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Synthesis and Modification of Hetero-Fused Pyrazoles Derived from Methyl 1-(2-Oxo-2-phenylethyl)-3-phenyl-1*H*-pyrazole-5-carboxylate

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Abstract—A modified procedure has been proposed for the synthesis of 2,7-diphenyl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]triazepin-4-one, and the possibility of transformation of the latter to the pyrazolo[1,5-*a*]pyrazine system has been demonstrated. Functionalization of 2,7-diphenyl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]-triazepin-4-one at the 4-position and fusion of a tetrazole or triazole ring at the C^4–N^5 bond have been performed.

Keywords: 5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]triazepin-4-one, pyrazolo[1,5-*a*]pyrazin-4-ol, pyrazolo-[1,5-*a*]pyrazin-4(5*H*)-one, 5-aminopyrazolo[1,5-*a*]pyrazin-4(5*H*)-one, 5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]-triazepine-4-thione, 4-(methylsulfanyl)-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine, 4-(morpholin-4-yl)-8*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine, 4-hydrazinyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine, 7*H*-pyrazolo[5,1-*d*][1,2,4]triazolo-[4,3-*b*][1,2,5]triazepine, 7*H*-pyrazolo[5,1-*d*]tetrazolo[1,5-*b*][1,2,5]triazepine

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Methyl 1-(2-aryl-2-oxoethyl)-1*H*-pyrazole-5-carboxylate derivatives can formally be regarded as 1,5-dicarbonyl compounds which offer great potential for molecular design and synthesis of new fused heterocyclic compounds as candidates for biological screening. In particular, pyrazolo[5,1-*c*][1,4]oxazines and pyrazolo[5,1-*d*][1,2,5]triazepin-4-ones containing an aryl, methyl, or carbohydrazide substituents in the 2-position have been reported [1–3]. 2,7-Diaryl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]triazepin-4-ones were found to inhibit endothelial cell apoptosis [2].

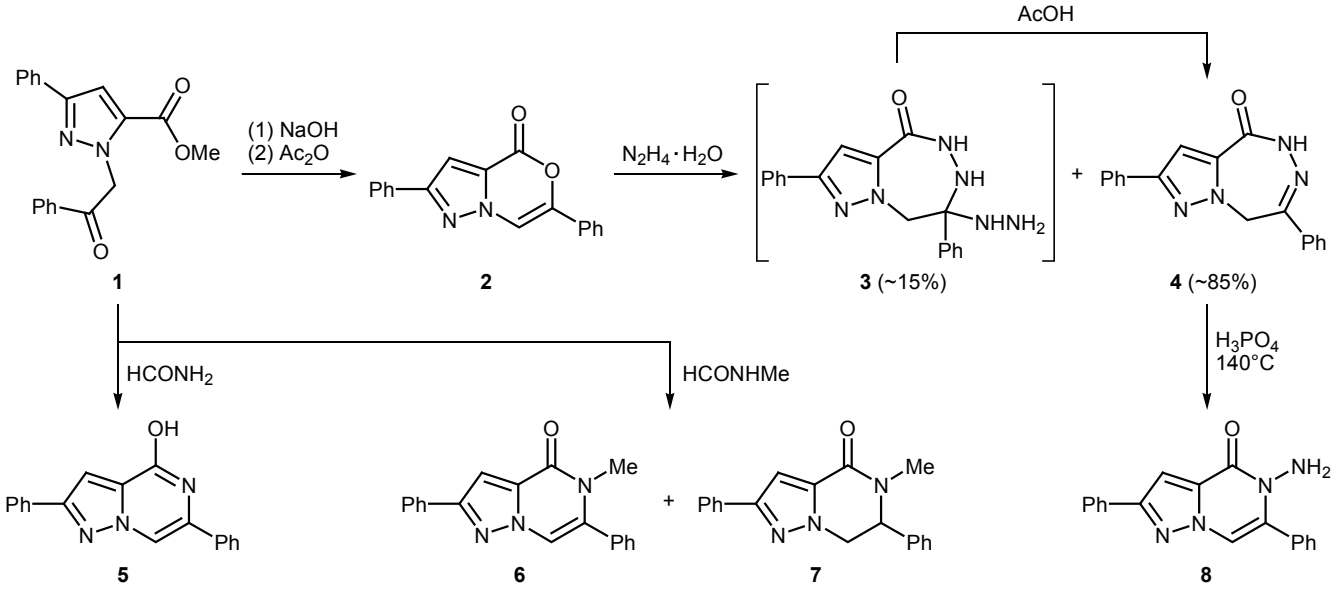
In continuation of our studies on the synthetic potential of methyl 1-(2-oxo-2-phenylethyl)-1*H*-pyrazole-5-carboxylate, the present work was aimed at synthesizing pyrazolo[1,5-*a*]pyrazines, taking into account the ability of 1,5-dicarbonyl compounds to undergo heterocyclization to pyridine derivatives. Pyrazolo-[1,5-*a*]pyrazine derivatives attract much interest as some of them have been found to exhibit anti-HIV-1 activity and be efficient in the prevention and treatment of some hematological diseases and diabetes [4, 5].

Thus, the goal of this work was to study reactions of methyl 1-(2-oxo-2-phenylethyl)-3-phenyl-1*H*-pyrazole-5-carboxylate (**1**) with nitrogen nucleophiles and modify the structure of 2,7-diphenyl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]triazepin-4-one at the seven-membered ring, specifically at the C^4–N^5 bond.

