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Chemistry of Diazopolycarbonyl Compounds: IX.* Synthesis of 6-Aryl-3-acyl-4-hydroxypyridazines by Heterocyclization of 1,5-Disubstituted 2-Diazo-1,3,5-pentanetriones

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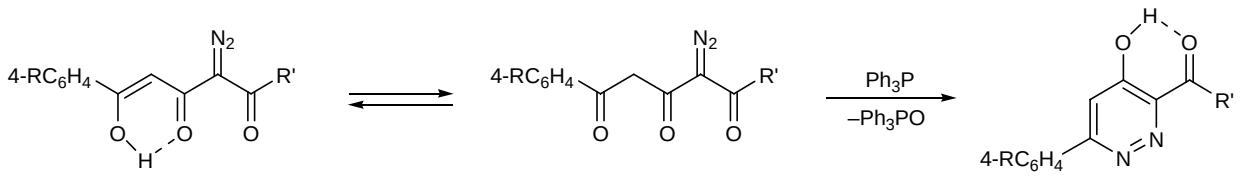
Abstract—5-Aryl-2-diazo-1,3,5-pentanetriones undergo intramolecular cyclization by the action of triphenylphosphine to give triphenylphosphine oxide and substituted 6-aryl-3-acyl-4-hydroxypyridazines.

We previously showed [2, 3] that some ethyl 5-aryl-2-diazo-5-hydroxy-3-oxo-4-pentenoates undergo intramolecular cyclization into ethyl 6-aryl-4-hydroxypyridazine-3-carboxylates by the action of triphenylphosphine. It was presumed that the cyclization involves the β-diketone tautomer of diazo esters. Later on, we found that the above diazo esters and structurally related 1,5-diaryl-2-diazo-5-hydroxy-4-pentene-1,3-diones in solution are enolized only partially [1]. In the present work we examined the possibility for analogous intramolecular cyclization of 5-aryl-2-diazo-1,3,5-pentanetriones having various substituents in position *1*. For this purpose, by reactions of aroyldiazomethanes, adamantylcarbonyldiazometanes, and phthalimido-α-diazoketones with aroylketenes [1] we synthesized 1,5-diaryl-2-diazo-1,3,5-pentanetriones **Ia**–**Ii**, 1-(1-adamantyl)-5-aryl-2-diazo-1,3,5-pentanetriones **Ij**–**Im**, and 5-aryl-2-diazo-1-phthalimidoalkyl-1,3,5-pentanetriones **In**–**It** (Table 1).

According to the ^{1}H NMR data, compounds **I** in solution are partially enolized [1]. Newly synthesized diazopentanetriones **In**, **Io**, and **Iq**–**It** containing a phthalimido group are also partially enolized in DMSO, the fraction of the diketone tautomer **B** being 22 to 43%. In the ^{1}H NMR spectra of compounds **In**, **Io**, and **Iq**–**It**, methylene protons of the β-diketone form (**B**) give a singlet at δ 4.32–4.51 ppm, while signals from the methine proton and proton of the hydroxy group of the enol form (**A**) appear, respectively, at δ 6.45–7.03 and 15.05–15.65 ppm.

The IR spectra of compounds **In**–**It** in mineral oil contain absorption bands at 1655–1682 cm^{-1} due to stretching vibrations of the ketone carbonyl (C^1=O) and at 1605–1615 cm^{-1}, the latter belonging to the

Scheme 1.



A **Ia–It** **B** **IIa–IIq**

I, **II**, R^1 = Ph, R = H (**a**), Me (**b**), MeO (**c**), Cl (**d**), Br (**e**); R^1 = 4-BrC$_6$H$_4$, R = MeO (**f**); R^1 = 4-NO$_2$C$_6$H$_4$, R = H (**g**), MeO (**h**), Br (**i**); R^1 = 1-Ad, R = H (**j**), Me (**k**), MeO (**l**), C1 (**m**); R^1 = PhthCH(Me), R = H (**n**), Me (**o**), MeO (**p**); R^1 = PhthCH$_2$CH$_2$, R = H (**q**); R^1 = PhthCH$_2$, R = Me (**r**); R^1 = PhthCH(CH$_2$CH$_3$), R = Me (**s**); R^1 = Phth(CH$_2$)$_3$, R = MeO (**t**); Phth is phthalimido.

* For communication VIII, see [1].

