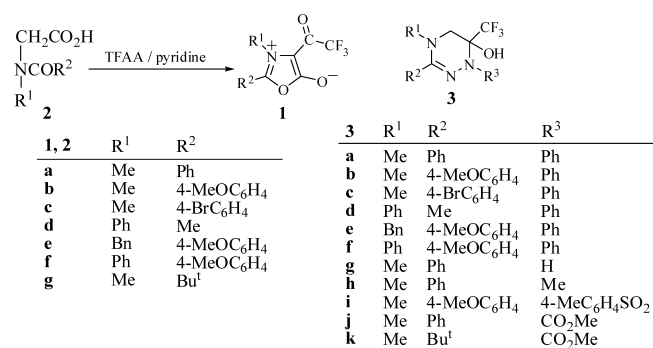


Chart 2

Table 1. Reactions of Compounds (1) with Phenylhydrazine

Run	Starting materials	Reaction conditions ^{a)}	Yields of products
1	1a	A	3a (74)
2	1b	A	3b (40)
3	1c	A	3c (68)
4	1d	A	3d (64)
5	1e	A	3e (88)
6	1f	A	3f (83)
7	1a	B	4a (63)
8	1b	B	4a (73)
9	1c	B	4a (46)
10	1e	B	4b (95)
11	1f	B	6a (24)+5d (25)
12	1a	B ^{b)}	4c (74)
13	1a	C	5a (62)
14	1b	C	5b (70)
15	1c	C	5c (48)
16	1d	C	5d (14)+4b (55)
17	1e	C	5e (41)

a) A: the reaction was done at room temperature for 24 h in DMF. B: the reaction mixture was refluxed for 2 h in benzene. C: the reaction was done at room temperature for 24 h in DCE. b) 4-Methoxyphenylhydrazine was used instead of phenylhydrazine.

Soft Acids and Bases (HSAB) theory.²¹⁾

We have carried out, besides the reaction of **1** with PH, the reaction of **1** with other hydrazine derivatives, such as hydrazine hydrate, methylhydrazine, hydrazine carbamate or tosylhydrazine, leading to the 1,2,4-triazine derivatives **3** in moderate yields, as shown in Table 2. On the other hand, the reaction of the semicarbazide with **1a** afforded only the non-cyclized semicarbazone **6b** in 76% yield.

Reaction of 1 with PH in Benzene The reaction of **1a**–**d** with PH in refluxing benzene solution afforded the 5-trifluoromethyl-3-hydroxypyrazoles **4** in good yields. At elevated temperature, the mesoionic **1** is in equilibrium with the trifluoroacetylketenes **10**. Similar ketene-type valence tautomers are often encountered during the cycloaddition of these mesoionic systems.²²⁾ Thus, PH attacked at the ketene

Table 2. Reactions of Compounds (1) with Hydrazine Derivatives^{a)}

Run	Starting materials	Hydrazine derivatives	Yields of products
1	1a	NH ₂ NH ₂	3g (48)
2	1a	CH ₃ NHNH ₂	3h (58)
3	1b	4-CH ₃ C ₆ H ₄ SO ₂ NHNH ₂	3i (17)
4	1a	NH ₂ NHCO ₂ CH ₃	3j (29)
5	1g	NH ₂ NHCO ₂ CH ₃	3k (14)
6	1f	NH ₂ NHCONH ₂	6b (76)

a) The reaction was done at room temperature for 24 h in DMF.

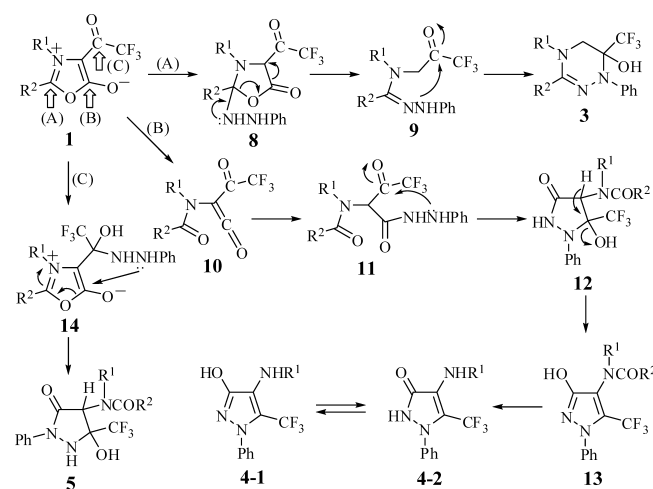


Chart 3

carbonyl of **10** and the subsequent intramolecular cyclization of **11** led to **12**, as shown in Chart 3 (route B). In this case, the intermediates **12** and **13** were not isolated, thus showing that the dehydration of **12** followed by hydrolysis of the resulting amide **13** easily occurred under the adopted reaction conditions. The driving force of the dehydration is probably due to stabilization by the formation of an aromatic pyrazole derivative.^{23,24)} The reason why the reaction of **1f** affords the different products **5d** and **6a** is unclear. In the reaction of **1a** with 4-methoxyphenylhydrazine instead of PH, **4c** was also isolated in 74% yield.

Reaction of 1 with PH in 1,2-Dichloroethane Compounds **1** were treated with PH at rt in a 1,2-dichloroethane solution to give the 3-trifluoromethyl-5-pyrazolones **5**. None of the 1,2,4-triazine derivative **3** was obtained in the reaction. The nucleophilic site in **1** was changed by the solvent polarity. Thus, the first step of the reaction consists of an attack at the trifluoromethyl ketone group by PH, as shown in Chart 3 (route C). The adduct **14** underwent intramolecular cyclization that led to the product **5**. The reaction of **1d** afforded **5d** in only 14% yield and **4b** was obtained as the main product in 55% yield. It is difficult to obtain a definitive explanation for the transformation.

Structural Determination of 3, 4 and 5 The structural determination of products **3**, **4**, and **5** were performed by spectral and analytical analyses. The ¹H-NMR spectrum of **3** exhibited the methylene signal of C-5 at around 3.4 ppm (d, *J*=13 Hz) and 3.8 ppm (d, *J*=13 Hz). In the ¹³C-NMR spectra, the C-5 carbon atom appears at around 52 ppm and the C-6 carbon atom at around 79 ppm (²*J*_{CF}=30 Hz). The carbon