2,7-Diaryl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]-triazepin-4-ones were synthesized for the first time in 68–82% yields by reaction of 2,6-diaryl-4*H*-pyrazolo-[1,5-*a*][1,4]oxazin-4-ones with hydrazine hydrate [1, 2]. We have found that, apart from pyrazolotriazepinone **4**, 7-hydrazinyl-2,7-diphenyl-5,6,7,8-tetrahydro-4*H*-pyrazolo[5,1-*d*][1,2,5]-triazepin-4-on (**3**) is also formed as minor product in the reaction of 2,6-diphenyl-4*H*-pyrazolo[1,5-*a*][1,4]oxazin-4-one (**2**) with hydrazine hydrate and that compound **3** is transformed to **4** on further heating in the presence of acetic acid. These findings prompted us to modify the procedure described in [2]; as a result, the yield of **4** was improved to 96% (Scheme 1).

Like 1,2-diazepinones, 1,2,5-triazepinones are known to undergo ring contraction by the action of hydrochloric acid to give six-membered *N*-aminopyrazine derivatives [6, 7]. However, as we showed previously [3], 1,2,5-triazepinone ring fused to a pyrazole ring did not change on heating in aqueous HCl. On the other hand, by heating pyrazolotriazepinone **4** in 85%

Scheme 1.



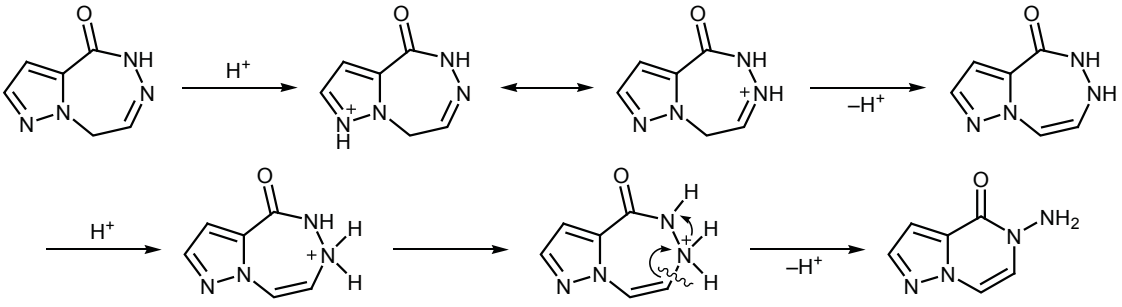
H_3PO_4 at 140°C for 1 h we obtained the corresponding ring contraction product, 5-amino-2,6-diphenylpyrazolo[1,5-*a*]pyrazin-4(5*H*)-one (**8**). This reaction can be regarded as a new method of synthesis of pyrazolo-[1,5-*a*]pyrazine derivatives.

Balci et al. [6] proposed a mechanism for triazepinone ring contraction in 4-methyl-2,5-dihydro-1*H*-pyrolo[2,1-*d*][1,2,5]triazepin-1-one by the action of trace amount of acid present in chloroform. The authors presumed initial protonation of the carbonyl oxygen atom, though protonation of N^3 seemed to be more probable since the N^3 atom possesses the highest electron density. Scheme 2 shows an alternative mechanism for acid-catalyzed triazepine ring contraction in 5,8-dihydro-4*H*-pyrazolo[5,1-*d*][1,2,5]triazepin-4-ones. We believe that initial protonation of the pyrazole nitrogen atom is responsible for the high stability of pyrazolotriazepinone **4** in acid medium in comparison to pyrrolo[2,1-*d*][1,2,5]triazepin-1-one and 2,5-dihydro-1*H*-2,3-benzodiazepin-1-ones [7].

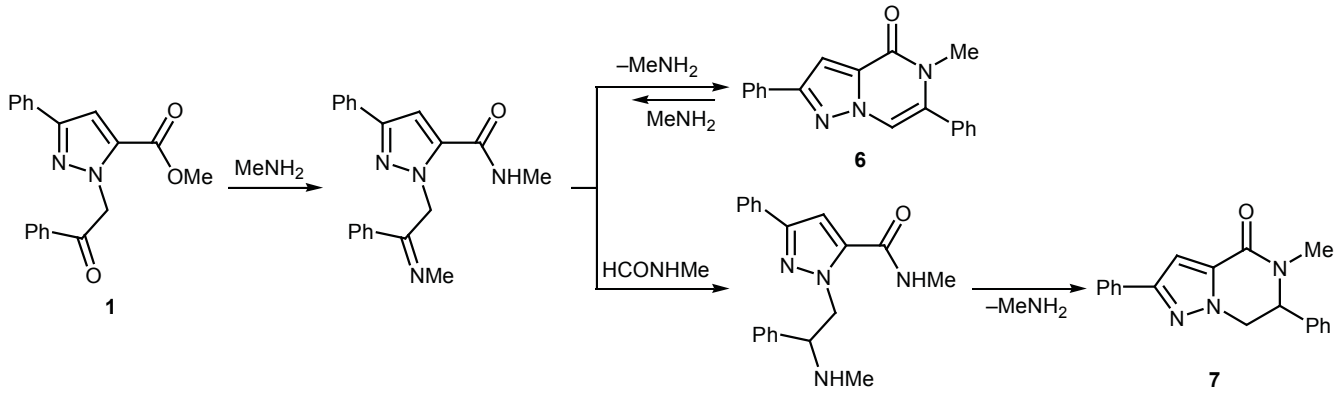
Pyrazolo[1,5-*a*]pyrazines can also be obtained directly from pyrazole **1**. The latter was quantitatively converted to 2,6-diphenylpyrazolo[1,5-*a*]pyrazin-4-ol (**5**) on heating for 1 h in boiling formamide, and compound **5** remained unchanged on further heating. When pyrazole **1** was refluxed in *N*-methylformamide for 1 h, a mixture of 5-methyl-2,6-diphenylpyrazolo-[1,5-*a*]pyrazin-4(5*H*)-one (**6**) and 5-methyl-2,6-diphenyl-6,7-dihydropyrazolo[1,5-*a*]pyrazin-4(5*H*)-one (**7**) at a ratio of ~72:28 was formed. The proportion of **7** increased on further heating, and the ratio **6**:**7** changed to the opposite (~30:70) after 20 h. In fact, this is the result of Leuckart–Wallach reaction. Presumably, the rate of reduction of **6** to **7** is determined by the rate of ring opening of pyrazinone **6**, which is followed by reduction and ring closure to pyrazinone **7** (Scheme 3).

