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A new Entry to [1,2,4]Triazolo[1,5-*a*][1,4]benzodiazepin-6-ones *via* Intramolecular Nitrilimine Cycloaddition to the Cyano Group

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Abstract: A series of [1,2,4]triazolo[1,5-*a*][1,4]benzodiazepin-6-ones of potential pharmacological interest have been synthesised by means of intramolecular nitrilimine cycloadditions to the cyano group.

In view of their well-known anti-convulsant and anti-anxiety activity, many 1,4-benzodiazepines and their oxo derivatives have acquired both pharmaceutical and economical relevance.[1] Among them, several triazolobenzodiazepines, *e.g.* triazolam,[2] estazolam,[3] and flumazenil were found to be effective in the treatment of some CNS disturbances.[4] Hence, a number of synthetic methods have been developed,[5] even in recent years,[6] providing interesting and useful routes to annulated 1,4-benzodiazepines.[7] We describe here a novel synthetic route, in which the intramolecular nitrilimine cycloaddition onto the cyano group is a fruitful source of [1,2,4]triazolo[1,5-*a*][1,4]benzodiazepin-6-ones.

Results and Discussion

Hydrazonoyl chlorides **4**, which we devised as the precursors of nitrilimines **5**, were synthesised as outlined in the Scheme. The synthetic route to *N*-phenyl substituted substrates **4a,b** starts with the cyanomethylation of (2-nitrobenzoyl)aniline or (5-chloro-2-nitrobenzoyl)aniline, while the preparation of *N*-benzyl substituted substrates **4c-i** involves, at the first step, the reaction of 2-nitrobenzoylchlorides with the proper 2-substituted 2-benzylaminoacetonitriles **1**. Reduction of nitro compounds **2**, in order to obtain the desired amino derivatives **3**, presented some difficulties. In fact, the reaction carried out by iron in aqueous acetic acid gave both compounds **3** and benzodiazepine diones **7**.

The formation of the latter can be ascribed to the intramolecular nucleophilic attack by the amino group of **3** onto the cyano moiety, which is a favoured 7-*Exo-Dig* ring closure according to Baldwin's rules.[8,9] Since compounds **7** are themselves of pharmaceutical interest,[10,11] we tried to improve their preparation. Actually,

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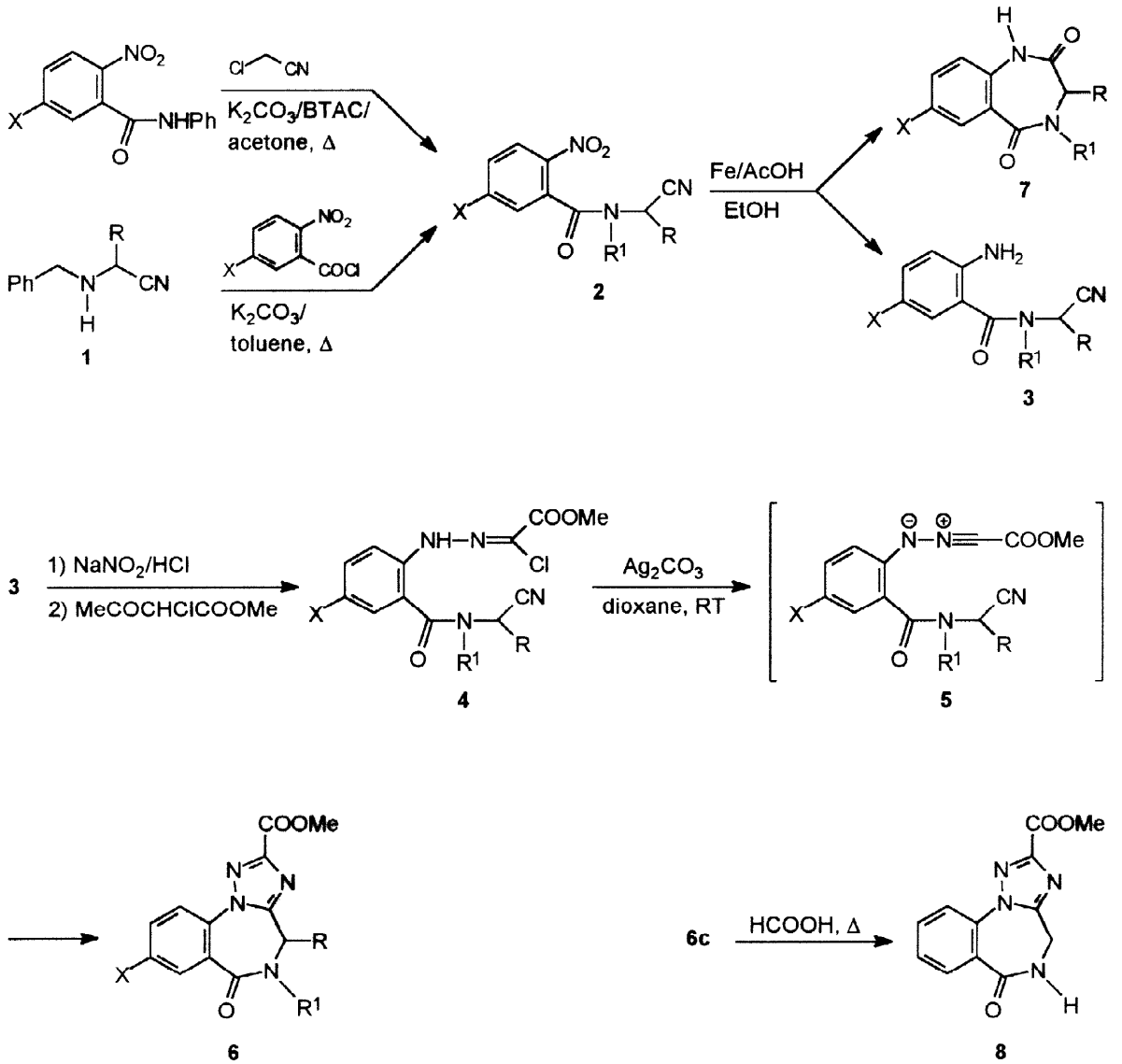
Scheme



