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Melamine trisulfonic acid (MTSA) as an efficient catalyst for the synthesis of triazolo[1,2-*a*]indazole-triones and some 2*H*-indazolo[2,1-*b*]phthalazine-triones

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ABSTRACT

Melamine trisulfonic acid (MTSA) as an efficient heterogeneous catalyst has been used for the one-pot preparation of triazolo[1,2-*a*]indazole-1,3,8-trione and 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives by the three-component condensation reaction of urazoles or phthalhydrazide, dimedone or 1,3-cyclohexanedione, and aldehydes under solvent-free conditions in good to excellent yields and short reaction times.

***Keywords**: Multi-component reaction, Melamine trisulfonic acid (MTSA), Urazole, Dimedone, 1,3-cyclohexanedione, Aldehyde, Phthalhydrazide.*

1. Introduction

Multi-component reactions (MCRs) make possible the speedy and efficient synthesis of molecular libraries that have a high degree of structural and molecular diversity [1]. One-pot MCR strategies have significant advantages over linear syntheses including convergence, productivity, time and cost-saving, high yields. They also help to avoid the usage of expensive, toxic, and hazardous solvents as the multi-step synthesis involves various steps for isolation and separation of the products after each step [2].
Development of heterogeneous catalysts for fine chemicals synthesis has become a major area of research. The application of heterogeneous catalysis in organic synthesis makes the reaction handling easier with special attention to product purification. A further advantage is represented by the possibility of performing reactions under solvent-free conditions [3].
Among a large variety of *N*-heterocyclic compounds, heterocycles containing a urazole and phthalhydrazide moiety are of interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities and clinical applications [4,5]. Among urazole and phthalazine derivatives, triazolo[1,2-*a*]indazole-trione and indazolo[2,1-*b*]phthalazine-trione derivatives are very interesting compounds and much attention has recently been given to the synthesis of them and its derivatives [6].

2. Experimental

2.1. General

All commercially available chemicals were obtained from *Merck* companies, and used without further purifications. Melamin trisulfonic acid was prepared as described [7]. Urazoles were synthesized according to the reported methods [8]. m.p. were measured on a *Büchi B-545* apparatus in open capillary tubes. The ^{1}H NMR (300/400 MHz) and ^{13}C NMR (75/100 mhz) spectra were run on a *Bruker Avance*, FT-NMR spectrometer (δ in ppm). IR spectra were conducted on a *Perkin Elmer GX FT IR* spectrometer. Microanalysis was performed on a *PerkineElmer 240-B* micro-analyzer.

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2.2. General procedure for the Synthesis of Triazolo[1,2-a]indazole-triones (4)

A mixture of *β*-diketone (dimedone or 1,3-cyclohexanedione)(1 mmol), urazole (1 mmol), aldehyde (1 mmol), and MTSA (15 mol %) was heated at 80 ˚C until completion of the reaction (TLC). Then, 15 mL of $CHCl_3$ was added to the mixture and the catalyst was recovered by filtration. The organic layer was concentrated and the crude product was recrystallized from AcOEt/ *n*-hexane (1:3) to afford the desired product (4).

2.3 General Procedure for the Synthesis of Indazolo[2,1-b]phthalazine-triones (5)

Aromatic aldehyde (1.0 mmol), dimedone or 1,3-cyclohexanedione (1.0 mmol), phthalhydrazide (1.0 mmol), and MTSA (15% mol) are mixed in a mortar. The mixture was then heated at 100 °C for an appropriate time (Table 3) until completion of the reaction (TLC). Then, the mixture was cooled, washed with acetone (15 mL) and evaporated under vacuum to give the product, which was crystallized from AcOEt/*n*-hexane (1:3) to afford pure product (5).

Selected spectral data:

*6,6-dimethyl-2-phenyl-9-p-tolyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4b)***.
White, IR (ν_{max}, cm^{-1}): 2956, 1781, 1719, 1665. ^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (6H, s, $2CH_3$), 2.35 (2H, s, CH_2), 2.37 (3H, s, CH_3), 2.93(2H, s, CH_2), 6.20 (1H, s, CH), 7.21-7.51 (9H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 28.3, 28.8, 34.8, 35.5, 51.4, 64.0, 120.2, 125.6, 127.0, 128.7, 129.3, 129.6, 130.8, 133.8, 138.8, 148.9, 150.5, 150.9, 192.0.

*9-(2-methoxyphenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4e)***.
White, IR (ν_{max}, cm^{-1}): 2961, 1778, 1734, 1620. ^1H NMR (400 MHz, $CDCl_3$): δ 1.10 (3H, s, CH_3), 1.20 (3H, s, CH_3), 2.20 (2H, AB system, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.80 (2H, AB system, $^2J_{HH}$ = 18.4 Hz, CH_2), 3.77 (3H, s, CH_3), 6.08 (1H, s, CH), 6.87–7.48 (9H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.1, 29.5, 34.5, 35.5, 51.2, 55.4, 64.4, 110.6, 118.5, 121.4, 125.3, 128.4, 129.2, 130.6, 131.2, 149.0, 150.2, 150.7, 156.9, 192.0.