Hetero-fused 1,2,5-triazepinethiones were reported [8] to be more reactive than their oxygen analogs. Therefore, it could be possible to perform their struc-

Scheme 2.

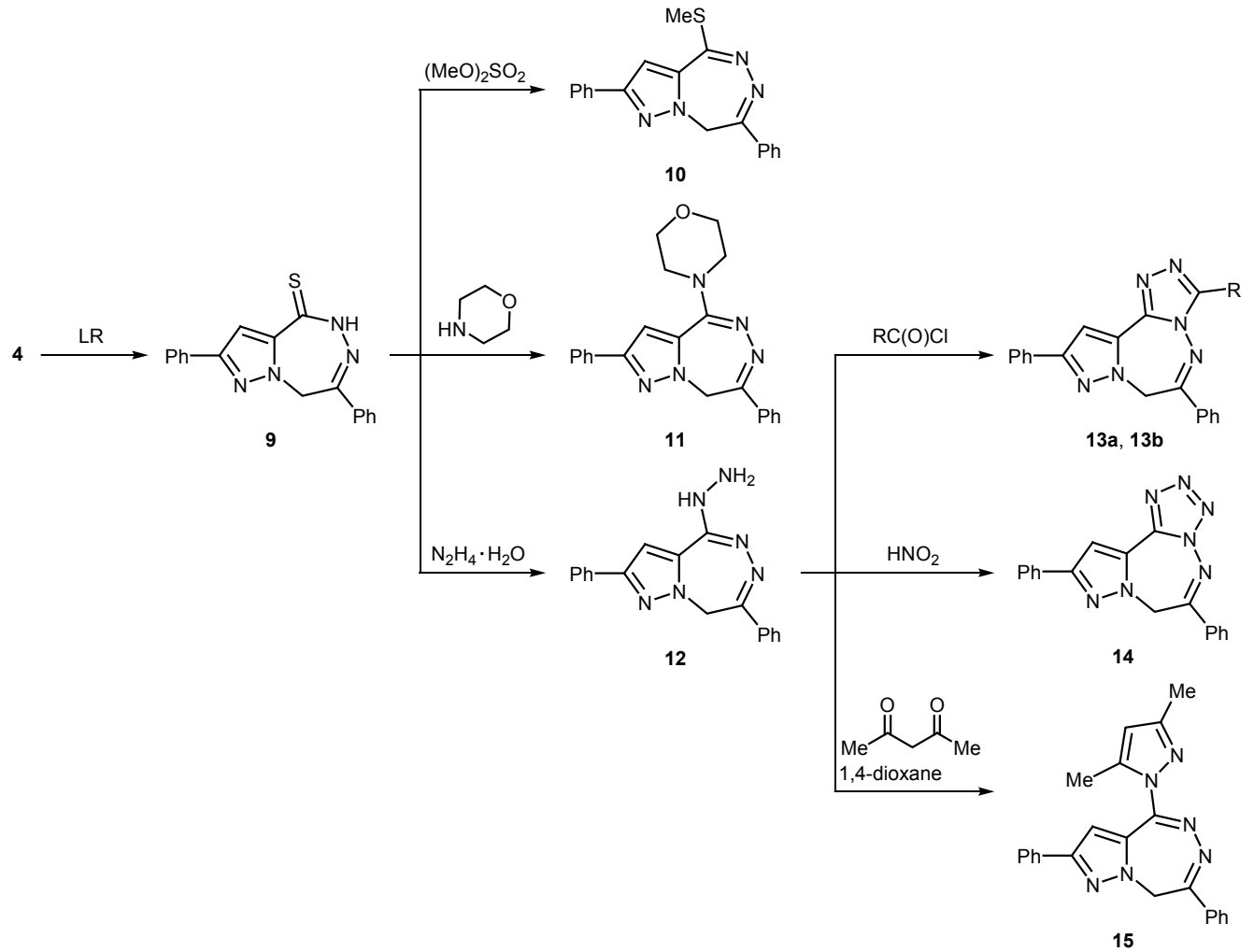


Scheme 3.