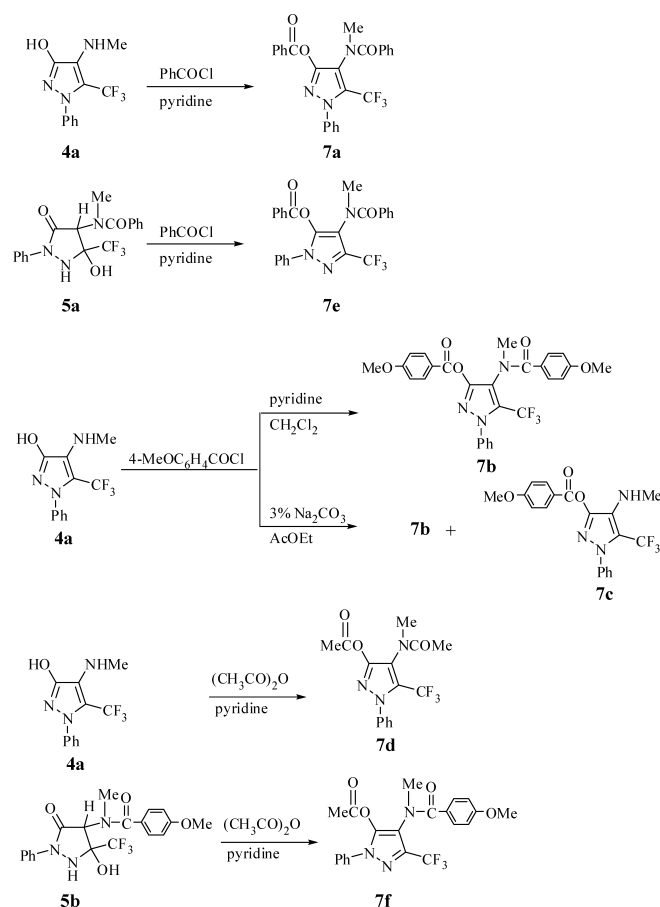


Chart 4

of CF₃ and the C-2 appear at around 123 ppm (¹J_{CF}=290 Hz) and 147 ppm, respectively. These ¹H- and ¹³C-NMR data are similar to the data for the 4-hydroxy-1-methyl-2-phenyl-4-trifluoromethyl-4,5-dihydro-imidazole.¹⁶⁾

The structure of **4a** was determined by the X-ray crystallography.²⁵⁾ Compound **4a** was treated with benzoyl chloride in the presence of pyridine to yield **7a** in 87% yield (Chart 4). When compound **5a** reacted with benzoic anhydride under reflux in benzene, compound **7e** was obtained in 59% yield, which was formed by dehydration and benzylation. Compound **7e** was the regioisomer of **7a**. Thus, these transformations confirmed the structure of **5a**. The regioisomeric pyrazoles **7a** and **7e** have significantly different ¹³C-NMR spectra as shown in Chart 5. The ¹³C-NMR spectral data of **7a** were similar to those of the 5-trifluoromethyl-3-hydroxyl-1-phenylpyrazole.²⁶⁾ The same was observed between **7e** and 3-trifluoromethyl-5-hydroxyl-1-phenyl-pyrazole²⁶⁾ as shown in Chart 5.

Compound **4a** was reacted with 4-methoxybenzoyl chloride in the presence of pyridine to yield **7b** in 95% yield. On the other hand, the same reaction of **4a** with 4-methoxybenzoyl chloride was done under Schotten–Baumann reaction condition to give a mixture of **7b** and **7c** in 9% and 17% yields, respectively. **4a** and **5b** were also treated with acetic anhydride in the presence of pyridine to yield **7d** and **7f** in 88% and 61%, respectively (Chart 4).

Conclusion

The selective synthesis of different products from the same

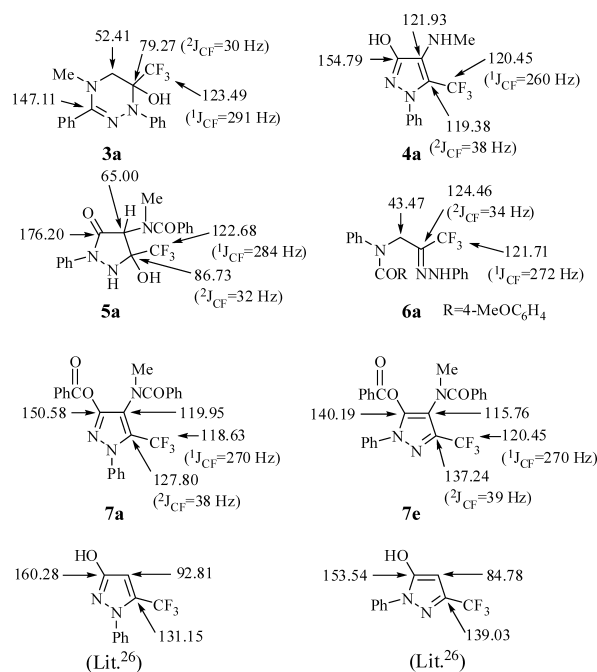


Chart 5. ¹³C-NMR Chemical Shifts of Representative Heterocycles Prepared in This Work and Two Related Pyrazoles

materials by only selecting different reaction conditions is an interesting research topic for chemists. We observed three different types of ring-opening reactions followed by ring-closure of the mesoionic oxazoles **1**. The reaction of **1** with PH affords a completely different product depending on the reaction solvent and temperature. With the application of different reaction conditions, the highly selective formation of 6-trifluoromethyl-1,2,4-triazines **3**, 5-trifluoromethyl-3-hydroxypyrazoles **4** and 3-trifluoromethyl-5-pyrazolones **5** can be realized. Regioselective attacks by PH on the mesoionic 4-trifluoroacetyl-1,3-oxazolium-5-olates **1** are a function of the solvent and the reaction temperature. Due to the easy availability of the starting materials and synthetic potential of the trifluoromethyl substituted heterocycles, this methodology will show its utility in organic synthesis. Further studies in this area are being pursued in our laboratory.

Experimental

General Methods All melting points were determined using a Yanagimoto hot-stage melting point apparatus and are uncorrected. ¹H-NMR spectra were measured on either a JEOL JNM-PMX60SI or JNM-GSX500 spectrometer with tetramethylsilane (Me₄Si) as an internal reference and CDCl₃ as the solvent. ¹³C-NMR spectra were obtained on a JEOL JNM-GSX500 spectrometer (at 127 MHz). Both ¹H- and ¹³C-NMR spectral data are reported in parts per million (δ) relative to Me₄Si. Infrared (IR) spectra were recorded on a JASCO IR810 spectrometer. Low- and high-resolution MS were obtained with a JEOL JMS-DX300 spectrometer with a direct inlet system at 70 eV. High-resolution (HR) ESI-MS of compound **6b** was performed with a microTOF-Q (Bruker Daltonics) mass spectrometer using acetonitrile as a solvent. Elemental analyses were carried out in the microanalytical laboratory of Josai University. Standard work-up means that the organic layers were finally dried over Na₂SO₄, filtered, and concentrated *in vacuo* below 45 °C using a rotary evaporator.

Materials The following compounds were prepared by reported procedures:

N-Benzoyl-N-methylglycine (2a) mp 101–104 °C (mp¹⁷⁾ 102–104 °C).

N-(4-Methoxybenzoyl)-N-methylglycine (2b) mp 101–104 °C (mp²⁷⁾ 102–104 °C).