*9-(2,4-dichlorophenyl)-6,6-dimethyl-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4f)***.
White, IR (ν_{max}, cm^{-1}): 2963, 1785, 1732, 1660. ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (6H, s, $2CH_3$), 2.31 (2H, AB system, $^2J_{HH}$ = 16.0 Hz, CH_2), 2.90 (2H, AB system, $^2J_{HH}$ = 18.8 Hz, CH_2), 6.33 (1H, s, CH), 7.30–7.50 (8H, m, H–Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.2, 28.9, 34.7, 35.4, 51.1, 62.9, 118.2, 125.7, 127.9, 128.8, 129.3, 130.6, 130.7, 131.0, 132.0, 133.6, 135.8, 148.4, 150.2, 151.0, 191.7; Anal. Calcd. for $C_{23}H_{19}C_{l2}N_3O_3$ (456.3): C, 60.54; H, 4.20; N, 9.21%. Found: C, 60.80; H, 4.13; N, 9.14%.

*2,9-bis(4-chlorophenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4g)***.
White, IR (ν_{max}, cm^{-1}): 2962, 1788, 1736, 1672. ^1H NMR (400 MHz, $CDCl_3$): δ 1.18 (6H, s, $2CH_3$), 2.32 (2H, s, CH_2), 2.89 (2H, s, CH_2), 6.15 (1H, s, CH), 7.35-7.49 (8H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 28.7, 34.8, 35.5, 51.2, 63.5, 119.8, 126.6, 128.6, 129.1, 129.3, 129.6, 134.5, 134.8, 135.3, 148.6, 150.7, 150.8, 191.9; Anal. Calcd for $C_{23}H_{19}Cl_2N_3O_3$ (456.3): C, 60.54; H, 4.20; N, 9.21%. Found: C, 60.60; H, 4.40; N, 8.85%

*9-(2,4-dichlorophenyl)-2-(3,4-dichlorophenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4h)***.
White, IR (ν_{max}, cm^{-1}): 2928, 1781, 1709, 1663. ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (6H, s, $2CH_3$), 2.33 (2H, AB system, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.92 (2H, AB system, $^2J_{HH}$ = 18.4 Hz, CH_2), 6.32 (1H, s, CH), 7.34-7.70 (6H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 28.9, 34.7, 35.4, 51.1, 63.1, 118.3, 124.5, 127.2, 128.0, 130.1, 130.3, 130.7, 130.9, 132.1, 132.9, 133.3, 133.4, 136.1, 147.4, 149.1, 150.6, 191.6; Anal. Calcd for $C_{23}H_{17}Cl_4N_3O_3$ (525.2): C, 52.60; H, 3.26; N, 8.00%. Found: C, 53.06; H, 3.09; N, 7.86%

*2-(4-tert-butylphenyl)-6,6-dimethyl-9-(2-nitrophenyl)-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4i)***.
White, IR (ν_{max}, cm^{-1}): 2962, 1787, 1741, 1661. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (3H, s, CH_3) 1.19 (3H, s, CH_3), 1.35 (9H, s, $3CH_3$), 2.28 (2H, AB system, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.91 (2H, s, CH_2), 6.98 (1H, s, CH), 7.39-7.98 (8H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.2, 28.7, 31.3, 34.7, 34.8, 35.5, 51.0, 61.2, 118.5, 125.3, 125.5, 126.4, 127.9, 129.9, 130.4, 130.7, 133.5, 148.8, 149.2, 151.4, 151.6, 152.1, 191.8; Anal. Calcd for $C_{27}H_{28}N_4O_5$ (488.5): C, 66.38; H, 5.78; N, 11.47%. Found: C, 66.32; H, 6.05; N, 11.89%.

*2-(4-chlorophenyl)-6,6-dimethyl-9-(3-nitrophenyl)-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione **(4j)***.
White, IR (ν_{max}, cm^{-1}): 2926, 1773, 1721, 1665. ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (6H, s, $2CH_3$), 2.35 (2H, s, CH_2), 2.94 (2H, AB system, $^2J_{HH}$ = 18.4 Hz, CH_2), 6.30 (1H, s, CH), 7.48 (4H, s, H-Ar), 7.60 (1H, t, $^3J_{HH}$ = 8 Hz, H-Ar), 7.89 (1H, d, $^3J_{HH}$ = 7.6 Hz, H-Ar), 8.20 (1H, d, $^3J_{HH}$ = 8 Hz, H-Ar), 8.29 (1H, s, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 28.6, 34.9, 35.5,

51.2, 63.3, 119.3, 121.8, 123.8, 126.7, 129.1, 129.6, 130.0, 133.8, 134.7, 139.1, 148.6, 148.8, 151.2, 151.4, 192.0; Anal. Calcd for $C_{23}H_{19}ClN_4O_5$ (466.8): C, 59.17; H, 4.10; N, 12.00%. Found: C, 58.88; H, 4.26; N, 12.46%.