Table 1. IR and ^{1}H NMR spectra and **A**:**B** tautomer ratios of compounds **In**–**It** and **IIa**–**IIq**

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm					A:B tautomer ratio, solvent
		aliphatic protons[a]	CH_2, s	=CH, s	Ar, m	OH, s	
In	2125 (N_2); 1768, 1712 (C=O, Phth); 1671 (C^1=O); 1606 (C^3=O)	1.58 d (3H, CH_3), 5.51 q and 5.38 q (1H, CH)	4.50	7.03	7.85	15.35	66:34, DMSO-d_6
Io	2129 (N_2); 1768, 1703 (C=O, Phth); 1665 (C^1=O); 1605 (C^3=O)	1.60 d and 1.50 d (3H, CH_3), 2.38 s and 2.52 s (3H, C**H**$_3$C$_6$H$_4$), 5.50 q and 5.38 q (1H, CH)	4.48	6.99	7.85	15.41	73:27, DMSO-d_6
Ip	2130 (N_2); 1771, 1720 (C=O, Phth); 1682 (C^1=O); 1607 (C^3=O)						
Iq	2138 (N_2); 1770, 1710 (C=O, Phth); 1655 (C^1=O); 1615 (C^3=O)	3.22 t and 3.11 t (2H, CH_2), 3.94 t and 3.82 t (2H, CH_2)	4.51	7.02	7.80	15.48	78:22, DMSO-d_6
Ir	2132 (N_2); 1770, 1720 (C=O, Phth); 1668 (C^1=O), 1608 (C^3=O)	2.45 s and 2.55 s (3H, CH_3), 4.82 s and 4.65 s (2H, CH_2)	4.32	6.45	7.71	15.32	60:40, $CDCl_3$
Is	2130 (N_2); 1770, 1728 (C=O, Phth); 1678 (C^1=O); 1605 (C^3=O)	1.03 t (3H, C**H**$_3$CH$_2$CH), 2.22 m (2H, CH$_3$C**H**$_2$CH), 2.42 s (3H, C**H**$_3$C$_6$H$_4$), 5.18 q (1H, CH$_3$CH$_2$C**H**)		6.85	7.67	15.05	$CDCl_3$
It[b]	2131 (N_2); 1767, 1714 (C=O, Phth); 1651 (C^1=O): 1598 (C^3=O)	2.05 m and 1.92 m (2H, CH_2), 2.80 t (2H, CH_2), 3.73 t and 3.65 t (2H, CH_2), 3.90 s (3H, CH_3)	4.32	6.82	7.70	15.65	78:22, DMSO-d_6
IIa	3200 sh (OH), 1684 (C=O)			6.70	7.65	13.61	DMSO-d_6–CCl_4 (1:3)
IIb	3234 (OH), 1673 (C=O)	2.32 s (3H, CH_3)		6.73	7.55	13.88	DMSO-d_6
IIc	3150 sh (OH), 1672 (C=O)	3.89 s (3H, CH_3)		6.64	7.50	13.42	DMSO-d_6–CCl_4 (1:3)
IId	3200 sh (OH), 1664 (C=O)			6.75	7.70	13.60	DMSO-d_6–CCl_4 (1:3)
IIe	3100 sh (OH), 1664 (C=O)			6.73	7.75	13.62	DMSO-d_6–CCl_4 (1:3)
IIf	3120 sh (OH); 1675, 1672 (C=O)						
IIg	3190 (OH), 1676 (C=O)			6.77	7.93	13.78	DMSO-d_6–CCl_4 (1:3)
IIh	3116 (OH), 1674 (C=O)						
IIi	3223 (OH), 1653 (C=O)						
IIj[c]	3237 (OH), 1690 (C=O)	1.87 m (15H, $C_{10}H_{15}$)		6.66	7.54		DMSO-d_6
IIk	3205 (OH), 1695 (C=O)	1.88 m (15H, $C_{10}H_{15}$), 2.35 s (3H, CH_3)		6.63	7.46	13.28	DMSO-d_6
IIl	3183 (OH), 1703 (C=O)						
IIm	3181 (OH), 1705 (C=O)						
IIn	1770, 1715, 1705 (C=O)	1.65 d (3H, CH_3), 5.72 q (1H, CH$_3$C**H**)		6.80	7.70	13.82	DMSO-d_6

Table 1. (Contd.)

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm				A:B tautomer ratio, solvent
		aliphatic protons	=CH, s	Ar, m	OH, s	
IIo	1773, 1710 br (C=O)	1.62 d (3H, C**H**$_3$CH), 2.38 s (3H, C**H**$_3$C$_6$H$_4$), 5.71 q (1H, CH$_3$C**H**)	6.75	7.65	13.75	DMSO-d_6
IIp[c]	3217 (OH); 1775, 1705, 1699 br (C=O)	1.63 d (3H, C**H**$_3$CH), 3.15 s (3H, C**H**$_3$OC$_6$H$_4$), 5.80 q (1H, CH)	6.74	7.60		DMSO-d_6
IIq	1773, 1710, 1697 (C=O)	3.40 t (2H, CH$_2$), 3.95 t (2H, CH$_2$)	6.78	7.73	13.71	DMSO-d_6

[a] The two sets of signals from aliphatic protons refer to the enol and ketone tautomers, respectively.