entry	a	b	c	d	e	f	g	h	i
X	H	Cl	H	Cl	H	H	H	H	H
R	H	H	H	H	Me	Ph	4-Me-C_6H_4	4-MeO-C_6H_4	4-Cl-C_6H_4
R^1	Ph	Ph	CH_2Ph	CH_2Ph	CH_2Ph	CH_2Ph	CH_2Ph	CH_2Ph	CH_2Ph

reduction of **2a** in basic medium **gave 7a in almost** quantitative yield, making this approach valuable on a preparative scale.

The *in situ* generation of **nitrilimines 5 was** accomplished by treating the corresponding hydrazonoyl chlorides with a two-fold molar **excess of silver carbonate** in dry dioxane at room temperature. Reaction times, eluants, products and yields are collected in the Table.

Table. Reaction of **4** with silver carbonate in dioxane at rt.

Entry	Time (h)	**6** (%)	Eluant[a]
a	70	54	AcOEt/LP 2:1
b	48	55	AcOEt/LP 1:1
c	120	95	–
d	48	85	AcOEt/LP 1:1
e	144	65	AcOEt/LP 10:1
f	168	70	AcOEt/LP 2:1
g	120	75	AcOEt/LP 1:1
h	96	70	Et_2O/CH_2Cl_2 10:1
i	120	70	–

[a]LP = light petroleum b.p. 40-60°C.

In the light of the poor dipolarophilic character of nitriles towards nitrilimines,[12] the extent of our intramolecular cycloadditions is fully satisfactory. This is somewhat surprising because benzoic esters structurally related to benzamides **4** gave poor results.[13] It may be that the lesser flexibility of the amide linkage with respect to the ester one is more favourable to the intramolecular approach of the addends.

Since further transformation of cycloadducts **6** could enhance their biological interest, the benzyl group of **6c** was removed with 95% formic acid[14] obtaining **8**, which represents a potential starting material for a variety of functionalisations.

Experimental Section

Melting points were determined with a Büchi apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 1725X spectrophotometer. Mass spectra were determined with a VG-70EQ apparatus. ^{1}H-NMR spectra were taken with a Bruker AC 300 instrument (in $CDCl_3$ solutions). Chemical shift are given as ppm from tetramethylsilane and coupling constants are given in Hz.

Chloroacetonitrile and 2-bromopropionitrile are commercially available. 2-Bromo-2-phenylacetonitrile,[15] 2-bromo-2-(4-methylphenyl)acetonitrile,[13] 2-bromo-2-(4-chlorophenyl) acetonitrile,[13] *N*-phenyl-2-nitrobenzamide[16] and *N*-phenyl-5-chloro-2-nitrobenzamide[17] are already known in the literature.

General procedure for the preparation of 2-substituted 2-benzylaminoacetonitriles 1. A solution of the 2-substituted 2-haloacetonitriles (20 mmol) in ethyl acetate (6 mL) was slowly added (1h) to benzylamine (4 28 g, 40 mmol) under vigorous stirring. The mixture was warmed gently to 45°C for 30 minutes, the white precipitate was filtered off, and the residue was evaporated under reduced pressure to give **1** as undistillable oils not analytically pure.

2-benzylaminoacetonitrile (2.50 g, 95% yield); IR (neat): 3333, 2234 (cm^{-1}); ^{1}H-NMR: 1.68 (1H, br s), 3.50 (2H, s), 3.90 (2H, s), 7.30-7.40 (5H, m); MS: *m/z* 132 (M^+).

2-benzylamino-2-methylacetonitrile (2.63 g, 90% yield); IR (neat): 3317, 2226 (cm^{-1}); ^{1}H-NMR: 1.50 (3H, d, *J*=8.7), 3.53 (1H, q, *J*=8.7), 3.82 (1H, d, *J*=13.1), 3.87 (1H, br s), 4.06 (1H, d, *J*=13.1), 7.30-7.45 (5H, m); MS: *m/z* 146 (M^+).

2-benzylamino-2-phenylacetonitrile (3.74 g, 90% yield); IR (neat): 3322, 2227 (cm^{-1}); ^{1}H-NMR: 2.10 (1H, br s), 3.93 (1H, d, *J*=13.0), 4.08 (1H, d, *J*=13.0), 4.76 (1H, s), 7.20-7.60 (10H, m); MS: *m/z* 208 (M^+).