2-(4-tert-butylphenyl)-9-(4-chlorophenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione ***(4k)***.
White, IR (ν_{max}, cm^{-1}): 2962, 1782, 1728, 1657. ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (6H, s, $2CH_3$), 1.36 (9H, s, $3CH_3$), 2.36 (2H, s, CH_2), 2.94 (2H, AB system, $^2J_{HH}$ = 18.4 Hz, CH_2), 6.21 (1H, s, CH), 7.37-7.53 (8H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 28.8, 31.2, 34.8, 35.6, 51.3, 63.5, 119.8, 125.2, 126.4, 127.8, 128.5, 129.1, 134.8, 135.5, 151.0, 151.5, 152.1, 192.0. Anal. Calcd for $C_{27}H_{28}ClN_3O_3$ (478.0): C, 67.85; H, 5.90; N, 8.79%. Found: C, 67.52; H, 6.10; N, 8.55%.

6,6-dimethyl-9-(naphthalen-2-yl)-2-phenyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione ***(4m)***.
White, IR (ν_{max}, cm^{-1}): 2958, 1780, 1728, 1665. ^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (6H, s, $2CH_3$), 2.37 (2H, s, CH_2), 2.98 (2H, s, CH_2), 6.41 (1H, s, CH), 7.43-7.96 (12H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 28.8, 34.8, 35.6, 51.4, 64.4, 120.2, 124.2, 125.6, 126.5, 126.6, 126.8, 127.7, 128.3, 128.8, 129.0, 129.4, 130.8, 133.2, 133.5, 134.1, 149.2, 150.7, 151.2, 192.0; Anal. Calcd for $C_{27}H_{23}N_3O_3$ (437.5): C, 74.12; H, 5.30; N, 9.60%. Found: C, 74.03; H, 5.59; N, 9.63%.

2-phenyl-9-propyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione ***(4n)***.
White, IR (ν_{max}, cm^{-1}): 2955, 1791, 1734, 1664. ^1H NMR (400 MHz, $CDCl_3$): δ 1.00 (3H, t, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.42-3.04 (10H, m, $5CH_2$), 5.25 (1H, b, CH), 7.40-7.51 (5H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 18.7, 21.9, 35.4, 37.1, 62.4, 120.9, 125.7, 128.7, 129.3, 130.9, 149.4, 151.8, 152.2, 193.1. Anal. Calcd for $C_{18}H_{19}N_3O_3$ (325.3): C, 66.45; H, 5.89; N, 12.91%. Found: C, 66.38; H, 5.75; N, 12.64%.

2-(4-chlorophenyl)-9-propyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione ***(4o)***.
White, IR (ν_{max}, cm^{-1}): 2962, 1795, 1742, 1659. ^1H NMR (400 MHz, $CDCl_3$): δ 1.00 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.49-3.04 (10H, m, $5CH_2$), 5.26 (1H, b, CH), 7.40 (4H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 18.7, 21.9, 35.4, 37.1, 62.5, 121.0, 126.7, 129.4, 129.5, 134.4, 149.0, 151.4, 152.0, 193.1. Anal. Calcd for $C_{18}H_{18}ClN_3O_3$ (359.8): C, 60.09; H, 5.04; N, 11.68%. Found: C, 66.18; H, 5.15; N, 11.64%.

9-(4-chlorophenyl)-2-ethyl-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione ***(4r)***.
White, IR (ν_{max}, cm^{-1}): 2963, 1787, 1728, 1664. ^1H NMR (400 MHz, $CDCl_3$): δ 1.19 (6H, s, $2CH_3$), 2.31 (3H, t, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.31 (2H, s, CH_2), 2.88 (2H, AB system, $^2J_{HH}$ = 18.4 Hz, CH_2), 3.66 (2H, AB system, $^2J_{HH}$ = 6.8 Hz, CH_2), 6.09 (1H, s, CH), 7.36 (4H, s, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.3, 28.3, 26.7, 34.8, 35.1, 35.5, 51.2, 63.1, 119.6, 128.4, 129.1, 134.6, 135.8, 150.5, 151.1, 152.6, 192.1. Anal. Calcd for $C_{19}H_{20}ClN_3O_3$ (373.8): C, 61.04; H, 5.39; N, 11.24%. Found: C, 61.12; H, 5.17; N, 11.13%.