[b] The mass spectrum of **It** contained the molecular ion peak, *m*/*z* 433 (I_{rel} 5%), and the following fragment ion peaks, *m*/*z* (I_{rel}, %): 405 (73) $[M–N_2]^+$, 273 (12) $[M – Phth(CH_2)_3]^+$, 245 (100) $[MeOC_6H_4COCH_2COCN_2CO]^+$, 216 (52) $[Phth(CH_2)_3CO]^+$, 188 (25) $[Phth(CH_2)_3]^+$, 160 (65) $[PhthCH_2]^+$, 135 (59) $[MeOC_6H_4CO]^+$.

[c] No signal from the enol hydroxy proton was observed in the ^{1}H NMR spectra of compounds **IIj** and **IIp**, presumably due to its considerable broadening.

C^3=O carbonyl group involved in intramolecular hydrogen bond (H-chelate ring).

We made an attempt to obtain triphenylphosphazines from diazotriketones **Ia**–**Iq** by reaction of the latter with triphenylphosphine. However, these reaction resulted in formation of triphenylphosphine oxide and the corresponding substituted 3-acyl-6-aryl-4-hydroxypyridazines **IIa**–**IIq** (Table 1). The IR spectra of compounds **IIa**–**IIq** contained a weak absorption band (or a plateau) in the region 3100–3237 cm^{-1}, which is typical of stretching vibrations of enol hydroxy group, and ketone carbonyl absorption at 1653–1705 cm^{-1}. In the ^{1}H NMR spectra of **IIa**–**IIs**, characteristic signals were a singlet at δ 6.63–6.80 ppm from 5-H in the pyridazine ring and a broadened singlet at δ 13.28–13.88 ppm from the enol hydroxy proton. The high-frequency shift of the carbonyl absorption band in the IR spectra of **II** and upfield position of the enol proton signal in their ^{1}H NMR spectra, as compared to initial diazopentanetriones **I**, indicate that the intramolecular hydrogen bond in **II** is weaker than in **I**. A probable reason is acoplanar arrangement of the pyridazine ring and the acyl substituent.

Presumably, the intramolecular cyclization of diazopentanetriones **I** begins with formation of intermediate triphenylphosphazine **C** which then undergoes ring closure to 4,5-dihydropyridazin-4-one **D** via elimination of triphenylphosphine oxide. Enolization of ketone **D** yields 4-hydroxypyridazine **II**. The cyclization is likely to involve the β-diketone form (**B**) of diazo compounds **I**.

EXPERIMENTAL

The IR spectra were recorded on an FSM-1201 spectrometer in mineral oil. The ^{1}H NMR spectra were obtained on a Bruker WR-80-SY instrument (80 MHz) using $CDCl_3$ or $(CD_3)_2SO$ as solvent and HMDS as internal reference. The mass spectrum of **It** (electron impact, 70 eV) was recorded on a Varian MAT-311A mass spectrometer (emission current 1000 mA, vaporizer temperature 120–150°C, ion source temperature 200°C). The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using diethyl ether–benzene–acetone (10:9:1) as eluent (development with iodine vapor).

4-Diazo-1-phenyl-6-phthalimido-1,3,5-heptanetrione (In). A solution of 2.43 g of (0.01 mol) of 1-diazo-3-phthalimidobutan-2-one and 1.74 g (0.01 mol) of 5-phenyl-2,3-dihydrofuran-2,3-dione [4] in 40 ml of anhydrous benzene was heated for 3 h under reflux. The mixture was evaporated, and the

Scheme 2.