N-(4-Bromobenzoyl)-N-methylglycine (2c) Yield 92%, mp 147–

150 °C (AcOEt–hexane), IR (Nujol) cm^{-1} : 1725, 2570 (br); $^1\text{H-NMR}$ (500 MHz, $\text{CDCl}_3 + \text{DMSO}-d_6$) δ : 3.11 + 3.03 (s, 3H), 3.92 + 4.22 (s, 2H), 7.31 + 7.37 (d, 2H, $J=8.2$), 7.53 + 7.56 (d, 2H, $J=8.2$); MS m/z : 271 (1.8) + 273 (1.8) (M^+ , 1:1), 183 (100) + 185 (98). *Anal.* Calcd for $\text{C}_{10}\text{H}_{10}\text{BrNO}_3$: C, 44.14; H, 3.70; N, 5.15. Found: C, 44.22; H, 3.58; N, 4.86.

***N*-Acetyl-*N*-phenylglycine (2d)** mp 196–198 °C (mp¹¹) 193–195 °C).

***N*-Benzyl-*N*-(4-methoxybenzoyl)glycine (2e)** Yield 84%, mp 149–151 °C (AcOEt–hexane), IR (Nujol) cm^{-1} : 1590, 1740, 2700 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.82 (s, 2H), 4.17 (s, 2H), 4.71 (s, 2H), 6.89 (d, 2H, $J=8.2$), 7.19–7.42 (m, 5H), 7.47–7.56 (br, 2H); MS m/z : 299 (M^+ , 10), 135 (100). *Anal.* Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_4$: C, 68.22; H, 5.72; N, 4.68. Found: C, 68.20; H, 5.91; N, 4.64.

***N*-Phenyl-*N*-(4-methoxybenzoyl)glycine (2f)** Yield 88%, mp 135–137 °C (AcOEt–hexane) (lit.²⁷) mp 158–163 °C), IR (Nujol) cm^{-1} : 1660, 1730, 3070 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.74 (s, 3H), 4.62 (s, 2H), 6.66 (d, 2H, $J=7.7$), 7.25 (t, 2H, $J=7.7$), 7.31 (d, 2H, $J=8.9$).

***N*-Methyl-*N*-pivaloylglycine (2g)** mp 75–76 °C (mp¹⁷) 75–76 °C).

General Procedure for the Preparation of 1 TFAA (11 ml, 78 mmol) was added to a stirred solution of *N*-acyl-*N*-alkylglycine (26 mmol) in CH_2CH_2 (50 ml) at 0 °C for 10 min. The mixture was stirred at 25 °C for 3 h and then extracted with CH_2Cl_2 (80 ml $\times$ 2). The combined extracts were washed successively with 3% HCl, H_2O , 1% Na_2CO_3 , and H_2O . After the standard workup, the residue was recrystallized from CH_2Cl_2 –hexane to give the 4-trifluoroacetyl-1,3-oxazolium-5-olates (1).

4-Trifluoroacetyl-3-methyl-2-phenyl-1,3-oxazolium-5-olate (1a) mp 161–163 °C (mp¹⁷) 162–163 °C).

2-(4-Bromophenyl)-4-trifluoroacetyl-3-methyl-1,3-oxazolium-5-olate (1b) mp 75–76 °C (mp¹⁷) 75–76 °C).

2-(4-Bromophenyl)-4-trifluoroacetyl-3-methyl-1,3-oxazolium-5-olate (1c) Yield 89%, mp 188–191 °C (CH_2Cl_2 –hexane), IR (Nujol) cm^{-1} : 1780; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 4.14 (s, 3H), 7.62 (d, 2H, $J=8.9$), 7.80 (d, 2H, $J=8.9$); MS m/z : 349 (23) + 351 (22) (M^+ , 1:1), 183 (100) + 185 (99). *Anal.* Calcd for $\text{C}_{12}\text{H}_7\text{BrF}_3\text{NO}_3$: C, 41.17; H, 2.02; N, 4.00. Found: C, 40.99; H, 2.10; N, 3.80.

2-(4-Bromophenyl)-4-trifluoroacetyl-3-methyl-1,3-oxazolium-5-olate (1d) mp 75–76 °C (mp¹⁷) 75–76 °C).

3-Benzyl-4-trifluoroacetyl-2-(4-methoxyphenyl)-1,3-oxazolium-5-olates (1e) mp 158–160 °C (AcOEt–hexane), IR (Nujol) cm^{-1} : 1780; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.89 (s, 3H), 5.78 (s, 2H), 7.02 (d, 2H, $J=9.0$), 7.18 (d, 2H, $J=7.2$), 7.37 (t, 1H, $J=7.2$), 7.41 (t, 2H, $J=7.2$), 7.65 (d, 2H, $J=9.0$); MS m/z : 377 (M^+ , 4), 91 (100). *Anal.* Calcd for $\text{C}_{19}\text{H}_{14}\text{F}_3\text{NO}_4$: C, 60.48; H, 3.74; N, 3.71. Found: C, 60.20; H, 3.86; N, 3.64.

4-Trifluoroacetyl-2-(4-methoxyphenyl)-3-phenyl-1,3-oxazolium-5-olates (1f) mp 182–185 °C (AcOEt–hexane), IR (Nujol) cm^{-1} : 1790; $^1\text{H-NMR}$ (60 MHz, CDCl_3) δ : 3.80 (s, 3H), 6.75 (d, 2H, $J=9.0$), 7.58 (d, 2H, $J=9.0$), 7.07–7.63 (m, 5H); MS m/z : 363 (M^+ , 19), 135 (100). *Anal.* Calcd for $\text{C}_{18}\text{H}_{12}\text{F}_3\text{NO}_4$: C, 59.51; H, 3.33; N, 3.86. Found: C, 59.38; H, 3.49; N, 4.02.

3-tert-Butyl-4-trifluoroacetyl-2-methyl-1,3-oxazolium-5-olate (1g) mp 120–121 °C (mp¹⁷) 120–121 °C).

General Procedure for the Reaction of 1 with PH in DMF Phenylhydrazine (162 mg, 1.5 mmol) was added to a solution of **1** (1 mmol) in dry DMF (5 ml) at 0 °C and the mixture was stirred at rt for 24 h. The mixture was diluted with AcOEt (30 ml) and washed with 3% Na_2CO_3 (20 ml), followed by brine (20 ml). After the standard work-up, the residue was purified by chromatography on silica gel with AcOEt–hexane (2:3).

6-Trifluoromethyl-1,4,5,6-tetrahydro-4-methyl-1,3-diphenyl-1,2,4-triazin-6-ol (3a) Oil, IR (oil) cm^{-1} : 1640, 3250 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.88 (s, 3H), 3.48 (dq, 1H, $J=2.1$, 12.8), 3.73 (d, 1H, $J=12.8$), 7.13–7.18 (m, 1H), 7.27–7.32 (m, 2H), 7.36–7.39 (m, 4H), 7.40–7.44 (m, 1H), 7.48–7.51 (m, 2H); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 40.47 (CH_3), 52.41 (CH_2), 79.27 (C, $^2J_{\text{CF}}=30$), 123.49 (CF_3 , $^1J_{\text{CF}}=291$), 125.56 (CH), 125.69 (CH), 128.32 (CH), 128.57 (CH), 128.71 (CH), 129.16 (CH), 133.82 (C), 144.58 (C), 147.11 (C); MS m/z : 335 (M^+ , 47), 77 (100). HR-MS Calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{N}_3\text{O}$: 335.1245. Found: 335.1215.