9,9'-(1,4-phenylene)bis(2-(4-tert-butylphenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione) ***(4s)***.
White, IR (ν_{max}, cm^{-1}): 2925, 1784, 1731, 1664. ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (12H, s, $4CH_3$), 1.36 (18H, s, $6CH_3$), 2.36 (4H, AB system, $^2J_{HH}$ = 16.2 Hz, $2CH_2$), 2.93 (4H, AB system, $^2J_{HH}$ = 18.6 Hz, $2CH_2$), 6.27 (2H, s, 2CH), 7.41 (4H, d, $^3J_{HH}$ = 8.8 Hz, H-Ar).7.52 (8H, m, H-Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 28.7, 29.7, 31.3, 34.8, 35.6, 51.3, 63.5, 119.8, 125.3, 126.4, 127.7, 127.9, 137.6, 151.1, 152.0, 192.1. Anal. Calcd for $C_{48}H_{52}N_6O_6$ (809.0): C, 71.27; H, 6.48; N, 10.39%. Found: C, 71.18; H, 6.35; N, 10.46%.

9,9'-(1,4-phenylene)bis(2-(4-chlorophenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4] triazolo[1,2-a]indazole-1,3,8(2H,5H,9H) -trione) ***(4t)***.
White, IR (ν_{max}, cm^{-1}): 2925, 1784, 1730, 1669. ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (12H, s, $4CH_3$), 2.38 (4H, AB system, $^2J_{HH}$ = 16.6 Hz, $2CH_2$), 2.92 (4H, AB system, $^2J_{HH}$ = 18.6 Hz, $2CH_2$), 6.25 (2H, s, 2CH), 7.49 (12H, m, H-Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 28.7, 34.8, 35.5, 51.3, 63.6, 119.9, 126.7, 127.7, 129.2, 129.6, 134.6, 137.4, 150.6, 150.7, 192.0. . Anal. Calcd for $C_{40}H_{34}Cl_2N_6O_6$ (765.6): C, 62.75; H, 4.48; N, 10.98%. Found: C, 62.63; H, 4.52; N, 10.76%.

2,2'-(4,4'-methylenebis(4,1-phenylene))bis(9-(4-bromophenyl)-6,6-dimethyl-6,7-dihydro-[1,2,4]triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione) ***(4u)***.
White, IR (ν_{max}, cm^{-1}): 2922, 1781, 1731, 1663; ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (12H, s, $4CH_3$), 2.36 (4H, s, $2CH_2$), 2.92 (4H, AB system, $^2J_{HH}$ = 18.6 Hz, $2CH_2$), 4.08 (2H, s, CH_2), 6.19 (2H, s, 2CH), 7.31-7.55 (16H, m, H-Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 28.8, 34.8, 35.5, 41.1, 51.3, 63.5, 119.7, 123.0, 125.8, 128.8, 128.9, 130.0, 132.1, 135.9, 141.1, 149.0, 150.9, 151.2, 192.0. Anal. Calcd for $C_{47}H_{40}Br_2N_6O_6$ (944.7): C, 59.76; H, 4.27; N, 8.90%. Found: C, 59.71; H, 4.24; N, 9.04%.

13-phenyl-3,4-dihydro-1H-indazolo[2,1-b]phthalazine-1,6,11(2H,13H)-trione ***(5a)***.
White, IR (ν_{max}, cm^{-1}): 2954, 1659, 1624, 1367, 1321, 1267. ^1H NMR (400 MHz, $CDCl_3$): δ 2.22-2.29 (2H, m, CH_2), 2.45-2.49 (2H, m, CH_2), 3.30-3.61 (2H, AB system, $^2J_{HH}$ = 19.2 Hz, CH_2), 6.46 (1H, s, CH), 7.27-7.45 (5H, m, H-Ar), 7.83-7.85 (2H, m, H-Ar),

8.25-8.27 (1H, m, H-Ar), 8.34-8.36 (1H, m, H-Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 24.5, 27.2, 36.9, 64.9, 119.7, 127.2, 127.7, 130.0, 128.1, 128.4, 128.7, 128.9, 129.1, 133.6, 134.6, 136.4, 152.3, 154.2, 156.0, 192.5.

3,3-dimethyl-13-phenyl-3,4-dihydro-1H-indazolo[2,1-b]phthalazine-1,6,11(2H,13H)-trione ***(5b)***.
Yellow, IR (ν_{max}, cm^{-1}): 2958, 1658, 1583. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (6H, s, $2CH_3$), 2.35 (2H, s, CH_2), 3.24-3.46 (2H, AB system, $^2J_{HH}$ = 19.2 Hz, CH_2), 6.47 (1H, s, CH), 7.30-8.38 (9H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 28.7, 34.7, 38.1, 51.0, 65.0, 118.6, 127.2, 127.7, 128.0, 128.7, 128.8, 129.0, 129.1, 133.6, 134.6, 136.4, 150.9, 154.3, 156.1, 192.2.

