4,5-DIOXO- AND 4-OXO-2,3-DIARYL-5-DIAZO-6,6-DIMETHYL-4,5,6,7-TETRAHYDROINDAZOLES

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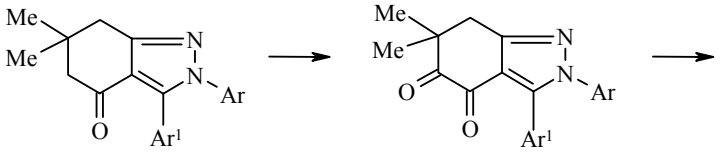
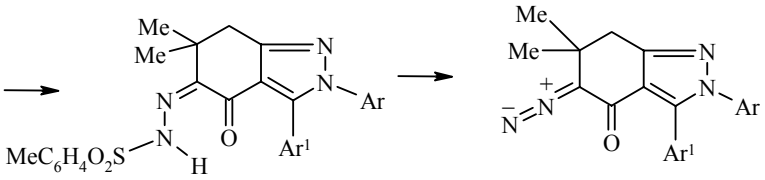
The oxidation of 2,3-diphenyl-, 3-(4-chlorophenyl)-2-phenyl-, 3-(4-dimethylaminophenyl)-2-phenyl-, 3-(4-methoxyphenyl)-2-phenyl-, 2-phenyl-3-(3-pyridyl)-, 3-phenyl-2-(2-pyridyl)-, and 3-(4-dimethylaminophenyl)-6,6-dimethyl-4-oxo-2-(2-pyridyl)-4,5,6,7-tetrahydroindazoles using H_2SeO_3 in acetic acid in the presence of sulfuric acid gave the corresponding 4,5-dioxo derivatives. Reaction of these with tosylhydrazine gave 4-oxo-5-tosylhydrazino derivatives which were decomposed by alkali to give the corresponding 2,3-diaryl-5-diazo-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazoles.

Keywords: α-diazo ketones, 2,3-diaryl-6,6-dimethyl-4,5-dioxo-4,5,6,7-tetrahydroindazoles.

6,6-Dimethyl-4,5-dioxo-4,5,6,7-tetrahydroindazoles have been prepared by oxidation of the corresponding 6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazoles using H_2SeO_3 [1] and have found a variety of uses in the modification of indazoles and pyrazoles [2-7]. On this basis pyrazole mono- and dicarboxylic acids have been prepared by subsequent oxidation of the α-diketone with hydrogen peroxide [1, 4, 5], a benzyl rearrangement [8], or cleavage of a tosylate monoxime [9]. The α-diketone group has been used in the synthesis of polycondensed pyrazolo[4,3-*a*]phenazine [2, 6, 7] and indazolo[4,5-*d*]imidazole [6] heterocyclic systems.



1a–g **2a–g**



3a–g **4a–g**

1-4 a Ar = Ar^1 = Ph; **b** Ar = Ph, Ar^1 = C_6H_4Cl-4; **c** Ar = Ph, Ar^1 = $C_6H_4NMe_2$-4; **d** Ar = Ph, Ar^1 = C_6H_4OMe-4; **e** Ar = Ph, Ar^1 = C_5H_4N-3; **f** Ar = C_5H_4N-2, Ar^1 = Ph; **g** Ar = C_5H_4N-2, Ar^1 = $C_6H_4NMe_2$-4