6-Trifluoromethyl-1,4,5,6-tetrahydro-3-(4-methoxyphenyl)-4-methyl-1-phenyl-1,2,4-triazin-6-ol (3b) Oil, IR (oil) cm^{-1} : 1610, 1670, 2900–3550; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.86 (s, 3H), 3.34 (d, 1H, $J=12.8$), 3.65 (d, 1H, $J=12.8$), 3.81 (s, 3H), 6.90 (d, 2H, $J=8.9$), 7.15 (t, 1H, $J=7.8$), 7.30 (t, 2H, $J=7.8$), 7.41 (d, 2H, $J=7.8$), 7.45 (d, 2H, $J=8.9$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 40.45 (CH_3), 52.41 (CH_2), 55.29 (CH_3), 79.42 (C, $^2J_{\text{CF}}=30$), 113.72 (CH), 123.50 (CF_3 , $^1J_{\text{CF}}=291$), 125.28 (CH), 125.47 (CH), 126.07 (C), 128.62 (CH), 129.93 (CH), 144.70 (C), 147.13 (C), 160.38 (C); MS m/z : 365 (M^+ , 100). HR-MS Calcd for $\text{C}_{18}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_2$:

365.1353. Found: 365.1352.

3-(4-Bromophenyl)-6-trifluoromethyl-1,4,5,6-tetrahydro-4-methyl-1-phenyl-1,2,4-triazin-6-ol (3c) Oil, IR (oil) cm^{-1} : 1610, 3250 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.89 (s, 3H), 3.52 (d, 1H, $J=12.8$), 3.76 (d, 1H, $J=12.8$), 7.15 (t, 1H, $J=7.8$), 7.28 (t, 2H, $J=7.8$), 7.38 (d, 2H, $J=8.5$), 7.40 (d, 2H, $J=7.8$), 7.51 (d, 2H, $J=8.5$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 40.48 (CH_3), 52.40 (CH_2), 79.52 (C, $^2J_{\text{CF}}=30$), 123.38 (CF_3 , $^1J_{\text{CF}}=290$), 123.93 (C), 125.59 (CH), 125.79 (CH), 128.68 (CH), 130.13 (CH), 131.63 (CH), 132.89 (C), 144.04 (C), 147.04 (C); MS m/z : 413 (100) + 415 (100) (M^+ , 1:1). HR-MS Calcd for $\text{C}_{17}\text{H}_{15}^{79}\text{BrF}_3\text{N}_3\text{O}$ ($\text{C}_{17}\text{H}_{15}^{81}\text{BrF}_3\text{N}_3\text{O}$): 413.0323 (415.0336). Found: 413.0337 (415.0333).

6-Trifluoromethyl-1,4,5,6-tetrahydro-3-methyl-1,4-diphenyl-1,2,4-triazin-6-ol (3d) mp 139–141 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1630, 3000 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 1.86 (s, 3H), 3.46 (dq, 1H, $J=1.5$, 11.9), 3.90 (d, 1H, $J=11.9$), 7.11 (d, 2H, $J=7.7$), 7.17 (t, 1H, $J=7.7$), 7.26 (t, 1H, $J=7.7$), 7.33 (t, 2H, $J=7.7$), 7.38 (t, 2H, $J=7.7$), 7.45 (d, 2H, $J=7.7$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 19.29 (CH_3), 52.09 (CH_2), 80.16 (C, $^2J_{\text{CF}}=30$), 123.30 (CF_3 , $^1J_{\text{CF}}=290$), 125.47 (CH), 125.69 (CH), 125.98 (CH), 126.49 (CH), 128.68 (CH), 129.36 (CH), 141.49 (C), 143.64 (C), 144.65 (C); MS m/z : 335 (M^+ , 100). *Anal.* Calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{N}_3\text{O}$: C, 60.89; H, 4.81; N, 12.53. Found: C, 60.67; H, 4.89; N, 12.46.

6-Trifluoromethyl-1,4,5,6-tetrahydro-3-(4-methoxyphenyl)-1-phenyl-4-phenylmethyl-1,2,4-triazin-6-ol (3e) Oil, IR (oil) cm^{-1} : 1610, 1740, 3300 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.45 (d, 1H, $J=13.0$), 3.69 (d, 1H, $J=13.0$), 3.79 (s, 3H), 4.36 (d, 1H, $J=16.0$), 4.48 (d, 1H, $J=16.0$), 6.88 (d, 2H, $J=8.8$), 7.26–7.43 (m, 10H), 7.52 (d, 2H, $J=8.8$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 49.59 (CH_3), 55.33 (CH_2), 55.64 (CH_2), 79.61 (C, $^2J_{\text{CF}}=30$), 114.06 (CH), 123.79 (CF_3 , $^1J_{\text{CF}}=279$), 126.15 (CH), 126.23 (C), 127.25 (CH), 127.84 (CH), 128.57 (CH), 128.85 (CH), 128.97 (CH), 129.27 (C), 129.82 (CH), 137.23 (C), 144.34 (C), 160.89 (C); MS m/z : 441 (M^+ , 47), 332 (100). HR-MS Calcd for $\text{C}_{24}\text{H}_{22}\text{F}_3\text{N}_3\text{O}_2$: 441.1664. Found: 441.1653.

6-Trifluoromethyl-1,4,5,6-tetrahydro-3-(4-methoxyphenyl)-1,4-diphenyl-1,2,4-triazin-6-ol (3f) mp 129–131 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1620, 3200 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.49 (dq, 1H, $J=2.1$, 12.8), 3.73 (s, 3H), 4.19 (d, 1H, $J=12.8$), 6.82–6.76 (m, 2H), 6.78 (d, 2H, $J=7.6$), 6.95–6.99 (m, 1H), 7.13–7.20 (m, 3H), 7.31–7.38 (m, 4H), 7.51 (d, 2H, $J=7.6$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 51.72 (CH_3), 55.17 (CH_2), 81.18 (C, $^2J_{\text{CF}}=30$), 113.48 (CH), 123.07 (CH), 123.31 (CF_3 , $^1J_{\text{CF}}=290$), 123.66 (CH), 124.25 (CH), 124.71 (CH), 125.56 (C), 128.71 (CH), 128.76 (CH), 129.91 (CH), 142.20 (C), 144.11 (C), 144.61 (C), 160.09 (C); MS m/z : 427 (M^+ , 100). HR-MS Calcd for $\text{C}_{23}\text{H}_{20}\text{F}_3\text{N}_3\text{O}_2$: 427.1507. Found: 427.1491.