2-benzylamino-2-(4-methylphenyl)acetonitrile (4.22 g, 95% yield); IR (neat): 3320, 2228 (cm^{-1}); ^{1}H-NMR: 1.85 (1H, br s), 2.32 (3H, s), 3.93 (1H, d, *J*=13.2), 4.05 (1H, d, *J*=13.2), 4.70 (1H, s), 7.15-7.40 (9H, m); MS: *m/z* 222 (M^+).

2-benzylamino-2-(4-methoxyphenyl)acetonitrile (4.84 g, 96% yield); IR (neat): 3321, 2249 (cm^{-1}); ^{1}H-NMR: 1.65 (1H, br s), 3.78 (1H, d, *J*=12.8), 3.81 (3H, s), 3.95 (1H, d, *J*=12.8), 4.65 (1H, s), 6.80-7.90 (9H, m); MS: *m/z* 252 (M^+).

2-benzylamino-2-(4-chlorophenyl)acetonitrile (4.60 g, 95% yield); IR (neat): 3322, 2225 (cm^{-1}); ^{1}H-NMR: 1.95 (1H, br s), 3.90 (1H, d, *J*=13.6), 4.07 (1H, d, *J*=13.6), 4.72 (1H, s), 7.30-7.50 (9H, m); MS: *m z* 242 (M^+).

General procedure for the preparation of 2-nitrobenzamides 2a,b. A solution of *N*-phenyl-2-nitrobenzamide (2.42 g, 10 mmol) or *N*-phenyl-5-chloro-2-nitrobenzamide (2.76 g, 10 mmol) in dry acetone (50 mL) was treated with potassium carbonate (4.14 g, 30 mmol) and benzyltriethylammonium chloride (0.57 g, 2.5 mmol). Chloroacetonitrile (0.75 g, 10 mmol) in dry acetone (2 mL) was added, and the reaction mixture was refluxed for 5 h. The undissolved material was filtered off, the organic layer was washed with water (50 mL) and then dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was crystallised from diisopropyl ether affording pure **2a,b**.

N-Phenyl-*N*-cyanomethyl-2-nitrobenzamide **2a** (2.28 g, 81% yield) as pale yellow solid having m.p. 126°C; IR (nujol): 3290, 1625 (cm^{-1}); ^{1}H-NMR: 4.80 (2H, s), 7.15-7.95 (9H, m); MS: *m/z* 281 (M^+). Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.04; H, 3.94; N, 14.95. Found: C, 64.10; H, 3.99; N, 15.02.

2b (2.43 g, 77% yield) as yellow solid having m.p. 120°C; IR (nujol): 3260, 1655 (cm^{-1}); ^{1}H-NMR: 4.80 (2H, s), 7.15-7.90 (8H, m); MS: *m/z* 315 (M^+). Anal. Calcd for $C_{15}H_{10}ClN_3O_3$: C, 57.14; H, 3.20; Cl, 11.10; N, 13.33. Found: C, 57.20; H, 3.22; Cl, 11.06; N, 13.28.

General procedure for the preparation of 2-nitrobenzamides 2c-i. A solution of 2-nitrobenzoyl chloride (1.85 g, 10 mmol) or 5-chloro-2-nitrobenzoyl chloride (2.19 g, 10 mmol) in dry toluene (50 mL) was

treated with potassium carbonate (3.45 g, 25 mmol). The proper 2-substituted 2-benzylaminoacetonitrile (10 mmol) in dry toluene (3 mL) was added, and the reaction mixture was refluxed for 5 h. The undissolved material was filtered off, the organic layer was washed with water (50 mL) and then dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was crystallised from diisopropyl ether affording pure **2c-i**.

N-Benzyl-*N*-cyanomethyl-2-nitrobenzamide **2c** (2.36 g, 80% yield) as pale yellow solid having m.p. 105°C; IR (nujol): 3270, 2250, 1650 (cm^{-1}); ^{1}H-NMR: 4.38 (2H, s), 4.44 (2H, s), 7.20-8.28 (9H, m); MS: *m/z* 295 (M^+). Anal. Calcd for $C_{16}H_{13}N_3O_3$: C, 65.06; H, 4.44; N, 14.24. Found: C, 65.00; H, 4.41; N, 14.32.

2d (0.92 g, 28% yield) as pale yellow solid having m.p. 98°C; IR (nujol): 3245, 2240, 1655 (cm^{-1}); ^{1}H-NMR: 4.36 (2H, s), 4.43 (2H, s), 7.20-8.30 (9H, m); MS: *m/z* 329 (M^+). Anal. Calcd for $C_{16}H_{12}ClN_3O_3$: C, 58.35; H, 3.68; Cl, 10.63; N, 12.77. Found: C, 58.31; H, 3.71; Cl, 10.70; N, 12.85.

2e (1.45 g, 44% yield) as white solid having m.p. 48°C; IR (nujol): 3250, 2247, 1655 (cm^{-1}); ^{1}H-NMR: 1.67 (3H, d, *J*=7.1), 4.28 (1H, d, *J*=15.2), 4.52 (1H, d, *J*=15.2), 4.58 (1H, q, *J*=7.1), 7.02-8.22 (9H, m); MS: *m/z* 309 (M^+). Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.58. Found: C, 65.92; H, 4.93; N, 13.64.