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TABLE 1. Characteristics of Compounds **2-4**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	Yield, %
		C	H	N	S		
2a	$C_{21}H_{18}N_2O_2$	76.11 / 76.34	5.55 / 5.49	8.41 / 8.48		162-163	68
2b	$C_{21}H_{17}ClN_2O_2$	69.00 / 69.13	4.55 / 4.70	7.62 / 7.68	—*	180-181	48
2c	$C_{23}H_{23}N_3O_2$	73.80 / 73.97	6.22 / 6.21	11.14 / 11.25		222-224	67
2d	$C_{22}H_{20}N_2O_3$	73.10 / 73.32	5.49 / 5.59	7.60 / 7.77		171-172	71
2e	$C_{20}H_{17}N_3O_2$	72.33 / 72.49	5.14 / 5.17	12.62 / 12.68		156-157	74
2f	$C_{20}H_{17}N_3O_2$	72.38 / 72.49	5.09 / 5.17	12.79 / 12.68		175-176	72
2g	$C_{22}H_{22}N_4O_2$	70.45 / 70.57	5.90 / 5.92	14.88 / 14.96		212-214	79
3a	$C_{28}H_{26}N_4O_3S$	67.37 / 67.45	5.21 / 5.26	11.11 / 11.24	6.30 / 6.43	153-154 (dec.)	41
3b	$C_{28}H_{25}ClN_4O_3S$	63.17 / 63.09	4.61 / 4.71	10.40 / 10.51		177-179 (dec.)	49
3c	$C_{30}H_{31}N_5O_3S$	66.36 / 66.52	5.70 / 5.77	12.78 / 12.93	5.70 / 5.92	187-188 (dec.)	39
3d	$C_{29}H_{28}N_4O_4S$	65.70 / 65.89	5.31 / 5.34	10.45 / 10.60	5.90 / 6.07	164-166 (dec.)	51
3e	$C_{27}H_{25}N_5O_3S$	64.72 / 64.91	4.92 / 5.04	14.14 / 14.02	6.20 / 6.42	153-154 (dec.)	36
3f	$C_{27}H_{25}N_5O_3S$	64.65 / 64.91	5.00 / 5.04	14.11 / 14.02	6.20 / 6.42	163-164 (dec.)	33
3g	$C_{29}H_{30}N_6O_3S$	64.02 / 64.19	5.43 / 5.57	15.40 / 15.49	5.70 / 5.91	181-182 (dec.)	27
4a	$C_{21}H_{18}N_4O$	73.55 / 73.66	5.21 / 5.30	16.21 / 16.36		161-163 (dec.)	70
4b	$C_{21}H_{17}ClN_4O$	66.76 / 66.93	4.40 / 4.55	14.69 / 14.87	—*[2]	168-169 (dec.)	66
4c	$C_{23}H_{23}N_5O$	71.50 / 71.66	5.89 / 5.01	18.00 / 18.17		170-171 (dec.)	60
4d	$C_{22}H_{20}N_4O_2$	70.88 / 70.95	5.29 / 5.41	14.90 / 15.05		140-142 (dec.)	39
4e	$C_{20}H_{17}N_5O$	69.80 / 69.95	5.02 / 4.99	20.20 / 20.40		170-171 (dec.)	68
4f	$C_{20}H_{17}N_5O$	69.90 / 69.95	4.82 / 4.99	20.22 / 20.40		142-143 (dec.)	65
4g	$C_{22}H_{22}N_6O$	68.28 / 68.37	5.62 / 5.74	21.80 / 21.75		161-163 (dec.)	70

* Found, %: Cl 9.60; calculated, %: Cl 9.72.

*[2] Found, %: Cl 9.20; calculated, %: Cl 9.41.

α-Oxocyclohexene heterocycles other than 4-oxo-4,5,6,7-tetrahydroindazoles were oxidized by selenious acid. The oxidation of 3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindoxazene [10] gives the corresponding 4,5-dioxo derivative while oxidation of 2-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinazolines [11] gives the 6,8-epidiseleno derivative.

Oxidation of the 2,3-diaryl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazoles **1a-g** [12, 13] was carried out using the method reported in [5-7]. The α-dicarbonyl structural fragment in the 4,5-dioxo derivatives **2a-g** produced gave two characteristic IR spectroscopic frequencies at 1735-1725 (ν $C_{(5)}$=O) and 1690-1670 cm^{-1} (ν $C_{(4)}$=O). Refluxing these dioxo derivatives **2a-g** with an equimolar amount of tosylhydrazine for 5 h gave the corresponding 4-oxo-5-tosylhydrazono-4,5,6,7-tetrahydroindazoles **3a-g** which contain an intramolecular

hydrogen bond (ν CO 1650-1640 cm^{-1}, δ NH 12.8 ppm). The decomposition of the α-diketone monohydrazones **3** using an aqueous ethanol solution of alkali [14] gave the diazo ketones **4a-g** which are characterized in the IR spectrum by the diazo group absorption at 2100-2080 cm^{-1} and the C=O absorption at 1630-1620 cm^{-1}. The ^{1}H NMR spectra of the diketone **2**, tosylhydrazones **3**, and diazo ketones **4** showed proton signals for all of the structural fragments in these compounds.