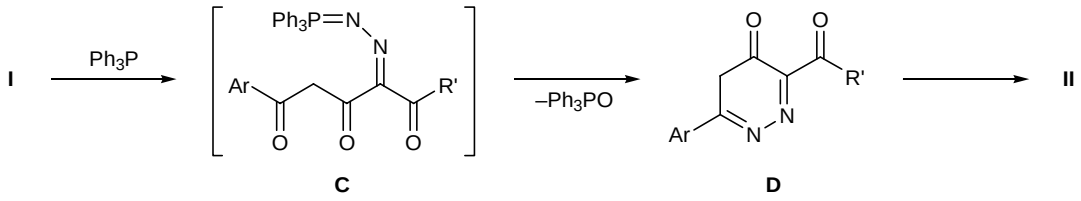


Table 2. Yields, melting points, and elemental analyses of compounds **In**–**It** and **IIa**–**IIq**

Comp. no.	Yield, %	mp, °C (decomp.)	Found, %				Formula	Calculated,%			
			C	H	N	Hlg		C	H	N	Hlg
In	39	149–149.5	64.82	3.72	10.87	–	$C_{21}H_{15}O_5N_3$	64.78	3.88	10.79	–
Io	40	153–154	64.89	4.07	10.56	–	$C_{22}N_{17}O_5N_3$	65.01	4.25	10.42	–
Ip	47	144–145	63.11	4.20	9.95	–	$C_{22}H_{17}O_6N_3$	63.00	4.08	10.02	–
Iq	40	133–134	64.62	4.01	10.75	–	$C_{21}H_{15}O_5N_3$	64.78	3.88	10.79	–
Ir	44	153–154	64.70	3.92	10.81	–	$C_{21}H_{15}O_6N_3$	64.78	3.88	10.79	–
Is	32	129–130	66.24	4.71	9.98	–	$C_{23}H_{19}O_5N_3$	66.18	4.59	10.07	–
It	17	112–115	63.65	4.54	9.56	–	$C_{23}H_{19}O_5N_3$	63.74	4.42	9.70	–
IIa	62	249–251	74.02	4.34	10.03	–	$C_{17}H_{12}O_2N_2$	73.90	4.38	10.14	–
IIb	68	230–231	74.31	4.79	9.74	–	$C_{18}H_{14}O_2N_2$	74.47	4.86	9.65	–
IIc	38	260–261	70.64	4.57	9.27	–	$C_{18}H_{14}O_3N_2$	70.58	4.61	9.15	–
IId	82	258–260	65.64	3.69	9.12	11.32	$C_{17}H_{11}O_2N_2Cl$	65.71	3.57	9.01	11.41
IIe	75	264–266	57.61	3.31	7.75	22.41	$C_{17}H_{11}O_2N_2Br$	57.49	3.12	7.89	22.50
IIf	21	296–298	56.05	3.29	7.15	20.83	$C_{18}H_{13}O_3N_2Br$	56.13	3.40	7.27	20.74
IIg	46	273–275	63.49	3.54	13.21	–	$C_{17}H_{11}O_4N_3$	63.55	3.45	13.08	–
IIh	81	295–297	61.59	3.85	12.05	–	$C_{18}H_{13}O_5N_3$	61.54	3.73	11.96	–
IIi	66	292–293	50.92	2.68	10.62	20.01	$C_{17}H_{10}O_4N_3Br$	51.02	2.52	10.50	19.97
IIj	78	208–209	73.31	6.53	8.04	–	$C_{21}H_{22}O_2N_2$	73.23	6.44	8.13	–
IIk	53	336–337	73.86	6.62	7.94	–	$C_{22}H_{24}O_2N_2$	73.72	6.75	7.82	–
IIl	25	288–291	72.40	6.51	7.80	–	$C_{22}H_{24}O_2N_3$	72.51	6.64	7.69	–
IIm		311–313	68.51	5.80	7.47	9.75	$C_{21}H_{21}O_2N_2Cl$	68.38	5.74	7.59	9.61
IIn	42	242–244	67.49	4.16	11.31	–	$C_{21}H_{15}O_4N_3$	67.55	4.05	11.26	–
IIo	35	246–248	68.19	4.16	10.71	–	$C_{22}H_{17}O_4N_3$	68.21	4.25	10.85	–
IIp	79	267–268	64.92	4.38	10.56	–	$C_{22}H_{17}O_5N_3$	65.01	4.25	10.42	–
IIq	56	218–221	67.67	4.19	11.30	–	$C_{21}H_{15}O_4N_3$	67.55	4.05	11.26	–

residue was recrystallized from acetone. Yield 1.52 g (39%). mp 149–149.5°C. Compounds **Io**–**It** were synthesized in a similar way.

3-Benzoyl-4-hydroxy-6-phenylpyridazine (II). A solution of 2.92 g (0.01 mol) of diazo compound **Ia** and 2.62 g (0.01 mol) of triphenylphosphine in 50 ml of anhydrous diethyl ether was kept for 48 h at 20–25°C. The mixture was evaporated, and the residue was recrystallized from dioxane. Yield 1.81 g (62%). Decomposition point 249–251°C. Compounds **IIb**–**IIq** were synthesized in a similar way.

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