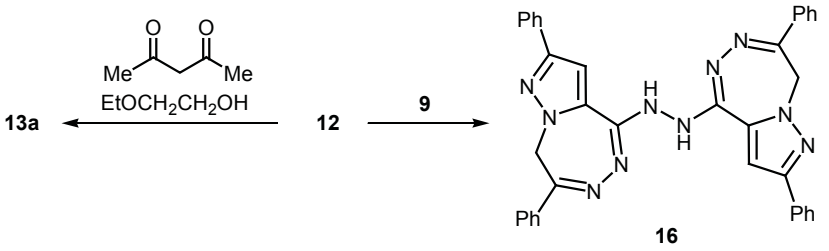
tural modifications at both sulfur atom and C^4–N^5 bond and thus extend the range of pyrazolo[1,2,5]triazepine derivatives. 2,7-Diphenyl-5,8-dihydro-4*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine-4-thione (**9**) was synthesized in high yield by treatment of **4** with Lawesson's reagent (Scheme 4). The alkylation of **9** with dimethyl sulfate gave 4-(methylsulfanyl)-2,7-diphenyl-8*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine (**10**). In the ^{1}H NMR spectrum of **10**, *ortho* protons in the phenyl ring on C^7 appeared as two doublets in the region δ 7.91–8.00 ppm with

Scheme 4.



R = Me (**a**), 4-$MeOC_6H_4$ (**b**); LR stands for Lawesson's reagent.

Scheme 5.



a coupling constant ^3J of 6.8 Hz, indicating their nonequivalence. Protons in the *para* and *meta* positions of the same phenyl substituent resonated as a narrow multiplet at δ 7.45–7.48 ppm.

The sulfur atom in pyrazolotriazepinethione **9** is readily replaced by a secondary amine moiety; for example, 4-(morpholin-4-yl)-2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine (**11**) was obtained in the reaction of **9** with morpholine. The reaction of **9** with hydrazine hydrate afforded 4-hydrazinyl-2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine (**12**), and the latter reacted with acetyl chloride and 4-methoxybenzoyl chloride to produce 3-methyl-6,10-diphenyl-7*H*-pyrazolo[5,1-*d*][1,2,4]triazolo[4,3-*b*][1,2,5]triazepine (**13a**) and 3-(4-methoxyphenyl)-6,10-diphenyl-7*H*-pyrazolo[5,1-*d*][1,2,4]triazolo[4,3-*b*][1,2,5]triazepine (**13b**), respectively (Scheme 4). 6,10-Diphenyl-7*H*-pyrazolo[5,1-*d*]tetrazolo[1,5-*b*][1,2,5]triazepine (**14**) was isolated in the reaction of **12** with sodium nitrite in acetic acid. The condensation of **12** with pentane-2,4-dione in 1,4-dioxane gave 4-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine (**15**) (Scheme 5), whereas the reaction in 2-ethoxyethanol unexpectedly afforded pyrazolotriazolotriazepine **13a**.

These findings may be rationalized assuming that intermediate hydrazone derived from pentane-2,4-dione and hydrazine **12** exists as different tautomers in polar and nonpolar solvent. In 2-ethoxyethanol, ketone cleavage of the pentane-2,4-dione hydrazone is accompanied by closure of triazole ring and elimination of acetone molecule (Scheme 6). Although the basicity of hydrazine **12** is not high, the configuration of nitrogen atoms therein is likely to favor the observed cleavage of pentane-2,4-dione hydrazone.

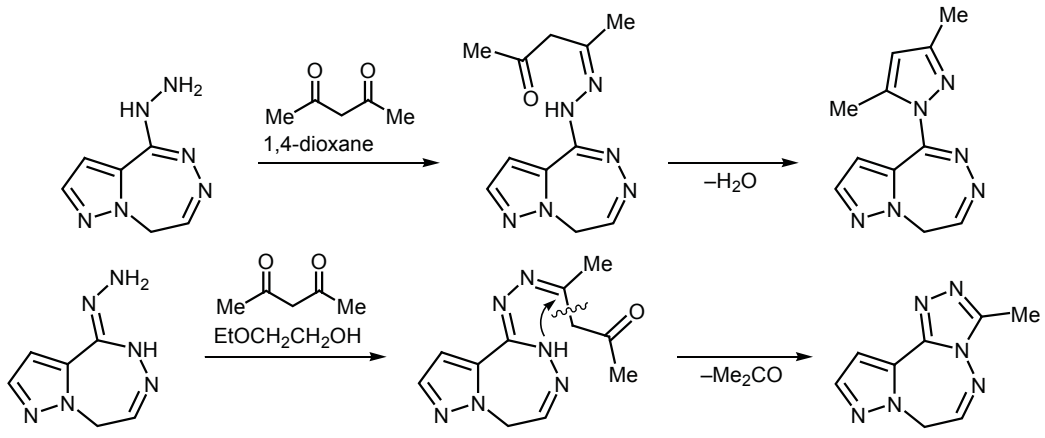
Pyrazolotriazepinethione **9** reacted with hydrazine **12** to give 4,4′-(hydrazine-1,2-diyl)bis(2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine (**16**) (Scheme 5). This should be taken into account while synthesizing compound **12** from thione **9**, and no less than 20 equiv of hydrazine hydrate should be used.

Thus, we have improved the procedure for synthesis of pyrazolotriazepinone **4**, found conditions for ring contraction of the triazepine ring therein, and obtained various derivatives of **4** via modification at C^4 and hetero-fusion to the C^4–N^5 bond.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II spectrometer (Germany) at 400 and 100 MHz, respectively, using DMSO-d_6 as solvent and tetramethylsilane as internal standard. The melting points were measured with a Boetius melting point apparatus and are uncorrected. Commercially available

Scheme 6.



reagents of chemically pure and analytical grades were used.