2f (0.74 g, 20% yield) as white solid having m.p. 137°C; IR (nujol): 3240, 2240, 1650 (cm^{-1}); ^{1}H-NMR: 4.10 (1H, d, *J*=15.0), 4.30 (1H, d, *J*=15.0), 5.70 (1H, s), 6.75-8.20 (14H, m); MS: *m/z* 371 (M^+). Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 71.11; H, 4.63; N, 11.39.

2g (1.54 g, 40% yield) as white solid having m.p. 159°C; IR (nujol): 3250, 2240, 1650 (cm^{-1}); ^{1}H-NMR: 2.40 (3H, s), 4.15 (1H, d, *J*=15.3), 4.27 (1H, d, *J*=15.3), 5.68 (1H, s), 6.80-8.15 (13H, m); MS: *m/z* 385 (M^+). Anal. Calcd for $C_{23}H_{19}N_3O_3$: C, 71.68; H, 4.97; N, 10.90. Found: C, 71.60; H, 4.93; N, 10.82.

2h (1.48 g, 37% yield) as pale yellow solid having m.p. 111°C; IR (nujol): 3250, 2240, 1645 (cm^{-1}); ^{1}H-NMR: 3.85 (3H, s), 4.20 (1H, d, *J*=15.1), 4.30 (1H, d, *J*=15.1), 5.65 (1H, s), 6.60-8.20 (13H, m); MS: *m/z* 401 (M^+). Anal. Calcd for $C_{23}H_{19}N_3O_4$: C, 68.80; H, 4.77; N, 10.47. Found: C, 68.89; H, 4.73; N, 10.52.

2i (0.36 g, 9% yield) as pale yellow solid having m.p. 134°C; IR (nujol): 3250, 2250, 1645 (cm^{-1}); ^{1}H-NMR: 4.20 (1H, d, *J*=15.4), 4.26 (1H, d, *J*=15.4), 5.65 (1H, s), 6.90-8.15 (13H, m); MS: *m/z* 405 (M^+). Anal. Calcd for $C_{22}H_{16}ClN_3O_3$: C, 65.11; H, 3.93; Cl, 8.74; N, 10.35. Found: C, 65.06; H, 3.90; Cl, 8.85; N, 10.42.

General procedure for the preparation of (2-aminocarbonyl)anilines 3. A solution of **2** (10 mmol) in ethanol (40 mL) and 20% aqueous acetic acid (7.5 mL) was treated with iron dust (4.4.7 g, 80 mmol). The mixture was refluxed for 2.5 h. The undissolved material was filtered off and the solvent was removed under reduced pressure. The residue was taken up with ethyl acetate (80 mL) and the organic solution was washed firstly with 5% aqueous sodium hydrogencarbonate (20 mL), then with water (50 mL). The organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. Crystallisation from diisopropyl ether gave solid **7** in the analytically pure state. The mother liquor was evaporated giving **3** as undistillable oils not analytically pure.

N-Phenyl-*N*-cyanomethyl-2-aminobenzamide **3a** (1.26 g, 50% yield); IR (neat): 3460, 3360, 3250, 2250, 1625 (cm^{-1}); ^{1}H-NMR: 4.68 (2H, s), 4.82 (2H, br s), 6.10-7.90 (9H, m); MS: *m/z* 251 (M^+).

3b (0.20 g, 7% yield); IR (neat): 3470, 3380, 3240, 2240, 1620 (cm^{-1}); ^{1}H-NMR: 4.60 (2H, s), 4.87 (2H, br s), 6.40-7.30 (8H, m); MS: *m/z* 285 (M^+).

3c (0.93 g, 35% yield); IR (neat): 3460, 3370, 3240, 2250, 1620 (cm^{-1}); ^{1}H-NMR: 4.22 (2H, s), 4.46 (2H, br s), 4.75 (2H, s), 6.70-7.40 (9H, m); MS: *m/z* 265 (M^+).

3d (1.47 g, 49% yield); IR (neat): 3460, 3365, 3235, 2245, 1625 (cm^{-1}); ^{1}H-NMR: 4.20 (2H, s), 4.48 (2H, br s), 4.70 (2H, s), 6.65-7.35 (8H, m); MS: *m/z* 299 (M^+).

3e (1.26 g, 45% yield); IR (neat): 3460, 3370, 3245, 2245, 1620 (cm^{-1}); ^{1}H-NMR: 1.48 (3H, d, *J*=7.1), 4.48 (2H, br s), 4.60 (1H, d, *J*=15.7), 4.88 (1H, d, *J*=15.7), 5.08 (1H, q, *J*=7.1), 6.68-7.35 (9H, m); MS: *m/z* 279 (M^+).

3f (0.68 g, 20% yield); IR (neat): 3460, 3360, 3250, 2250, 1620 (cm^{-1}); ^{1}H-NMR: 4.23 (1H, d, *J*=15.7), 4.38 (2H, br s), 4.75 (1H, d, *J*=15.7), 6.43 (1H, s), 6.65-7.30 (14H, m); MS: *m/z* 341 (M^+).