6-Trifluoromethyl-1,4,5,6-tetrahydro-4-methyl-3-phenyl-1,2,4-triazin-6-ol (3g) The procedure was the same as described above, except that phenylhydrazine was replaced with hydrazine: Yield 45%, mp 159–161 °C (Et_2O), IR (Nujol) cm^{-1} : 1620, 3000 (br), 3310; $^1\text{H-NMR}$ (500 MHz, $\text{CDCl}_3 + \text{DMSO}-d_6$, 5:1) δ : 2.76 (s, 3H), 3.35 (dd, 1H, $J=2.5$, 11.6), 3.60 (d, 1H, $J=11.6$), 5.53 (s, 1H), 6.63 (s, 1H), 7.36–7.37 (m, 3H), 7.42–7.44 (m, 2H); $^{13}\text{C-NMR}$ (125 MHz, $\text{CDCl}_3 + \text{DMSO}-d_6$, 5:1) δ : 40.28 (CH_3), 51.55 (CH_2), 77.42 (C, $^2J_{\text{CF}}=30$), 123.69 (CF_3 , $^1J_{\text{CF}}=287$), 128.11 (CH), 128.26 (CH), 128.76 (CH), 134.40 (C), 148.54 (C); MS m/z : 259 (M^+ , 25), 241 (100). *Anal.* Calcd for $\text{C}_{11}\text{H}_{12}\text{F}_3\text{N}_3\text{O}$: C, 50.97; H, 4.67; N, 16.21. Found: C, 51.01; H, 4.77; N, 16.13.

6-Trifluoromethyl-1,4,5,6-tetrahydro-1,4-dimethyl-3-phenyl-1,2,4-triazin-6-ol (3h) The procedure was the same as described above, except that phenylhydrazine was replaced with methylhydrazine: Yield 58%, mp 153–154 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1610, 3000 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.76 (s, 3H), 2.87 + 2.88 (s, 3H), 3.27 (dd, 1H, $J=1.3$, 11.9), 3.54 (d, 1H, $J=11.9$), 7.36–7.39 (m, 3H), 7.41–7.44 (m, 2H); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 38.32 + 38.33 (CH_3), 39.94 (CH_2), 53.52 (CH_2), 79.67 (C, $^2J_{\text{CF}}=30$), 123.50 (CF_3 , $^1J_{\text{CF}}=290$), 128.44 (CH), 128.56 (CH), 129.18 (CH), 133.63 (C), 148.23 (C); MS m/z : 273 (M^+ , 68), 255 (100). *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{F}_3\text{N}_3\text{O}$: C, 52.75; H, 5.16; N, 15.38. Found: C, 53.01; H, 5.25; N, 15.36.

6-Trifluoromethyl-1,4,5,6-tetrahydro-3-(4-methoxyphenyl)-4-methyl-1-(4-methylbenzenesulfonyl)-1,2,4-triazin-6-ol (3i) The procedure was the same as described above, except that phenylhydrazine was replaced with tosylhydrazine: Yield 17%, oil, IR (oil) cm^{-1} : 1610, 1670, 1740, 3450; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.43 (s, 3H), 2.81 (s, 3H), 3.38 (dd, 1H, $J=3.1$, 13.4), 3.66 (d, 1H, $J=13.4$), 3.82 (s, 3H), 6.87 (d, 2H, $J=8.9$), 7.29 (d, 2H, $J=8.9$), 7.31 (d, 2H, $J=8.2$), 7.91 (d, 2H, $J=8.2$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 21.60 (CH_3), 40.13 (CH_2), 51.84 (CH_2), 55.30 (CH_2), 80.41 (C, $^2J_{\text{CF}}=33$), 113.65 (CH), 123.10 (CF_3 , $^1J_{\text{CF}}=291$), 124.74 (C), 128.64 (CH), 129.03 (CH), 130.25 (CH), 135.03 (C), 144.21 (C), 148.06 (C), 160.91 (C);

MS m/z : 443 (M^+ , 4), 148 (100). HR-MS Calcd for $C_{19}H_{20}F_3N_3O_4S$: 443.1126. Found: 443.1118.

6-Trifluoromethyl-1,4,5,6-tetrahydro-1-methoxycarbonyl-4-methyl-3-phenyl-1,2,4-triazin-6-ol (3j) The procedure was the same as described above, except that phenylhydrazine was replaced with methyl hydrazinocarboxylate: mp 122–123 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1620, 1690, 3375; 1H -NMR (500 MHz, $CDCl_3$) δ : 2.85 (s, 3H), 3.54 (dq, 1H, $J=2.7$, 13.4), 3.71 (d, 1H, $J=13.4$), 3.87 (s, 3H), 7.37–7.42 (m, 3H), 7.44–7.47 (m, 2H); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 40.31 (CH_3), 51.11 (CH_3), 53.90 (CH_2), 79.87 (C, $^2J_{CF}=32$), 123.83 (CF_3 , $^1J_{CF}=292$), 128.60 (CH), 128.90 (CH), 130.02 (CH), 132.84 (C), 148.85 (C), 156.20 (C); MS m/z : 317 (M^+ , 41), 228 (100). Anal. Calcd for $C_{13}H_{14}F_3N_3O_3$: C, 49.21; H, 4.45; N, 13.24. Found: C, 49.06; H, 4.44; N, 13.20.

3-tert-Butyl-6-trifluoromethyl-1,4,5,6-tetrahydro-1-methoxycarbonyl-4-methyl-1,2,4-triazin-6-ol (3k) The procedure was the same as described above, except that phenylhydrazine was replaced with methyl hydrazinocarboxylate: Yield 14%, mp 93–94 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1610, 1670, 3250 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 1.28+1.29 (s, 9H), 3.10 (s, 3H), 3.28 (dq, 1H, $J=2.8$, 13.4), 3.45 (d, 1H, $J=13.4$), 3.85+3.86 (s, 3H); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 28.93 ($CH_3 \times 3$), 37.11 (C), 40.96 (CH_3), 52.96 (CH_3), 53.63 (CH_2), 79.75 (C, $^2J_{CF}=32$), 124.20 (CF_3 , $^1J_{CF}=291$), 152.86 (C), 156.11 (C); MS m/z : 297 (M^+ , 39), 208 (100). HR-MS Calcd for $C_{11}H_{18}F_3N_3O_3$: 297.1301. Found: 297.1297.