2,7-Diphenyl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*]-[1,2,5]triazepin-4-one (4). A mixture of 3.35 g (11.63 mmol) of 2,6-diphenyl-4*H*-pyrazolo[5,1-*c*][1,4]-oxazin-4-one (**2**) and 1.2 mL (24.0 mmol) of hydrazine hydrate in 10 mL of 2-ethoxyethanol was refluxed for 4 h. Acetic acid, 1.5 mL, was added to the hot mixture, and the mixture was refluxed for an additional 30 min. After cooling, the mixture was diluted with 80 mL of water under stirring, and the precipitate was filtered off and washed with water. Yield 3.4 g (97%), colorless crystals, mp 227–228°C; published data [2]: mp 230–232°C. ^{1}H NMR spectrum, δ, ppm: 5.53 s (2H, CH_2), 7.27 s (1H, CH), 7.28 t (1H, Ph, *J* = 7.6 Hz), 7.37 t (2H, Ph, *J* = 7.2 Hz), 7.40–7.48 m (3H, Ph), 7.81 d (2H, Ph, *J* = 7.2 Hz), 7.90 d (1H, Ph, *J* = 6.8 Hz), 7.91 d (1H, Ph, *J* = 6.8 Hz), 11.44 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 48.6 (CH_2), 106.6 (CH), 125.2 (2C), 126.6 (2C), 127.7, 128.3 (2C), 128.5 (2C), 130.2, 132.0, 134.3, 137.1, 150.1, 154.4, 157.5 (CO). Found, %: C 71.50; H 4.70; N 18.52; O 5.28. $C_{18}H_{14}N_4O$. Calculated, %: C 71.51; H 4.67; N 18.53; O 5.29.

2,6-Diphenylpyrazolo[1,5-*a*]pyrazin-4-ol (5). A mixture of 0.5 g (1.56 mmol) of compound **1** and 3 mL of formamide was refluxed for 1 h. The mixture was cooled and diluted with 8 mL of water, and the precipitate was filtered off and washed with water. Yield 0.42 g (93%), fine colorless crystals, mp 242–243°C. ^{1}H NMR spectrum, δ, ppm: 7.33 t (1H, Ph, *J* = 6.8 Hz), 7.38 s (1H, CH), 7.40–7.49 m (5H, Ph), 7.73 d (2H, Ph, *J* = 7.2 Hz), 7.91 s (1H, CH), 7.93 d (2H, Ph, *J* = 7.6 Hz), 11.55 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 101.5 (CH), 107.9 (CH), 126.1 (2C), 126.7 (2C), 128.5, 128.9 (2C), 129.0 (3C), 129.2, 129.3, 131.7, 132.5, 134.2, 152.2, 156.12. Found, %: C 75.29; H 4.60; N 14.59; O 5.52. $C_{18}H_{13}N_3O$. Calculated, %: C 75.25; H 4.56; N 14.62; O 5.57.

5-Methyl-2,6-diphenylpyrazolo[1,5-*a*]pyrazin-4(5*H*)-one (6) and 5-methyl-2,6-diphenyl-6,7-dihydropyrazolo[1,5-*a*]pyrazin-4(5*H*)-one (7). A mixture of 0.5 g (1.56 mmol) of compound **1** and 3 mL of *N*-methylformamide was refluxed for 20 h. The mixture was cooled and diluted with 10 mL of water, and the resin-like material was separated by decanting. The product was dissolved in 1 mL of methanol on heating under reflux, and the solution was left overnight. The crystalline solid was filtered off and washed with a small amount of methanol. Yield of **7** 0.19 g (40%), fine colorless crystals, mp 154–156°C. ^{1}H NMR spectrum, δ, ppm: 3.02 s (3H, CH_3), 4.52 d.d (1H, CH_2, *J* = 13.4, 1.2 Hz), 4.80 d.d (1H, CH_2, *J* = 13.4, 5.2 Hz), 5.15 q (1H, CH, *J* = 3.2 Hz), 7.14–7.20 m (3H, Ph, CH), 7.25 t (2H, Ph, *J* = 6.8 Hz), 7.27–7.37 m (4H, Ph), 7.77 d (2H, Ph, *J* = 7.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 33.0 (CH_3), 52.6 (CH_2), 60.7 (CH), 104.0, 125.5 (2C), 126.5 (2C), 128.8 (2C), 129.0, 129.2 (2C), 129.8, 132.7, 135.6, 138.5, 151.0, 157.6. Found, %: C 75.26; H 5.68; N 13.88; O 5.18. $C_{19}H_{17}N_3O$. Calculated, %: C 75.23; H 5.65; N 13.85; O 5.27.

The mother liquor was evaporated to dryness under reduced pressure, 10 mL of heptane was added to the residue, and the mixture was heated to the boiling point with stirring. The hot solution was separated from the undissolved resin and was left overnight. The crystalline solid was filtered off and washed with heptane. Yield of **6** 0.14 g (30%), fine colorless crystals, mp 106–108°C. ^{1}H NMR spectrum, δ, ppm: 3.26 s (3H, CH_3), 7.38–7.44 m (4H, Ph), 7.46–7.55 m (6H, Ph, CH), 7.93 d (2H, Ph, *J* = 6.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 32.0 (CH_3), 101.1, 109.3, 125.5 (2C), 127.9, 128.3 (2C), 128.4 (2C), 129.0, 129.2 (2C), 131.4, 131.7, 131.8, 133.0, 151.7, 154.8. Found, %: C 75.78; H 5.05; N 13.97; O 5.50. $C_{19}H_{15}N_3O$. Calculated, %: C 75.73; H 5.02; N 13.94; O 5.31.