3g (1.17 g, 33% yield); IR (neat): 3460, 3370, 3250, 2250, 1620 (cm^{-1}); ^{1}H-NMR: 2.36 (3H, s), 4.22 (1H, d, *J*=15.8), 4.46 (2H, br s), 4.79 (1H, d, *J*=15.8), 6.45 (1H, s), 6.68-7.35 (14H, m); MS: *m/z* 355 (M^+).

3h (2.34 g, 63% yield); IR (neat): 3460, 3370, 3250, 2245, 1615 (cm^{-1}); ^{1}H-NMR: 3.84 (3H, s), 4.23 (1H, d, *J*=15.4), 4.36 (2H, br s), 4.76 (1H, d, *J*=15.4), 6.43 (1H, s), 6.70-7.30 (13H, m); MS: *m/z* 371 (M^+).

3i (2.25 g, 60% yield); IR (neat): 3460, 3370, 3250, 2250, 1620 (cm^{-1}); ^{1}H-NMR: 4.28 (1H, d, *J*=15.6), 4.36 (2H, br s), 4.75 (1H, d, *J*=15.6), 6.44 (1H, s), 6.70-7.30 (13H, m); MS: *m/z* 375 (M^+).

4-Phenyl-3*H*-1,4-benzodiazepine-2,5-dione **7a** (0.76 g, 30% yield) as white solid having m.p. 140°C; IR (nujol): 3240, 1700, 1620 (cm^{-1}); ^{1}H-NMR: 4.30 (2H, s), 6.70-8.00 (9H, m), 8.50 (1H, br s); MS: *m z* 252 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.48; H, 4.83; N, 11.11.

7b (1.00 g, 35% yield) as white solid having m.p. 151°C; IR (nujol): 3245, 1690, 1630 (cm^{-1}); ^{1}H-NMR: 4.28 (2H, s), 6.70-7.40 (8H, m), 8.54 (1H, br s); MS: *m/z* 286 (M^+). Anal. Calcd for $C_{15}H_{11}ClN_2O_2$: C, 62.84; H, 3.87; Cl, 12.37; N, 9.77. Found: C, 62.93; H, 3.90; Cl, 12.46; N, 9.82.

7c (0.82 g, 31% yield) as white solid having m.p. 163°C; IR (nujol): 3245, 1700, 1625 (cm^{-1}); ^{1}H-NMR: 3.78 (2H, s), 4.87 (2H, s), 6.95-8.05 (9H, m), 8.75 (1H, br s); MS: *m/z* 266 (M^+). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.11; H, 5.34; N, 10.60.

7d (1.32 g, 44% yield) as white solid having m.p. 175°C; IR (nujol): 3240, 1690, 1640 (cm^{-1}); ^{1}H-NMR: 3.80 (2H, s), 4.85 (2H, s), 6.90-7.40 (8H, m), 8.60 (1H, br s); MS: *m/z* 300 (M^+). Anal. Calcd for $C_{16}H_{13}ClN_2O_2$: C, 63.90; H, 4.36; Cl, 11.79; N, 9.31. Found: C, 63.97; H, 4.39; Cl, 11.86; N, 9.40.

7e (1.12 g, 40% yield) as white solid having m.p. 149°C; IR (nujol): 3240, 1690, 1620 (cm^{-1}); ^{1}H-NMR: 1.50 (3H, d, *J*=7.1), 4.28 (1H, q, *J*=7.1), 4.76 (2H, s), 6.90-8.10 (9H, m), 8.50 (1H, br s); MS: *m z* 280 (M^+). Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.87; H, 5.80; N, 9.95.

7f (0.27 g, 8% yield) as white solid having m.p. 198°C; IR (nujol): 3250, 1690, 1620 (cm^{-1}); ^{1}H-NMR: 4.32 (1H, d, *J*=13.8), 4.98 (1H, s), 5.80 (1H, d, *J*=13.8), 6.70-7.70 (14H, m), 8.65 (1H, br s); MS: *m/z* 342 (M^+). Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.23; H, 5.30; N, 8.24.

7g (1.25 g, 35% yield) as white solid having m.p. 185°C; IR (nujol): 3270, 1685, 1625 (cm^{-1}); ^{1}H-NMR: 2.12 (3H, s), 4.25 (1H, d, *J*=15.3), 4.89 (1H, s), 5.86 (1H, d, *J*=15.3), 6.70-7.70 (14H, m), 8.60 (1H, br s); MS: *m/z* 356 (M^+). Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.48; H, 5.63; N, 7.90.

7h (1.19 g, 32% yield) has white solid having m.p. 210°C; IR (nujol): 3265, 1685, 1630 (cm^{-1}); ^{1}H-NMR: 3.64 (3H, s), 4.26 (1H, d, *J*=14.5), 4.90 (1H, s), 5.90 (1H, d, *J*=14.5), 6.70-7.70 (13H, m), 8.55 (1H, br s); MS: *m/z* 372 (M^+). Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.16; H, 5.42; N, 7.53. Found: C, 74.21; H, 5.45; N, 7.58.