TABLE 2. IR and ^{1}H NMR Spectra of the Compounds Synthesized

Com-pound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
2a	1730, 1685	1.35 (6H, s, $2CH_3$); 3.12 (2H, s, CH_2); 7.29 (10H, m, $2C_6H_5$)
2b	1727, 1688	1.36 (6H, s, $2CH_3$); 3.11 (2H, s, CH_2); 7.33 (9H, m, C_6H_4, C_6H_5)
2c	1733, 1690	1.37 (6H, s, $2CH_3$); 2.92 (6H, s, $N(CH_3)_2$); 3.12 (2H, s, CH_2); 6.57 (2H, m, ^3J = 8, C_6H_4); 7.27 (7H, m, C_6H_4, C_6H_5)
2d	1732, 1690-1680	1.36 (6H, s, $2CH_3$); 3.09 (2H, s, CH_2); 3.73 (3H, s, OCH_3); 6.81 (2H, m, ^3J = 8.5, C_6H_4); 7.22 (7H, m, C_6H_4, C_6H_5)
2e	1735, 1685	1.41 (6H, s, $2CH_3$); 3.25 (2H, s, CH_2); 7.26 (5H, m, C_6H_5); 7.89 (2H, dt, ^3J = 8, ^4J = 1.5, C_5H_4N); 8.47 (1H, d, ^4J=1.5, C_5H_4N); 8.61 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N)
2f	1730, 1680	1.42 (6H, s, $2CH_3$); 3.24 (2H, s, CH_2); 7.16-7.82 (8H, m, C_5H_4N, C_6H_5); 8.56 (1H, dd, ^3J = 5, J = 1.5, C_5H_4N)
2g	1728, 1685	1.33 (6H, s, $2CH_3$); 2.91 (6H, s, $N(CH_3)_2$); 3.14 (2H, s, CH_2); 6.51 (2H, m, ^3J = 8, C_6H_4); 7.01-7.71 (5H, m, C_6H_4, C_5H_4N); 8.53 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N)
3a	1645, 3190	1.22 (6H, s, $2CH_3$); 2.37 (3H, s, CH_3); 2.86 (2H, s, CH_2); 7.25 (12H, m, $2C_6H_5$, C_6H_4); 7.81 (2H, m, ^3J = 8, C_6H_4); 12.83 (1H, br. s, NH)
3b	1642; 3200	1.22 (6H, s, $2CH_3$); 2.33 (3H, s, CH_3); 2.29 (2H, s, CH_2); 7.28 (11H, m, C_6H_5, $2C_6H_4$); 7.75 (2H, m, ^3J = 8, C_6H_4); 12.81 (1H, br. s, NH)
3c	1640, 3170	1.22 (6H, s, $2CH_3$); 2.36 (3H, s, CH_3); 2.86 (2H, s, CH_2); 2.94 (6H, s, $N(CH_3)_2$); 6.53 (2H, m, ^3J = 8, C_6H_4); 7.28 (9H, m, C_6H_5, C_6H_4); 7.83 (2H, m, ^3J = 8, C_6H_4); 12.81 (1H, br. s, NH)
3d	1644, 3200-3170	1.25 (6H, s, $2CH_3$); 2.31 (3H, s, CH_3); 2.94 (2H, s, CH_2); 3.78 (3H, s, OCH_3); 6.78 (2H, m, ^3J = 8, C_6H_4); 7.17 (9H, m, C_6H_5, C_6H_4); 7.72 (2H, m, ^3J = 8, C_6H_4); 12.81 (1H, br. s, NH)
3e	1641, 3200	1.21 (6H, s, $2CH_3$); 2.39 (3H, s, CH_3); 2.89 (2H, s, CH_2); 7.19-7.81 (11H, m, C_6H_5, C_6H_4, C_5H_4N); 8.42 (1H, d, ^4J = 1.5, C_5H_4N); 8.47 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N); 12.81 (1H, br. s, NH)
3f	1640, 3180	1.19 (6H, s, $2CH_3$); 2.36 (3H, s, CH_3); 2.92 (2H, s, CH_2); 7.28-7.83 (12H, m, C_6H_5, C_6H_4, C_5H_4N); 8.33 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N); 12.84 (1H, br. s, NH)
3g	1644, 3190	1.20 (6H, s, $2CH_3$); 2.39 (3H, s, CH_3); 2.92 (2H, s, CH_2); 2.98 (6H, s, $N(CH_3)_2$); 6.58 (2H, m, ^3J = 8, C_6H_4); 7.30-7.44 (7H, m, C_6H_4, C_5H_4N); 7.81 (2H, m, ^3J = 8, C_6H_4); 8.50 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N); 12.92 (1H, br. s, NH)
4a	1620, 2090	1.33 (6H, s, $2CH_3$); 2.84 (2H, s, CH_2); 7.26 (10H, m, $2C_6H_5$)
4b	1623, 2095	1.34 (6H, s, $2CH_3$); 2.92 (2H, s, CH_2); 7.28 (9H, m, C_6H_5, C_6H_4)
4c	1622, 2095	1.33 (6H, s, $2CH_3$); 2.82 (2H, s, CH_2); 2.86 (6H, s, $N(CH_3)_2$); 6.56 (2H, m, ^3J = 8, C_6H_4); 7.22 (7H, m, C_6H_5, C_6H_4)
4d	1620, 2090	1.33 (6H, s, $2CH_3$); 2.84 (2H, s, CH_2); 3.73 (3H, s, OCH_3); 6.81 (2H, m, ^3J = 8, C_6H_4); 7.22 (5H, m, C_6H_5); 7.24 (2H, m, ^3J = 8, C_6H_4)
4e	1620, 2100	1.40 (6H, s, $2CH_3$); 2.93 (2H, s, CH_2); 7.22 (6H, m, C_6H_5, C_5H_4N); 7.87 (1H, m, C_5H_4N); 8.47 (2H, m, C_5H_4N)
4f	1622, 2100	1.36 (6H, s, $2CH_3$); 2.93 (2H, s, CH_2); 6.95-7.71 (8H, m, C_6H_5, C_5H_4N); 8.40 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N)
4g	1619, 2095	1.36 (6H, s, $2CH_3$); 2.93 (2H, s, CH_2); 2.95 (6H, s, $N(CH_3)_2$); 6.53 (2H, m, ^3J = 8, C_6H_4); 6.97-7.68 (5H, m, C_5H_4N, C_6H_4); 8.51 (1H, dd, ^3J = 5, ^4J = 1.5, C_5H_4N)