13-(4-chlorophenyl)-3,3-dimethyl-3,4-dihydro-1H-indazolo[2,1-b]phthalazine-1,6,11(2H,13H)-trione ***(5c)***.
Yellow, IR (ν_{max}, cm^{-1}): 2959, 1659, 1625. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (6H, s, $2CH_3$), 2.36 (2H, s, CH_2), 3.24-3.45 (2H, AB system, $^2J_{HH}$ = 19.2 Hz, CH_2), 6.44 (1H, s, CH), 7.32-8.39 (8H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 28.7, 34.7, 38.1, 50.9, 64.4, 118.1, 127.8, 128.1, 128.6, 128.9, 129.0, 129.1, 133.7, 134.6, 134.7, 135.0, 151.1, 154.4, 156.0, 192.2.

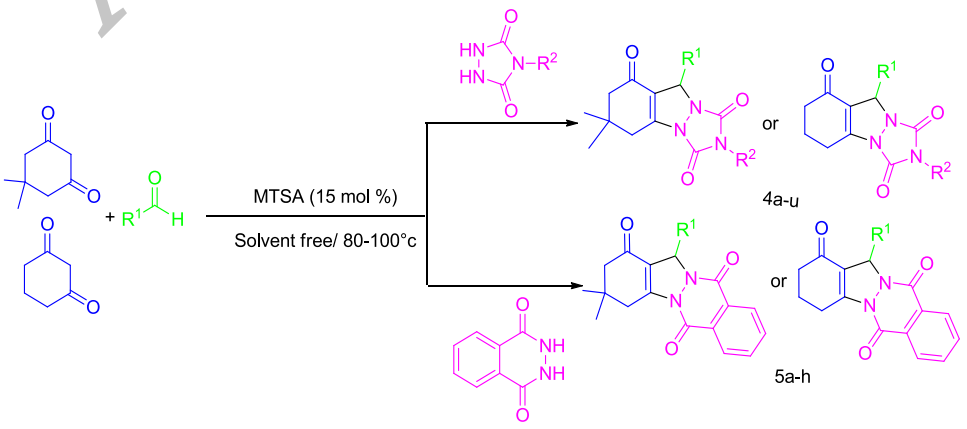
3,3-dimethyl-13-(3-phenoxyphenyl)-3,4-dihydro-1H-indazolo[2,1-b]phthalazine-1,6,11(2H,13H)-trione ***(5d)***.
Yellow, IR (ν_{max}, cm^{-1}): 2950, 1655, 1626. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19-1.27 (6H, m, $2CH_3$), 2.36 (2H, s, CH_2), 3.21-3.42 (2H, AB system, $^2J_{HH}$ = 18.8 Hz, CH_2), 6.44 (1H, s, CH), 6.89-8.39 (13H, m, H-Ar),. ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 28.7, 34.6, 38.0, 51.0, 64.6, 117.1, 118.3, 118.6, 119.1, 122.4, 123.5, 127.8, 128.0, 129.0, 129.1, 129.7, 130.0, 133.6, 134.6, 138.4, 151.0, 154.4, 156.0, 156.7, 157.6, 192.1.

3,4-Dihydro-3,3-dimethyl-13-(4-nitrophenyl)-1H-indazolo[2,1-b]phthalazine-1,6,11(13H)-trione ***(5e)***.
Yellow, IR (ν_{max}, cm^{-1}): 2958, 1693, 1660, 1618. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21-1.27 (6H, m, $2CH_3$), 2.36 (2H, s, CH_2), 3.21-3.43 (2H, AB system, $^2J_{HH}$ = 19.2 Hz, CH_2), 6.52 (1H, s, CH), 7.61-8.41 (8H, m, H-Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 28.7, 34.7, 38.0, 50.8, 64.1, 117.3, 124.0, 127.8, 128.1, 128.6, 128.9, 134.0, 143.4, 147.9, 151.7, 154.5, 155.9, 192.1.

13-(4-methoxyphenyl)-3,4-dihydro-1H-indazolo[2,1-b]phthalazine-1,6,11(2H,13H)-trione ***(5h)***.
Yellow, IR (ν_{max}, cm^{-1}): 2896, 1663, 1625,.^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27-2.31 (2H, m, CH_2), 2.47-2.51 (2H, m, CH_2), 3.32-3.62 (2H, AB system, $^2J_{HH}$ = 19.2 Hz, CH_2), 3.78 (3H, s, CH_3), 6.44 (1H, s, CH), 6.87-6.89 (2H, m, H-Ar), 7.36-7.38 (2H, m, H-Ar), 7.85-7.87 (2H, m, H-Ar), 8.28–8.38 (2H, m, H-Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 24.5, 36.9, 55.2, 64.6, 114.1, 119.6, 127.7, 127.9, 128.3, 128.6, 128.9, 129.1, 133.4, 134.5, 152.1, 154.2, 156.0, 157.7, 192.6.