7i (1.43 g, 38% yield) as white solid having m.p. 238°C; IR (nujol): 3270, 1680, 1630 (cm^{-1}); ^{1}H-NMR: 4.28 (1H, d, *J*=14.5), 4.87 (1H, s), 5.85 (1H, d, *J*=14.5), 6.70-7.70 (13H, m), 8.50 (1H, br s); MS: *m/z* 376 (M^+). Anal. Calcd for $C_{22}H_{17}ClN_2O_2$: C, 70.12; H, 4.55; Cl, 9.41; N, 7.43. Found: C, 70.07; H, 4.52; Cl, 9.52; N, 7.51.

General procedure for the preparation of hydrazonoyl chlorides 4. A solution of **3** (7.5 mmol) in 6M hydrochloric acid (6.5 mL) and methanol (8 mL) was treated with sodium nitrite (0.73 g, 10.5 mmol) under vigorous stirring and ice cooling. After 30 min, the cold mixture was adjusted to pH 5 with sodium acetate and cold methyl 2-chloroacetoacetate (1.13 g, 7.5 mmol) in methanol (1.5 mL) was added dropwise. The mixture was stirred under cooling for 4 h, then at room temperature for 15 h. The solvent was partly removed under reduced pressure, and the residue was taken up with diethylether (75 mL). The organic layer was washed firstly with aqueous sodium hydrogencarbonate (25 mL), then with water (50 mL), and dried over sodium sulfate. The solvent was evaporated and the residue was crystallised from diisopropyl ether giving **4** in the analytically pure form.

N-Cyanomethyl-*N*-phenyl-2-[2-(1-chloro-2-methoxy-2-oxoethylidene)hydrazino]benzamide **4a** (1.97 g, 71% yield) as pale yellow solid having m.p. 120°C; IR (nujol): 3260, 2360, 1725, 1645 (cm^{-1}); ^{1}H-NMR: 3.92 (3H, s), 4.75 (2H, s), 6.50-7.70 (9H, m), 10.52 (1H, br s); MS: *m/z* 370 (M^+). Anal. Calcd for $C_{18}H_{15}ClN_4O_3$: C, 58.31; H, 4.08; Cl, 9.56; N, 15.11. Found: C, 58.36; H, 4.11; Cl, 9.63; N, 15.07.

4b (1.27 g, 42% yield) as yellow solid having m.p. 161°C; IR (nujol): 3265, 2370, 1730, 1645 (cm^{-1}); ^{1}H-NMR: 3.93 (3H, s), 4.72 (2H, s), 6.85-7.60 (8H, m), 10.46 (1H, br s); MS: *m/z* 404 (M^+). Anal. Calcd for $C_{18}H_{14}Cl_2N_4O_3$: C, 53.35; H, 3.48; Cl, 17.50; N, 13.83. Found: C, 53.31; H, 3.52; Cl, 17.58; N, 13.90.

4c (2.59 g, 90% yield) as yellow solid having m.p. 146°C; IR (nujol): 3270, 2250, 1735, 1640 (cm^{-1}); ^{1}H-NMR: 3.93 (3H, s), 4.25 (2H, s), 4.79 (2H, s), 7.00-7.64 (9H, m), 10.40 (1H, br s); MS: *m/z* 384 (M^+). Anal. Calcd for $C_{19}H_{17}ClN_4O_3$: C, 59.36; H, 4.46; Cl, 9.10; N, 14.58. Found: C, 59.41; H, 4.42; Cl, 9.17; N, 14.63.

4d (2.41 g, 77% yield) as yellow solid having m.p. 150°C; IR (nujol): 3270, 2250, 1740, 1640 (cm^{-1}); ^{1}H-NMR: 3.92 (3H, s), 4.24 (2H, s), 4.76 (2H, s), 7.20-7.68 (8H, m), 9.78 (1H, br s); MS: *m/z* 418 (M^+). Anal.

Calcd for $C_{19}H_{16}Cl_2N_4O_3$: C, 54.54; H, 3.86; Cl, 16.73; N, 13.40. Found: C, 54.59; H, 3.90; Cl, 16.62; N, 13.44.

4e (1.34 g, 45% yield) as yellow solid having m.p. 95°C; IR (nujol): 3270, 2250, 1735, 1640 (cm^{-1}); ^{1}H-NMR: 1.50 (3H, d, *J*=7.3), 3.90 (3H, s), 4.54 (1H, d, *J*=15.8), 4.87 (1H, d, *J*=15.8), 5.03 (1H, q, *J*=7.3), 6.85-7.67 (9H, m), 9.65 (1H, br s); MS: *m/z* 398 (M^+). Anal. Calcd for $C_{20}H_{19}ClN_4O_3$: C, 60.28; H, 4.81; Cl, 8.78; N, 14.07. Found: C, 60.31; H, 4.85; Cl, 8.85; N, 14.00.

4f (1.48 g, 64% yield) as pale yellow solid having m.p. 64°C; IR (nujol): 3270, 2245, 1740, 1635 (cm^{-1}); ^{1}H-NMR: 3.93 (3H, s), 4.38 (1H, d, *J*=15.6), 4.78 (1H, d, *J*=15.6), 6.54 (1h, s), 6.70-7.70 (14H, m), 9.56 (1H, br s); MS: *m/z* 460 (M^+). Anal. Calcd for $C_{25}H_{21}ClN_4O_3$: C, 65.20; H, 4.60; Cl, 7.60; N, 12.17. Found: C, 65.11; H, 4.56; Cl, 7.63; N, 12.21.