N-[2,2,2-Trifluoro-2-(semicarbazono)propyl]-N-methylbenzamide (6b) The procedure was the same as described above, except that phenylhydrazine was replaced with semicarbazide: Yield 76%, IR (Nujol) cm^{-1} : 1640, 1700 (br), 3000–3600; 1H -NMR (500 MHz, $CDCl_3$) δ : 3.04 (s, 3H), 4.45 (s, 2H), 6.19 (s, 2H), 7.30–7.43 (m, 5H), 10.67 (s, 1H); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 38.44 (CH_3), 41.54 (CH_2), 121.04 (CF_3 , $^1J_{CF}=273$), 127.44 (CH), 128.53 (CH), 130.59 (CH), 130.73 (C, $^2J_{CF}=35$), 133.91 (C), 156.59 (C), 172.87 (C); MS m/z : 302 (M^+ , 0.5), 105 (100). HR-MS Calcd for $C_{12}H_{12}F_3N_4O_2$ (M-H): 301.0912. Found: 301.0911.

General Procedure for the Reaction of 1 with PH in Benzene Phenylhydrazine (162 mg, 1.5 mmol) was added to a solution of **1** (1 mmol) in dry benzene (5 ml) at 0 °C and the mixture was refluxed for 3 h. The mixture was diluted with AcOEt (30 ml) and washed with 3% Na_2CO_3 (20 ml), followed by brine (20 ml). After the standard work-up, the residue was purified by chromatography on silica gel with AcOEt–hexane (2 : 3).

5-Trifluoromethyl-1,2-dihydro-4-(methylamino)-1-phenyl-3H-pyrazol-3-one (4a) mp 117–119 °C (cyclohexane), IR (Nujol) cm^{-1} : 1600, 3000 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 2.86 (s, 3H), 7.34–7.41 (m, 3H), 7.42–7.46 (m, 2H); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 34.91 (CH_3), 119.38 (C, $^2J_{CF}=38$), 120.45 (CF_3 , $^1J_{CF}=260$), 121.93 (C), 125.33 (CH), 128.37 (CH), 129.09 (CH), 139.05 (C), 154.79 (C); MS m/z : 257 (M^+ , 100). Anal. Calcd for $C_{11}H_{10}F_3N_3O$: C, 51.37; H, 3.92; N, 16.34. Found: C, 51.98; H, 4.10; N, 16.23.

5-Trifluoromethyl-1,2-dihydro-1-phenyl-4-[(phenylmethyl)amino]-3H-pyrazol-3-one (4b) mp 99–105 °C (cyclohexane), IR (Nujol) cm^{-1} : 1605, 3000 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 4.30 (s, 2H), 7.23–7.32 (m, 5H), 7.33–7.37 (m, 3H), 7.38–7.45 (m, 2H); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 51.48 (CH_2), 119.70 (C, $^2J_{CF}=37$), 120.43 (CF_3 , $^1J_{CF}=269$), 120.93 (C), 125.38 (CH), 127.32 (CH), 127.91 (CH), 128.44 (CH), 128.48 (CH), 129.08 (CH), 138.91 (C), 139.61 (C), 154.70 (C); MS m/z : 333 (M^+ , 55), 91 (100). Anal. Calcd for $C_{17}H_{14}F_3N_3O$: C, 61.26; H, 4.23; N, 12.61. Found: C, 61.17; H, 4.32; N, 12.70.

5-Trifluoromethyl-1,2-dihydro-1-(4-methoxyphenyl)-4-(methylamino)-3H-pyrazol-3-one (4c) mp 170–172 °C (cyclohexane), IR (Nujol) cm^{-1} : 1615, 3000 (br), 3400; 1H -NMR (500 MHz, $CDCl_3$) δ : 2.84 (s, 3H), 3.84 (s, 3H), 6.93 (d, 2H, $J=9.1$), 7.27 (d, 2H, $J=9.1$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 35.09 (CH_3), 55.44 (CH_2), 114.15 (CH), 120.00 (C, $^2J_{CF}=37$), 120.39 (CF_3 , $^1J_{CF}=269$), 121.05 (C), 127.09 (CH), 131.88 (CH), 154.55 (C), 159.54 (C); MS m/z : 287 (M^+ , 100). Anal. Calcd for $C_{12}H_{12}F_3N_3O_2$: C, 50.18; H, 4.21; N, 14.63. Found: C, 50.39; H, 4.27; N, 14.72.

N-[2,2,2-Trifluoro-2-(phenylhydrazono)propyl]-N-phenyl-4-methoxybenzamide (6a) Oil, IR (oil) cm^{-1} : 1730, 3030 (br), 3240 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 3.71 (s, 3H), 4.91 (s, 2H), 6.64 (d, 2H, $J=7.1$), 6.91–7.02 (m, 3H), 7.18–7.34 (m, 7H), 7.28 (d, 2H, $J=7.1$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 43.47 (CH_2), 55.17 (CH_3), 113.11 (CH), 113.71 (CH), 121.71 (CF_3 , $^1J_{CF}=272$), 121.77 (CH), 124.46 (C, $^2J_{CF}=34$), 125.79 (C), 127.78 (CH), 127.88 (CH), 129.29 (CH), 129.47 (CH), 131.28 (CH), 141.65 (C), 143.69 (C), 161.25 (C), 171.56 (C); MS m/z : 427 (M^+ , 6), 135 (100). HR-MS Calcd for $C_{23}H_{20}F_3N_3O_2$: 427.1508. Found: 427.1509.

General Procedure for the Reaction of 1 with PH in 1,2-Dichloroethane Phenylhydrazine (162 mg, 1.5 mmol) was added to a solution of **1** (1 mmol)

in dry 1,2-dichloroethane (5 ml) at 0 °C and the mixture was stirred at rt for 24 h. The mixture was diluted with AcOEt (30 ml) and washed with 3% Na_2CO_3 (20 ml), followed by brine (20 ml). After the standard work-up, the residue was purified by chromatography on silica gel with AcOEt–hexane (2 : 3).

N-(3-Trifluoromethyl-3-hydroxy-5-oxo-1-phenyl-4-pyrazolidinyl)-N-methylbenzamide (5a) Oil, IR (oil) cm^{-1} : 1635, 1720, 3200 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 3.21 (s, 3H), 4.28–4.48 (br, 1H, D_2O changeable), 5.16 (s, 1H, D_2O changeable), 7.19 (t, 1H, $J=7.6$), 7.36 (t, 2H, $J=7.6$), 7.44 (t, 2H, $J=7.6$), 7.50 (t, 1H, $J=7.6$), 7.58 (d, 2H, $J=7.6$), 7.76 (d, 2H, $J=7.6$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 41.10 (CH_3), 65.00 (CH), 86.73 (C, $^2J_{CF}=32$), 118.92 (CH), 122.68 (CF_3 , $^1J_{CF}=284$), 125.70 (CH), 127.78 (CH), 128.60 (CH), 128.92 (CH), 131.26 (CH), 133.32 (C), 137.08 (C), 161.10 (C), 176.20 (C); MS m/z : 379 (M^+ , 3), 105 (100). HR-MS Calcd for $C_{18}H_{16}F_3N_3O_3$: 379.1143. Found: 379.1151.