5-Amino-2,6-diphenylpyrazolo[1,5-*a*]pyrazin-4(5*H*)-one (8). A mixture of 0.1 g (0.33 mmol) of **4** and 0.5 mL of 85% H_3PO_4 was heated with stirring to 140°C until complete dissolution. The mixture was kept for 1 h at that temperature, cooled, diluted with 5 mL of water, and adjusted to pH ~9 with 30% aqueous ammonia. An oily material separated and crystallized on grinding. The precipitate was filtered off, dried, and recrystallized from toluene. Yield 0.096 g (96%), fine colorless crystals, mp 138–139°C. ^{1}H NMR spectrum, δ, ppm: 5.43 s (2H, NH_2), 7.34 t (1H, Ph, *J* = 6.8 Hz), 7.38–7.52 m (6H, Ph, CH), 7.57 s (1H, CH), 7.62 t (2H, Ph, *J* = 3.6 Hz), 7.93 d (2H, Ph, *J* = 7.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 101.6, 109.3, 126.2 (3C), 128.1 (2C), 128.6, 128.9 (2C), 130.3 (2C), 132.2, 132.54, 133.0, 133.7, 152.5, 154.7. Found, %: C 71.52; H 4.69; N 18.54; O 5.25. $C_{18}H_{14}N_4O$. Calculated, %: C 71.51; H 4.67; N 18.53; O 5.29.

2,7-Diphenyl-5,8-dihydro-4*H*-pyrazolo[5,1-*d*]-[1,2,5]triazepine-4-thione (9). A mixture of 3.0 g (9.97 mmol) of **4** and 3 g (7.48 mmol) of Lawesson's reagent in 30 mL of anhydrous toluene was refluxed

for 2 h. The solvent was completely removed under reduced pressure, 30 mL of methanol was added to the residue, and the mixture was refluxed for 2 h and left overnight. The precipitate was filtered off and washed with methanol. Yield 1.9 g (60%), fine yellow crystals, mp 159–160°C. ^{1}H NMR spectrum, δ, ppm: 5.55 s (2H, CH_2), 7.25–7.42 m (4H, Ph), 7.45–7.53 m (3H, Ph, CH), 7.79 d (2H, Ph, *J* = 6.8 Hz), 7.97 d (2H, Ph, *J* = 4.0 Hz), 13.13 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 49.4 (CH_2), 110.5 (CH), 125.7 (2C), 127.7 (2C), 128.3, 128.8 (2C), 129.2 (2C), 131.6, 132.4, 133.8, 142.3, 150.8, 158.8, 180.5. Found, %: C 67.92; H 4.45; N 17.57; S 10.06. $C_{18}H_{14}N_4S$. Calculated, %: C 67.90; H 4.43; N 17.60; S 10.07.

4-(Methylsulfanyl)-2,7-diphenyl-8*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine (10). Dimethyl sulfate, 0.19 mL (1.15 mmol), was added with vigorous stirring to a mixture of 0.4 g (1.26 mmol) of compound **9** and 0.1 g (2.52 mmol) of sodium hydroxide in 10 mL of acetone. The mixture was stirred for 1 h at room temperature and diluted with 30 mL of water, and the precipitate was filtered off and washed with water. Yield 0.41 g (98%), fine pale yellow needles, mp 168–169°C. ^{1}H NMR spectrum, δ, ppm: 2.64 s (3H, CH_3), 3.13 s (2H, CH_2), 7.00 s (1H, CH), 7.28 t (1H, Ph, *J* = 7.2 Hz), 7.37 t (2H, Ph, *J* = 7.6 Hz), 7.41–7.48 m (3H, Ph), 7.79 d (2H, Ph, *J* = 7.2 Hz), 7.91–8.00 m (2H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 14.0 (CH_3), 48.9 (CH_2), 103.5 (CH), 125.8 (2C), 127.4 (2C), 128.2, 128.8 (2C), 129.0 (2C), 130.8, 132.5, 134.7, 135.7, 147.3, 151.0, 152.9. Found, %: C 68.67; H 4.88; N 16.86; S 9.59. $C_{19}H_{16}N_4S$. Calculated, %: C 68.65; H 4.85; N 16.85; S 9.65.

4-(Morpholin-4-yl)-2,7-diphenyl-8*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine (11). A mixture of 0.12 g (0.32 mmol) of compound **9** and 0.5 mL of morpholine was refluxed for 1 h. The mixture was cooled, 1 mL of water was added, an oily material separated and crystallized on grinding, and the crystalline solid was filtered off and washed with water. Yield 0.13 g (93%), fine yellow crystals, mp 185–187°C. ^{1}H NMR spectrum, δ, ppm: 3.49–3.56 m (4H, CH_2), 3.64–3.73 m (2H, CH_2), 3.76–3.84 m (2H, CH_2), 4.84 d (1H, CH_2, *J* = 14.4 Hz), 5.64 d (1H, CH_2, *J* = 14.4 Hz), 6.91 s (1H, CH), 7.27 t (2H, Ph, *J* = 7.2 Hz), 7.34 t (2H, Ph, *J* = 7.6 Hz), 7.39–7.46 m (3H, Ph), 7.78 d (2H, Ph, *J* = 7.2 Hz), 7.89 d (2H, Ph, *J* = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 47.5 (2C, CH_2), 47.8 (CH_2), 65.9 (2C, CH_2), 103.1 (CH), 125.3 (2C), 126.4 (2C), 127.6, 128.2 (2C), 128.3 (2C), 129.6, 131.2, 132.3, 135.0, 145.6, 150.3, 153.4. Found, %: C 71.15; H 5.73; N 18.82; O 4.30. $C_{22}H_{21}N_5O$. Calculated, %: C 71.14; H 5.70; N 18.85; O 4.31.