4g (1.71 g, 48% yield) as pale yellow solid having m.p. 59°C; IR (nujol): 3270, 2250, 1740, 1640 (cm^{-1}); ^{1}H-NMR: 2.36 (3H, s), 3.84 (3H, s), 4.35 (1H, d, *J*=15.0), 4.68 (1H, d, *J*=15.0), 6.51 (1H, s), 6.95-7.60 (13H, m), 9.56 (1H, br s); MS: *m/z* 474 (M^+). Anal. Calcd for $C_{26}H_{23}Cl_2N_4O_3$: C, 65.80; H, 4.89; Cl, 7.38; N, 11.81. Found: C, 65.85; H, 4.92; Cl, 7.46; N, 11.89.

4h (3.31 g, 90% yield) as pale yellow solid having m.p. 47°C; IR (nujol): 3270, 2250, 1730, 1640 (cm^{-1}); ^{1}H-NMR: 3.79 (3H, s), 3.93 (3H, s), 4.39 (1H, d, *J*=15.9), 4.69 (1H, d, *J*=15.9), 6.50 (1H, s), 6.75-7.65 (13H, m), 9.59 (1H, br s); MS: *m/z* 490 (M^+). Anal. Calcd for $C_{26}H_{23}ClN_4O_4$: C, 63.33; H, 4.73; Cl, 7.13; N, 11.43. Found: C, 63.29; H, 4.75; Cl, 7.20; N, 11.51.

4i (2.33 g, 63% yield) as yellow solid having m.p. 80°C; IR (nujol): 3270, 2245, 1735, 1640 (cm^{-1}); ^{1}H-NMR: 3.92 (3H, s), 4.44 (1H, d, *J*=15.2), 4.67 (1H, d, *J*=15.2), 6.52 (1H, s), 6.95-7.60 (13H, m), 9.58 (1H, br s); MS: *m/z* 494 (M^+). Anal. Calcd for $C_{25}H_{20}Cl_2N_4O_3$: C, 60.72; H, 4.08; Cl, 14.15; N, 11.34. Found: C, 60.77; H, 4.11; Cl, 14.23; N, 11.40.

General procedure for the reaction of hydrazonoyl chlorides 4 with silver carbonate in dioxane. A solution of **4** (4 mmol) in dry dioxane (200 mL) was treated with silver carbonate (2.21 g, 8 mmol). The mixture was stirred in the dark at room temperature for the time indicated in the Table. The undissolved material was filtered off, the solvent was evaporated and the residue was chromatographed on a silica gel column (entries **a**,**b**, **d-g**) or crystallised (entries **c**,**h**,**i**). Eluents and isolation yields are collected in the Table. [1,2,4]Triazolo [1,5-*a*][1,4]benzodiazepin-6-ones **6** were obtained in analytical pure state by recrystallisation from diisopropyl ether.

Methyl 5,6-dihydro-6oxo-5-phenyl-4*H*-[1,2,4]triazolo[1,5-*a*][1,4]benzodiazepine-2-carboxylate **6a** (0.72 g, 54% yield) as white solid having m.p. 143°C; IR (nujol): 1740, 1650 (cm^{-1}); ^{1}H-NMR: 4.05 (3H, s), 4.96 (2H, s), 7.30-8.20 (9H, m); MS: *m/z* 334 (M^+). Anal. Calcd for $C_{18}H_{14}N_4O_3$: C, 64.54; H, 4.22; N, 16.76. Found: C, 64.58; H, 4.25; N, 16.80.

6b (0.81 g, 55% yield) as pale yellow solid having m.p. 165°C; IR (nujol): 1742, 1656 (cm^{-1}); ^{1}H-NMR: 4.05 (3H, s), 4.94 (2H, s), 7.28-8.14 (8H, m); MS: *m/z* 368 (M^+). Anal. Calcd for $C_{18}H_{13}ClN_4O_3$: C, 58.68; H, 3.56; Cl, 9.50; N, 15.22. Found: C, 58.61; H, 3.60; Cl, 9.58; N, 15.27.

6c (1.32 g, 95% yield) as white solid having m.p. 63°C; IR (nujol): 1740, 1640 (cm^{-1}); ^{1}H-NMR: 4.03 (3H, s), 4.45 (2H, s), 4.86 (2H, s), 7.20-8.20 (9H, m); MS: *m/z* 348 (M^+). Anal. Calcd for $C_{19}H_{16}N_4O_3$: C, 65.49; H, 4.63; N, 16.09. Found: C, 65.55; H, 4.66; N, 16.13.

6d (1.30 g, 85% yield) as white solid having m.p. 70°C; IR (nujol): 1740, 1642 (cm^{-1}); ^{1}H-NMR: 4.02 (3H, s), 4.43 (2H, s), 4.82 (2H, s), 7.20-8.20 (8H, m); MS: *m/z* 382 (M^+). Anal. Calcd for $C_{19}H_{15}ClN_4O_3$: C, 59.67; H, 3.96; Cl, 9.15; N, 14.66. Found: C, 59.61; H, 4.00; Cl, 9.18; N, 14.73.