N-(3-Trifluoromethyl-3-hydroxy-5-oxo-1-phenyl-4-pyrazolidinyl)-4-methoxy-N-methylbenzamide (5b) Oil, IR (oil) cm^{-1} : 1610, 1720, 3200; 1H -NMR (500 MHz, $CDCl_3$) δ : 3.27 (s, 3H), 3.85 (s, 3H), 4.35 (br s, 1H, D_2O changeable), 5.13 (s, 1H, D_2O changeable), 6.93 (d, 2H, $J=8.9$), 7.18 (t, 1H, $J=7.9$), 7.36 (t, 2H, $J=7.9$), 7.59 (d, 2H, $J=8.9$), 7.76 (d, 2H, $J=7.9$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 41.33 (CH_3), 55.41 (CH_3), 65.34 (CH_2), 86.76 (C, $^2J_{CF}=32$), 113.83 (CH), 118.89 (CH), 122.72 (CF_3 , $^1J_{CF}=282$), 125.01 (C), 125.65 (CH), 128.90 (CH), 130.39 (CH), 137.08 (C), 161.04 (C), 162.14 (C), 176.00 (C); MS m/z : 409 (M^+ , 3), 135 (100). HR-MS Calcd for $C_{19}H_{18}F_3N_3O_4$: 409.1249. Found: 409.1243.

4-Bromo-N-(3-trifluoromethyl-3-hydroxy-5-oxo-1-phenyl-4-pyrazolidinyl)-N-methylbenzamide (5c) Oil, IR (oil) cm^{-1} : 1645, 1685, 3200 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 3.19 (s, 3H), 4.38 (brs, 1H), 5.18 (s, 1H), 7.19 (t, 1H, $J=7.7$), 7.37 (t, 2H, $J=7.7$), 7.44 (d, 2H, $J=8.3$), 7.58 (d, 2H, $J=8.3$), 7.74 (dd, 2H, $J=1.2$, 7.7); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 40.93 (CH_3), 65.07 (CH), 86.66 (C, $^2J_{CF}=32$), 118.92 (CH), 122.63 (CF_3 , $^1J_{CF}=282$), 125.80 (CH), 125.91 (C), 128.96 (CH), 129.40 (CH), 131.93 (CH), 132.14 (C), 137.00 (C), 160.95 (C), 175.08 (C); MS m/z : 457 (2.6)+459 (2.5) (M^+ , 1 : 1), 183 (100)+185 (99). HR-MS Calcd for $C_{18}H_{15}^{79}BrF_3N_3O_3$ ($C_{17}H_{15}^{81}BrF_3N_3O_3$): 457.0212 (459.0189). Found: 457.0175 (459.0209).

N-(3-Trifluoromethyl-3-hydroxy-5-oxo-1-phenyl-4-pyrazolidinyl)-4-methoxy-N-phenylbenzamide (5d) Oil, IR (oil) cm^{-1} : 1650, 1670, 3100 (br); 1H -NMR (500 MHz, $CDCl_3$) δ : 3.72 (s, 3H), 4.80 (s, 1H), 5.22 (s, 1H), 6.64 (d, 2H, $J=8.7$), 7.16–7.40 (m, 10H), 7.81 (d, 2H, $J=8.7$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 55.23 (CH_3), 68.09 (CH), 86.66 (C, $^2J_{CF}=32$), 113.20 (CH), 118.94 (CH), 122.59 (CF_3 , $^1J_{CF}=284$), 124.82 (CH), 125.20 (C), 125.70 (CH), 127.95 (CH), 128.92 (CH), 129.65 (C), 129.77 (CH), 131.87 (CH), 137.15 (C), 143.99 (C), 161.87 (C), 174.38 (C); MS m/z : 471 (M^+ , 6), 135 (100). HR-MS Calcd for $C_{24}H_{20}F_3N_3O_4$: 471.1392. Found: 471.1399.

N-(3-Trifluoromethyl-3-hydroxy-5-oxo-1-phenyl-4-pyrazolidinyl)-4-methoxy-N-(phenylmethyl)benzamide (5e) Oil, IR (oil) cm^{-1} : 1610, 1720, 3200; 1H -NMR (500 MHz, $CDCl_3$) δ : 3.81 (s, 3H), 4.32 (s, 1H, D_2O changeable), 4.54 (d, 1H, $J=17.1$), 5.05 (s, 1H, D_2O changeable), 5.12 (d, 1H, $J=17.1$), 6.88 (d, 2H, $J=8.9$), 7.18 (t, 1H, $J=7.6$), 7.35 (t, 2H, $J=7.6$), 7.37 (t, 1H, $J=7.6$), 7.45 (t, 2H, $J=7.6$), 7.56 (d, 2H, $J=7.6$), 7.64 (d, 2H, $J=8.9$), 7.76 (d, 2H, $J=7.6$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 55.23 (CH_3), 55.41 (CH_3), 61.54 (CH), 87.12 (C, $^2J_{CF}=32$), 113.99 (CH), 118.93 (CH), 122.58 (CF_3 , $^1J_{CF}=282$), 124.68 (C), 125.64 (CH), 126.95 (CH), 128.30 (CH), 128.90 (CH), 129.35 (CH), 129.97 (CH), 134.51 (C), 137.09 (C), 161.16 (C), 162.45 (C), 176.49 (C); MS m/z : 485 (M^+ , 8), 91 (100). HR-MS Calcd for $C_{25}H_{22}F_3N_3O_4$: 485.1580. Found: 485.1571.

N-(3-Benzoyloxy-5-trifluoromethyl-1-phenyl-1H-pyrazol-4-yl)-N-methylbenzamide (7a) Benzoyl chloride (0.3 ml, 2.6 mmol) was added to a stirred solution of **4a** (230 mg, 0.89 mmol) and pyridine (1 ml, 12 mmol) in CH_2Cl_2 (2 ml) at 0 °C and the mixture was stirred at rt for 24 h. The mixture was diluted with AcOEt (30 ml) and washed with 3% Na_2CO_3 (20 ml), followed by brine (20 ml). After the standard work-up, the residue was purified by column chromatography on silica gel with AcOEt:hexane (1 : 3): Yield 87%, mp 102–104 °C (Et_2O –hexane), IR (Nujol) cm^{-1} : 1660, 1720, 3050; 1H -NMR (500 MHz, $CDCl_3$) δ : 3.41 (s, 3H), 7.32 (d, 3H, $J=7.6$), 7.37–7.47 (m, 7H), 7.55 (t, 2H, $J=7.6$), 7.70 (t, 1H, $J=7.6$), 8.15 (d, 2H, $J=7.6$); ^{13}C -NMR (125 MHz, $CDCl_3$) δ : 37.26 (CH_3), 118.63 (CF_3 , $^1J_{CF}=270$), 119.95 (C), 125.70 (CH), 127.32 (C), 127.75 (CH), 127.80 (C, $^2J_{CF}=38$), 127.85 (CH), 128.82 (CH), 129.13 (CH), 129.81 (CH), 130.37 (CH), 130.57 (CH), 134.60 (CH), 134.81 (C), 138.40 (C), 150.58 (C), 163.34 (C), 171.19 (C); MS m/z : 465 (M^+ , 14), 105 (100). Anal. Calcd for $C_{25}H_{18}F_3N_3O_3$: C, 64.52; H, 3.90; N, 9.03. Found: C, 64.63; H, 4.13; N, 9.01.