4-Hydrazinyl-2,7-diphenyl-8*H*-pyrazolo-[5,1-*d*][1,2,5]triazepine (12). A mixture of 1.15 g (3.63 mmol) of compound **9** and 3.63 mL (72.55 mmol) of hydrazine hydrate in 19 mL of 2-ethoxyethanol was refluxed with stirring. The mixture was cooled, 80 mL of water and 3 g of sodium chloride were added, and the precipitate was filtered off and washed with water. Yield 1.03 g (90%), fine yellowish needles, mp 110–111°C. ^{1}H NMR spectrum, δ, ppm: 5.40 s (2H, CH_2), 5.67 br.s (2H, NH_2), 6.78 s (1H, CH), 7.21 t (1H, Ph, *J* = 7.2 Hz), 7.31 t (2H, Ph, *J* = 7.6 Hz), 7.34– 7.41 m (3H, Ph, CH), 7.72 d (2H, Ph, *J* = 7.6 Hz), 7.81 d (2H, Ph, *J* = 6.8 Hz), 9.28 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 47.6 (CH_2), 101.9 (CH), 125.1 (2C), 126.0 (2C), 127.2, 128.1, 128.4, 129.4, 132.6, 134.7, 135.2, 137.9, 149.3, 154.8. Found, %: C 68.37; H 5.14; N 26.49. $C_{18}H_{16}N_6$. Calculated, %: C 68.34; H 5.10; N 26.56.

3-Methyl-6,10-diphenyl-7*H*-pyrazolo[5,1-*d*]-[1,2,4]triazolo[4,3-*b*][1,2,5]triazepine dihydrochloride (13a) and 3-(4-methoxyphenyl)-6,10-diphenyl-7*H*-pyrazolo[5,1-*d*][1,2,4]triazolo[4,3-*b*]-[1,2,5]triazepine dihydrochloride (13b) (*general procedure***).** Acetyl chloride, 0.05 mL (0.633 mmol), or 4-methoxybenzoyl chloride, 0.11 mL (0.633 mmol), was added to a solution of 0.1 g (0.316 mmol) of compound **12** in 0.2 mL of anhydrous dioxane. The mixture was refluxed for 5 min, saturated with gaseous hydrogen chloride, and refluxed for an additional 2 h. The mixture was cooled, diluted with 10 mL of diethyl ether, and left to stand for 1 h. The resin-like material was separated by decanting and treated with 0.3 mL of propan-2-ol. The resin dissolved on heating with grinding, and fine colorless crystals began to separate from the solution. After 1 h, the precipitate was filtered off and washed with propan-2-ol.

Compound **13a**. Yield 0.056 g (43%), fine colorless crystals, mp 194–195°C. ^{1}H NMR spectrum, δ, ppm: 2.69 s (3H, CH_3), 5.76 s (2H, CH_2), 7.30 t (1H, Ph, *J* = 7.2 Hz), 7.31–7.45 m (3H, Ph, CH), 7.50–7.62 m (3H, Ph), 7.84 d (2H, Ph, *J* = 7.6 Hz), 8.13 d (2H, Ph, *J* = 7.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.9 (CH_3), 48.6 (CH_2), 103.9 (CH), 125.3 (2C), 127.9, 128.0 (2C), 128.3 (2C), 128.8 (2C), 130.3, 131.8, 132.2, 133.0, 140.6, 151.4, 151.7, 161.3. Found, %: C 58.10; H 4.41; Cl 17.13; N 20.36. $C_{20}H_{16}N_6 \cdot 2HCl$. Calculated, %: C 58.12; H 4.39; Cl 17.16; N 20.33.

Compound **13b**. Yield 0.062 g (39%), fine colorless crystals, mp 205–206°C. ^{1}H NMR spectrum, δ, ppm: 3.88 s (3H, CH_3), 5.81 s (2H, CH_2), 7.07 d (2H, Ph, J = 8.8 Hz), 7.30 t (1H, Ph, J = 7.6 Hz), 7.32–7.42 m (3H, Ph, CH), 7.51–7.62 m (3H, Ph), 7.86 d (2H, Ph, J = 7.6 Hz), 7.97 d (2H, Ph, J = 8.8 Hz), 8.08 d (2H, Ph, J = 6.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.4 (CH_2), 55.0 (CH_3), 103.4 (CH), 113.7, 117.9, 125.3 (2C), 127.7, 127.8 (2C), 128.3 (2C), 128.8 (2C), 130.3 (2C), 131.0 (2C), 131.8, 132.0, 133.3, 141.5, 151.2, 152.8, 160.5, 160.9. Found, %: C 61.80; H 4.43; Cl 14.01; N 16.67; O 3.09. $C_{26}H_{20}N_6O\cdot 2HCl$. Calculated, %: C 61.79; H 4.39; Cl 14.03; N 16.63; O 3.17.