3. Results and Discussion

In continuation of our interest in using solid acid catalysts in organic transformations [9], herein we wish to report the catalytic activity of melamine trisulfonic acid (MTSA) for the synthesis of triazolo[1,2-*a*]indazole-triones and 2*H*-indazolo[2,1-*b*]phthalazine-triones derivatives *via* the one-pot three-component reaction of dimedone or 1,3-cyclohexanedione, aldehydes, and 4-substituted urazoles or phthal-hydrazide under solvent-free conditions (Scheme 1).
In our previous work, we manufactured the catalyst for the first time and named it 1, 3, 5-triazine-2,4,6-triyltrisulfamic acid (TTSA) [7], but later, this catalyst was used in literature with the name melamine trisulfonic acid (MTSA) [10]. Melamine trisulfonic acid (MTSA) is a versatile catalyst which is prepared from the reaction of melamine and chlorosulfonic acid [7]. The use of MTSA in organic synthesis has received considerable attention as a non-toxic, easily producible and powerful solid protic acid catalyst for various organic functional group transformations [10].



Scheme 1. Synthesis of triazolo[1,2-a]indazole-triones and 2*H*-Indazolo[2,1-b]phthalazine-triones.

Table 1. Effect of different amounts of the catalyst (MTSA) in the reaction of benzaldehyde with dimedone and phenyl urazole (1:1:1) at 80 °C under solvent-free conditions.

Entry	Catalyst Amount (mol%)	Time (min)	Yield[a] (%)
1	-	360	trace
2	5	30	45
3	10	30	75
4	15	30	94
5	20	30	93

[a]Yield of isolated product.

To optimize the reaction conditions, the condensation between dimedone (1 mmol), benzaldehyde (1 mmol), and 4-phenylurazole (1 mmol) to give 4a was selected as a model reaction in the presence of various amount of catalyst, and the obtained results were summarized in Table 1. It was found that the yield of 4a increases with increasing amounts of catalyst, from 45% to 94% with increasing catalyst from 5 mol % to 15 mol %. The results were good in terms of yields and product purity in the presence of MTSA, while without MTSA and over long period of time (5–6 h), the yield of product was trace.

In the next step, the efficiency of the catalyst was explored under the optimized reaction conditions for the condensation of various 4-substituted urazoles with structurally diverse aldehydes and dimedone or 1,3-cyclohexanedione (Scheme 1). The results are displayed in Table 2.

Table 2. Synthesis of triazolo[1,2-*a*]indazole-trione (4a–u).

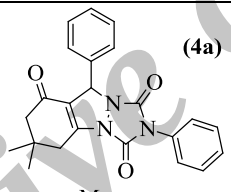
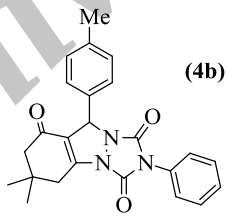
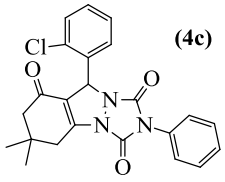
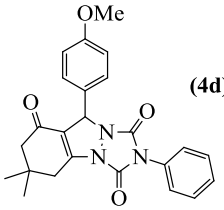
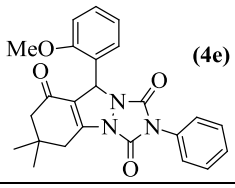
Entry	R^1	R^2	Product (4)	Time (min)	Yield [a] (%)	mp °C (mp °C)[lit]	Ref.
1	C_6H_5	C_6H_5	 **(4a)**	30	94	190-192 (188-190)	[6h]
2	4-Me-C_6H_4	C_6H_5	 **(4b)**	30	86	163-165 (160-162)	[6h]
3	2-Cl-C_6H_4	C_6H_5	 **(4c)**	35	82	183-185 (173-175)	[6h]
4	4-MeO-C_6H_4	C_6H_5	 **(4d)**	30	85	166-168 (165-167)	[6e]
5	2-MeO-C_6H_4	C_6H_5	 **(4e)**	35	88	196-198	-