EXPERIMENTAL

IR spectra were recorded on a Specord IR-75 instrument for a suspension of the material in vaseline oil (1800-1500 cm^{-1} region) and in hexachlorobutadiene (3600-2000 cm^{-1} region). Only the carbonyl absorption bands are reported for the region 1800-1500 cm^{-1}. The absorption bands for the C–H stretching vibrations in the region 3050-2800 cm^{-1} are not reported. ^1H NMR spectra were recorded on a Bruker WH/90 DS instrument (90 MHz) using $CDCl_3$ solvent and HMDS as internal standard (δ 0.05 ppm).

2,3-Diaryl-6,6-dimethyl-4,5-dioxo-4,5,6,7-tetrahydroindazoles 2a-g. Finely pulverized H_2SeO_3 (4 mmol) in conc. H_2SO_4 (4 mmol, in the case of **1c-g** 8 mmol) was added to a solution of the 4-oxo-4,5,6,7-tetrahydroindazole **1a-g** (4 mmol) in glacial acetic acid (15 ml). The reaction mixture was left for 4 days with occasional shaking and then heated for 2 h on a boiling water bath. The hot mixture was filtered from the black selenium precipitate. The filtrate was poured into crushed ice and a dilute (1:1) solution of ammonium hydroxide was added until turbidity ceased and a precipitate was formed. The precipitate of the diketone **2** was filtered off. Compounds **2a,e-g** were recrystallized from a mixture of ethyl acetate and hexane (1:1), **2b,d** from ethyl acetate, and **2c** from a mixture of ethyl acetate and benzene.

2,3-Diaryl-6,6-dimethyl-4-oxo-5-tosylhydrazono-4,5,6,7-tetrahydroindazoles 3a-g. Separately prepared, hot solutions of diketone **2** (2 mmol) in ethanol (20 ml) and of tosylhydrazine (2 mmol) in ethanol (10 ml) were mixed and heated for 6 h. Hot water (5 ml) was added to the hot mixture and the product was allowed to stand for 1 day in the fridge. The precipitated tosylhydrazone **3** was filtered off and recrystallized from 80% ethanol (compounds **3a,b**), ethanol (**3c-f**), or a mixture of ethyl acetate and hexane (**3g**).

2,3-Diaryl-5-diazo-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazoles 4a-g. A suspension of the tosylhydrazone **3** (0.5 mmol) in aqueous sodium hydroxide (2%, 15 ml) was heated for 1 h on a boiling water bath, gradually adding ethanol (3 ml). The reaction mixture was cooled and the precipitated yellow diazo ketone **4** was filtered off, carefully washed with water on the filter to the disappearance of an alkaline reaction, and recrystallized from a mixture of ethyl acetate and hexane (**4a,c-g**) or a mixture of benzene and hexane (**4b**).

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