3-Methyl-6,10-diphenyl-7*H*-pyrazolo[5,1-*d*]-[1,2,4]triazolo[4,3-*b*][1,2,5]triazepine (13a) (*alternative method*). A mixture of 0.1 g (0.316 mmol) of compound **12** and 0.06 mL (0.60 mmol) of pentane-2,4-dione in 0.4 mL of 2-ethoxyethanol was refluxed for 1 h. The solvent was distilled off under reduced pressure, 0.1 mL of methanol was added to the residue, and the mixture was heated to the boiling point. The oily material crystallized on grinding, and the crystals were filtered off and washed with methanol. Yield 0.053 g (49%), fine colorless crystals, mp 176–178°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 5.68 s (2H, CH_2), 7.25–7.35 m (2H, Ph, CH), 7.39 t (2H, Ph, J = 7.2 Hz), 7.53–7.62 m (3H, Ph), 7.85 d (2H, Ph, J = 7.2 Hz), 8.11 d (2H, Ph, J = 6.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 10.1 (CH_3), 48.4 (CH_2), 103.0 (CH), 125.3 (2C), 127.8 (3C), 128.3 (2C), 128.8 (2C), 131.4, 131.8, 132.0, 133.4, 140.7, 151.1, 151.6, 159.4. Found, %: C 70.59; H 4.73; N 24.68. $C_{20}H_{16}N_6$. Calculated, %: C 70.57; H 4.74; N 24.69.

6,10-Diphenyl-7*H*-pyrazolo[5,1-*d*]tetrazolo-[1,5-*b*][1,2,5]triazepine (14). Sodium nitrite, 0.03 g (0.32 mmol), was added in one portion to a solution of 0.1 g (0.316 mmol) of compound **12** in 1 mL of acetic acid, and the mixture was stirred for 1 h at room temperature. The precipitate was filtered off and washed with a small amount of acetic acid and with water. Yield 0.059 g (57%), fine colorless crystals, mp 206–207°C. ^{1}H NMR spectrum, δ, ppm: 5.83 s (2H, CH_2), 7.30 t (1H, Ph, J = 7.2 Hz), 7.38 t (2H, Ph, J = 7.6 Hz), 7.51–7.61 m (3H, Ph, CH), 7.64 t (1H, Ph, J = 7.2 Hz), 7.85 d (2H, Ph, J = 7.2 Hz), 8.16 d (2H, Ph, J = 7.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 49.5 (CH_2), 105.5 (CH), 125.9 (2C), 128.6, 128.9, 129.0 (4C), 129.5 (2C), 132.0, 133.0, 133.3, 141.7, 152.5, 162.0. Found, %: C 66.07; H 4.03; N 29.90. $C_{18}H_{13}N_7$. Calculated, %: C 66.05; H 4.00; N 29.95.

4-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine (15). A mixture of 0.05 g (0.158 mmol) of compound **12** and 0.025 mL (0.25 mmol) of pentane-2,4-dione in 0.25 mL of dioxane was refluxed for 4 h. The mixture was diluted with 0.5 mL of water, and the yellow resinous material was separated by decanting and dissolved in 0.25 mL of methanol on heating. After cooling, the precipitate was filtered off and washed with methanol. Yield 0.031 g (52%), fine colorless crystals, mp 170–172°C. ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, CH_3), 2.70 s (3H, CH_3), 4.94 br.s (1H, CH_2), 5.93 br.s (1H, CH_2), 6.12 s (1H, CH), 6.89 s (1H, CH), 7.28 t (1H, Ph, J = 7.2 Hz), 7.37 t (2H, Ph, J = 7.6 Hz), 7.47–7.50 m (3H, Ph), 7.78 d (2H, Ph, J = 7.6 Hz), 7.95–8.12 m (2H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 13.4 (CH_3), 13.6 (CH_3), 48.8 (CH_2), 105.6 (CH), 109.2 (CH), 125.3 (2C), 127.1 (2C), 127.6, 128.3 (2C), 128.5 (2C), 128.8, 130.5, 132.2, 133.7, 139.2, 142.2, 149.7, 150.3, 153.2. Found, %: C 72.65; H 5.27; N 22.08. $C_{23}H_{20}N_6$. Calculated, %: C 72.61; H 5.30; N 22.09.

4,4′-(Hydrazine-1,2-diyl)bis(2,7-diphenyl-8*H*-pyrazolo[5,1-*d*][1,2,5]triazepine) (16). A mixture of 0.05 g (0.16 mmol) of compound **9** and 0.06 g (0.19 mmol) of **12** in 0.2 mL of 2-ethoxyethanol was refluxed for 4 h. The mixture was cooled and slowly diluted with 2 mL of water while grinding the separating solid. The precipitate was filtered off and washed with water. Yield 0.091 g (96%), fine yellow crystals, mp 88–92°C. ^{1}H NMR spectrum, δ, ppm: 5.56 s (4H, CH_2), 7.25–7.39 m (8H, Ph, CH), 7.48–7.55 m (6H, Ph), 7.79 d (4H, Ph, J = 7.2 Hz), 7.98 d (4H, Ph, J = 5.6 Hz), 13.12 s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 49.4 (2C, CH_2), 110.5 (2C, CH), 125.7 (4C), 127.7 (4C), 128.3 (2C), 128.8 (4C), 129.2 (4C), 131.6 (2C). 132.4 (2C), 142.3 (2C), 150.8 (2C), 158.9 (2C), 180.5 (2C). Found, %: C 72.02; H 4.75; N 23.23. $C_{38}H_{28}N_{10}$. Calculated, %: C 71.98; H 4.70; N 23.32.

CONFLICT OF INTEREST

The authors declare the absence of conflict of interest.

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