Table 2. *(Continued).*

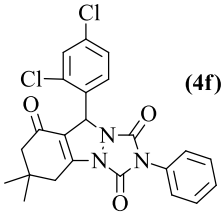
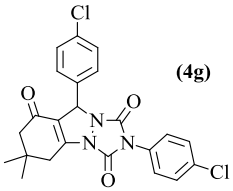
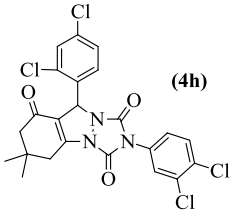
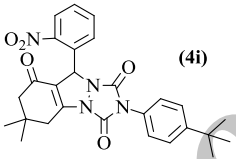
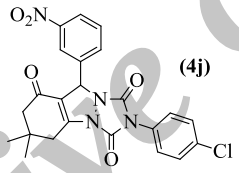
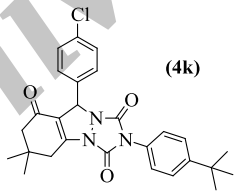
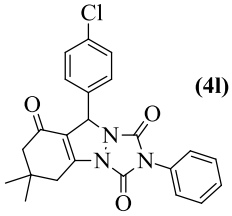
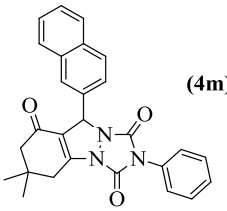
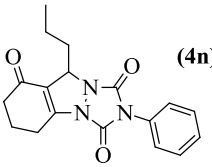
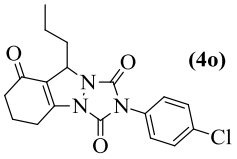
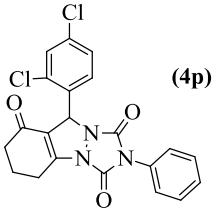
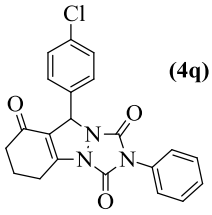
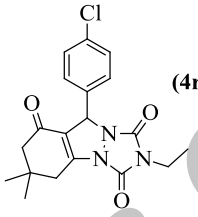
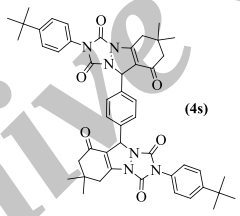
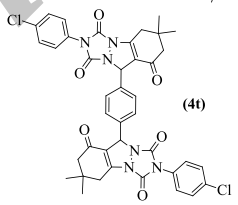
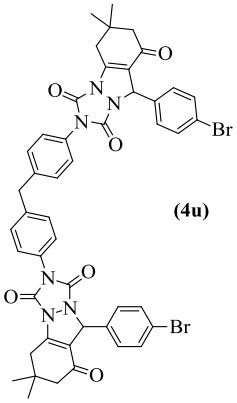
6	2,4-di-Cl-C_6H_3	C_6H_5	 **(4f)**	45	87	195-197	-
7	4-Cl-C_6H_4	4-Cl-C_6H_4	 **(4g)**	40	83	204-206	-
8	2,4-di-Cl-C_6H_3	3,4-di-Cl-C_6H_3	 **(4h)**	45	84	192-194	-
9	2-NO_2-C_6H_4	4-tert-Bu-C_6H_4	 **(4i)**	30	85	256-258	-
10	3-NO_2-C_6H_4	4-Cl-C_6H_4	 **(4j)**	20	89	177-179	-
11	4-Cl-C_6H_4	4-tert-Bu-C_6H_4	 **(4k)**	35	81	266-268	-
12	4-Cl-C_6H_4	C_6H_5	 **(4l)**	40	87	170-172 (166-168)	[6h]
13	2-Naphthyl	C_6H_5	 **(4m)**	40	96	135-137 (139-142)	[6f]
14	C_3H_7	C_6H_5	 **(4n)**	80	75	210-212	-

Table 2. *(Continued).*

15	C_3H_7	4-Cl-C_6H_4	 (4o)	80	79	230-232	-
16	2,4-di-Cl-C_6H_3	C_6H_5	 (4p)	40	74	207-209	-
17	4-Cl-C_6H_4	C_6H_5	 (4q)	35	76	203-205	-
18	4-Cl-C_6H_4	Et	 (4r)	25	79	175-177	-
19[b]	4-OHC-C_6H_4	4-tert-Bu-C_6H_4	 (4s)	120	75	319-321	-
20[b]	4-OHC-C_6H_4	4-Cl-C_6H_4	 (4t)	120	80	324-326	-
21[c]	4-Br-C_6H_4	C_6H_4-CH_2-C_6H_4	 (4u)	120	78	210-212	-

[a] Yields of isolated product.
[b] Reaction conditions: dimedone (2 equiv.), urazole (2 equiv.) and terephthaldehyde (1 equiv.)
[c] Reaction conditions: dimedone (2 equiv.), urazole (1 equiv.) and 4-Br-benzaldehyde (2 equiv.)