N-[5-Trifluoromethyl-3-(4-methoxyphenyl)carbonyloxy-1-phenyl-1H-

pyrazol-4-yl]-N-methyl-4-methoxybenzamide (7b) The procedure was the same as described above, except that benzoyl chloride was replaced with 4-methoxybenzoyl chloride: Yield 95%, oil, IR (oil) cm^{-1} : 1610, 1750; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.35 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 6.79 (d, 2H, $J=8.5$), 6.97 (d, 2H, $J=9.0$), 7.31–7.45 (m, 5H), 7.38 (d, 2H, $J=9.0$), 8.07 (d, 2H, $J=8.5$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 37.44 (CH_3), 55.24 (CH_3), 55.53 (CH_3), 113.13 (CH), 114.12 (CH), 118.73 (CF_3 , $^1J_{\text{CF}}=271$), 119.51 (C), 125.28 (C), 125.70 (CH), 126.89 (C), 127.47 (C, $^2J_{\text{CF}}=37$), 129.10 (CH), 129.69 (CH), 130.03 (CH), 132.83 (CH), 138.56 (C), 150.71 (C), 161.24 (C), 163.04 (C), 164.66 (C), 170.96 (C); MS m/z : 525 (M^+ , 4), 135 (100). HR-MS Calcd for $\text{C}_{27}\text{H}_{22}\text{F}_3\text{N}_3\text{O}_5$: 525.1511. Found: 525.1487.

5-Trifluoromethyl-3-(4-methoxyphenyl)carbonyloxy-4-methylamino-1-phenyl-1H-pyrazole (7c) and 7b 4-Methoxybenzoyl chloride (0.15 ml, 11 mmol) was added to a stirred solution of **4a** (300 mg, 12 mmol) and 3% Na_2CO_3 (5 ml) in AcOEt (5 ml) at 0°C and the mixture was stirred at rt for 3.5 h. The mixture was diluted with AcOEt (30 ml) and washed with 3% Na_2CO_3 (20 ml), followed by brine (20 ml). After the standard work-up, the residue was purified by column chromatography on silica gel with AcOEt:hexane (2:3) to give **7c** (80 mg, 17%) and **7b** (55 mg, 9%). **7c**: the less polar fraction, Yield 17%, mp 129–130 $^\circ\text{C}$ (Et₂O–hexane), IR (Nujol) cm^{-1} : 1735, 3400 (br); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.85 (s, 3H), 3.89 (s, 3H), 6.99 (d, 2H, $J=8.9$), 7.38–7.48 (m, 5H), 8.17 (d, 2H, $J=8.9$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 34.03 (CH_3), 55.57 (CH_3), 114.07 (CH), 118.84 (C, $^2J_{\text{CF}}=38$), 120.35 (C), 120.52 (CF_3 , $^1J_{\text{CF}}=267$), 125.54 (CH), 126.44 (C), 128.76 (CH), 128.98 (CH), 132.79 (CH), 139.51 (C), 146.72 (C), 163.98 (C), 164.42 (C); MS m/z : 391 (M^+ , 4), 135 (100). Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_5$: C, 58.31; H, 4.12; N, 10.74. Found: C, 58.30; H, 4.23; N, 10.67.

N-(3-Acetoxy-5-trifluoromethyl-1-phenyl-1H-pyrazol-4-yl)-N-methylacetamide (7d) The procedure was the same as described for **7a**, except that benzoyl chloride was replaced with acetic anhydride: Yield 88%, mp 127–129 $^\circ\text{C}$ (cyclohexane), IR (Nujol) cm^{-1} : 1680, 1780; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.00 (s, 3H), 2.34 (s, 3H), 3.17 (s, 3H), 7.47–7.53 (m, 5H); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 20.26 (CH_3), 21.47 (CH_3), 36.22 (CH_3), 118.66 (CF_3 , $^1J_{\text{CF}}=271$), 118.94 (C), 125.63 (CH), 128.49 (C, $^2J_{\text{CF}}=35$), 129.24 (CH), 129.92 (CH), 138.44 (C), 151.00 (C), 167.65 (C), 171.17 (C); MS m/z : 341 (M^+ , 6), 257 (100). Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{F}_3\text{N}_3\text{O}_5$: C, 52.79; H, 4.13; N, 12.31. Found: C, 52.68; H, 4.19; N, 12.37.

N-(5-Benzoyloxy-3-trifluoromethyl-1-phenyl-1H-pyrazol-4-yl)-N-methylbenzamide (7e) The procedure was the same as described for **7a**: Yield 59%, oil, IR (oil) cm^{-1} : 1765, 1770; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 3.41 (s, 3H), 7.27–7.37 (m, 10H), 7.52 (t, 2H, $J=7.7$), 7.49 (t, 1H, $J=7.7$), 7.94 (d, 2H, $J=7.7$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 37.02 (CH_3), 115.76 (C), 120.45 (CF_3 , $^1J_{\text{CF}}=270$), 123.20 (CH), 126.03 (C), 127.53 (CH), 127.80 (CH), 129.00 (CH), 129.04 (CH), 129.41 (CH), 130.22 (CH), 130.68 (CH), 135.11 (C), 135.24 (CH), 136.57 (C), 137.24 (C, $^2J_{\text{CF}}=39$), 140.19 (C), 161.56 (C), 171.23 (C); MS m/z : 465 (M^+ , 2), 105 (100). HR-MS Calcd for $\text{C}_{25}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_5$: 465.1316. Found: 465.1308.

N-(5-Acetoxy-3-trifluoromethyl-1-phenyl-1H-pyrazol-4-yl)-N-methyl-4-methoxybenzamide (7f) The procedure was the same as described for **7a**, except that benzoyl chloride was replaced with acetic anhydride: Yield 61%, oil, IR (oil) cm^{-1} : 1610, 1790; $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ : 2.22 (s, 3H), 3.32 (s, 3H), 3.78 (s, 3H), 6.78 (d, 2H, $J=8.5$), 7.32–7.46 (m, 5H), 7.39 (d, 2H, $J=8.5$); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ : 20.03 (CH_3), 37.38 (CH_3), 55.29 (CH_3), 113.28 (CH), 116.14 (C), 120.44 (CF_3 , $^1J_{\text{CF}}=270$), 123.40 (CH), 127.18 (C), 129.12 (CH), 129.49 (CH), 129.63 (CH), 136.73 (C), 137.17 (C, $^2J_{\text{CF}}=38$), 140.19 (C), 161.21 (C), 165.78 (C), 171.07 (C); MS m/z : 433 (M^+ , 0.8), 135 (100). HR-MS Calcd for $\text{C}_{21}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_4$:

433.1249. Found: 433.1251.

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