6e (0.94 g, 65% yield) as white solid having m.p. 63°C; IR (nujol): 1738, 1640 (cm^{-1}); ^{1}H-NMR: 1.08 (3H, d, *J*=6.2), 4.02 (3H, s), 4.36 (1H, d, *J*=15.0), 5.03 (1H, q, *J*=6.2), 5.36 (1H, d, *J*=15.0), 7.20-8.20 (9H, m); MS: *m/z* 362 (M^+). Anal. Calcd for $C_{20}H_{18}N_4O_3$: C, 66.27; H, 5.01; N, 15.47. Found: C, 66.33; H, 4.96; N, 15.55.

6f (1.19 g, 70% yield) as pale yellow solid having m.p. 124°C; IR (nujol): 1740, 1640 (cm^{-1}); ^{1}H-NMR: 4.08 (3H, s), 4.93 (1H, d, *J*=14.4), 5.18 (1H, d, *J*=14.4), 6.25 (1H, s), 7.00-7.90 (14H, m); MS: *m/z* 424 (M^+). Anal. Calcd for $C_{25}H_{20}N_4O_3$: C, 70.73; H, 4.75; N, 13.21. Found: C, 70.66; H, 4.72; N, 13.26.

6g (1.31 g, 75% yield) as white solid having m.p. 118°C; IR (nujol): 1742, 1638 (cm^{-1}); ^{1}H-NMR: 2.09 (3H, s), 4.07 (3H, s), 4.92 (1H, d, *J*=14.4), 5.15 (1H, d, *J*=14.4), 6.21 (1H, s), 7.05-7.93 (13H, m); MS: *m/z* 438 (M^+). Anal. Calcd for $C_{26}H_{22}N_4O_3$: C, 71.21; H, 5.06; N, 12.78. Found: C, 71.17; H, 5.02; N, 12.77.

6h (1.27 g, 70% yield) as white solid having m.p. 105°C; IR (nujol): 1740, 1640 (cm^{-1}); ^{1}H-NMR: 3.60 (3H, s), 4.07 (3H, s), 4.88 (1H, d, *J*=14.4), 5.15 (1H, d, *J*=14.4), 6.19 (1H, s), 7.05-7.92 (13H, m); MS: *m/z* 454 (M^+). Anal. Calcd for $C_{26}H_{22}N_4O_4$: C, 68.70; H, 4.88; N, 12.33. Found: C, 68.66; H, 4.84; N, 12.37.

6i (1.28 g, 70% yield) as pale yellow solid having m.p. 130°C; IR (nujol): 1740, 1640 (cm^{-1}); ^{1}H-NMR: 4.07 (3H, s), 4.80 (1H, d, *J*=14.3), 5.21 (1H, d, *J*=14.3), 6.20 (1H, s), 6.58-7.90 (13H, m); MS: *m/z* 458 (M^+). Anal. Calcd for $C_{25}H_{19}ClN_4O_3$: C, 65.49; H, 4.18; Cl, 7.63; N, 12.23. Found: C, 65.56; H, 4.13; Cl, 7.70; N, 12.30.

Preparation of methyl 5,6-dihydro-6-oxo-4*H*-[1,2,4]triazolo[1,5-*a*][1,4]benzodiazepine-2-carboxylate 8. A solution of **6c** (0.50 g, 1.5 mmol) in 95% formic acid (1.5 mL) was stirred at room temperature for 2 h, and then at 50°C for 2 h. The mixture was taken up with dichloromethane (15 mL) and washed with water (25 mL); the organic layer was dried over sodium sulfate and the solvent was evaporated. Crystallisation from diisopropyl ether gave pure **8** (0.31 g, 80% yield) as white solid having m.p. 187°C; IR (nujol): (cm^{-1}); ^{1}H-NMR: 3.89 (3H, s), 4.86 (2H, s), 6.92-7.10 (4H, m), 9.11 (1H, br s); MS: *m/z* 258 (M^+). Anal. Calcd for $C_{12}H_{10}N_4O_3$: C, 55.80; H, 3.91; N, 21.70. Found: C, 55.73; H, 3.87; N, 21.77.

Preparation of 1,4-benzodiazepine-2,5-dione 7a. A solution of **2a** (1.40 g, 5 mmol) in ethanol (25 mL) and 30% aqueous ammonium hydroxide (3.0 mL) was treated with iron (II) sulfate heptahydrate (4.17 g, 15 mmol). The mixture was refluxed for 1.5 h. The undissolved material was filtered off and the solvent was removed under reduced pressure. The residue was taken up with dichloromethane (80 mL) and the organic

solution was washed with water (50 mL). The organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. Crystallisation from diisopropyl ether gave pure **7a** (1.21 g, 96% yield) as white solid having m.p. 140°C; IR (nujol): 3240, 1700, 1620 (cm^{-1}); ^{1}H-NMR: 4.30 (2H, s), 6.70-8.00 (9H, m), 8.50 (1H, br s); MS: *m/z* 252 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.44; H, 4.80; N, 11.14.

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