The triazolo[1,2-*a*]indazole-trione derivatives (4) were obtained in high yields and short reaction times. Aliphatic aldehydes react under the same conditions with longer reaction time (Table 2, entries 14, 15). The influence of electron-withdrawing and electron-donating substituents on the aromatic ring of aldehydes upon the reaction yields was also investigated. The results showed that both electron-withdrawing and electron-donating substituents had no significant effect on the reaction yields (Table 2, entries 2-10). Interestingly, the catalyst was successfully applied for the synthesis of bis-triazolo[1,2-*a*]indazole-triones, by the condensation reaction between arylaldehydes/bis-arylaldehydes, dimedone and urazoles/bis-urazoles (Table 2, entries 19-21). In the next step, this catalyst was used for the preparation of indazolo[2,1-*b*]phthalazine-triones (Scheme 1). Thus, different aldehydes were reacted with dimedone or 1,3-cyclohexanedione and phthalhydrazine using MTSA (15 mol%) at 100 °C under solvent-free conditions (Table 3). The catalyst efficiently promoted the reaction, and afforded the desired products in excellent yields and in short reaction times.

The products 4a-u and 5a-h were characterized on the basis of their physical and spectral (IR, ^{1}H NMR, ^{13}C NMR) data which were in accord with those reported in the literature [6].

A comparison of the efficacy of MTSA catalyst with some of those reported in the literature is presented in Table 4. The model reaction of dimedone, phthalhydrazide and benzaldehyde was considered as a representative example. It is apparent that MTSA is an equally or more efficient catalyst for this three-component reaction (Table 4).

4. Conclusions

In conclusion, we have developed a highly efficient and simple method for the preparation of a wide range of triazolo [1,2-*a*] indazole-trione and indazolo [2,1-*b*] phthalazine-trione derivatives *via* the one-pot multi-component condensation of aldehydes with *β*-diketones

Table 3. Synthesis of indazolo[2,1-*b*]phthalazine-triones (5a-h).

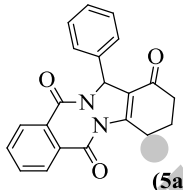
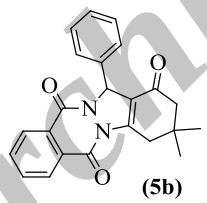
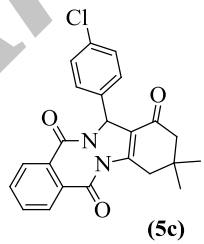
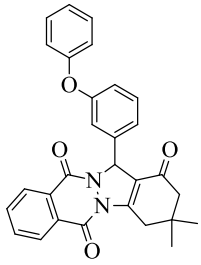
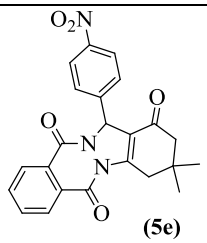
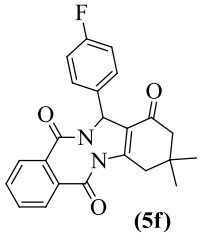
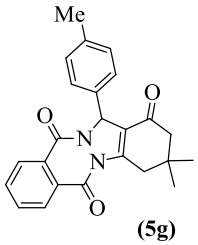
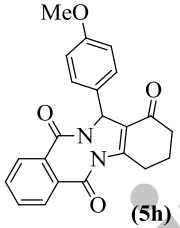
Entry	R^1	Product (5)	Time (min)	Yield[a] (%)	m.p. °C (m.p. °C)[lit]	Ref.
1	C_6H_5	 **(5a)**	10	84	220-222 (222-224)	[6d]
2	C_6H_5	 **(5b)**	10	85	204-206 (204-206)[6a]	[6a]
3	4-Cl-C_6H_4	 **(5c)**	15	80	261-263 (262-264)[6a]	[6a]
4	3-phO-C_6H_4	 **(5d)**	20	78	175-177	-

Table 3. *(Continued).*

5	4-NO_2-C_6H_4	 **(5e)**	10	83	226-229 (223-225)[6a]	[6a]
6	4-F-C_6H_4	 **(5f)**	10	92	219-221 (217-219)[6a]	[6a]
7	4-Me-C_6H_4	 **(5g)**	10	89	225-227 (227-229)[6a]	[6a]
8	4-MeO-C_6H_4	 **(5h)**	10	91	255-257 (254–255)[6d]	[6d]

[a] Yields of isolated product.

and urazoles or phthalhydrazine in the presence of 15 mol % of melamine trisulfonic acid (MTSA) as an efficient solid acid catalyst, which can be prepared from available inexpensive starting materials. The described method has many advantages, such as generality, simple work-up procedure, relatively mild reaction conditions, clean production of the products in high yields.

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Table 4. Influence of different catalysts on the reaction of benzaldehyde, dimedone and phthalhydrazide.

Entry	Catalyst	Amount(mol%)	Time	Yield (%)[a]	Ref
1	*p*-TSA	30	10	86	[6a]
2	DPA	10	10	96	[6k]
3	SSA	6.5	8	87	[6b]
4	H_2SO_4	15	30	86	[6d]
5	TBBDA	0.05g	10	82	[6i]
6	MTSA	15	10	85	This work

[a] Yields of isolated product.

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