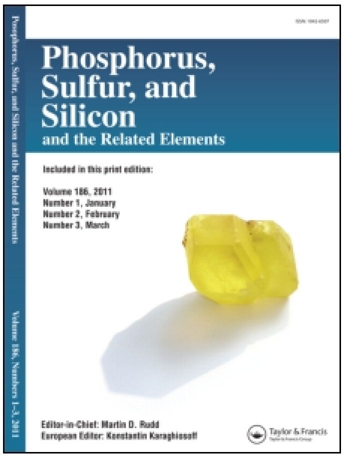

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INVESTIGATION ON SOME REACTIONS OF SACCHARINYL BENZOIC ACID AZIDES

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Communication

INVESTIGATION ON SOME REACTIONS OF SACCHARINYL BENZOIC ACID AZIDES

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Saccharinyl benzoic acid azides **2a–c** were used to synthesize a number of noncondensed heterocyclic systems. Thus azides **2a** or **2c** reacted with glycine to give 1,3-oxazolin-5-one derivatives **3a** and **3b**. However azide **2b** reacted to give diaryl urea derivative which was easily cyclized to give imidazol -2,5- dione (**6**). Also azides **2a–c** reacted with glycolic acid to give 1,3-oxazolin -2,5-dione derivatives (**7a–c**) and with aroyl hydrazines to give the corresponding hydrazides (**8a–f**) which were cyclized to 1,3,5-oxadiazole derivatives (**9a–f**).

Keywords: Saccharin; benzoic acid azide

In considering possible approaches to the development of new heterocyclic side chains derived from saccharinyl benzoic acid azides,[1,2] it was found that o- and p- (N-saccharinyl)-benzoic acid azides[2] (**2a** and **2c**) reacted with glycine to give 2-(2'N- phenyl saccharinyl)- 1,3 -oxazolin- 5- one (**3a**) and 2-(4' N-phenylsaccharinyl)-1,3- oxazolin- 5- one (**3b**) respectively.

The structures of **3a** and **3b** were established by (i) Direct comparison (m.m.p) with authentic specimens prepared by the reaction of 2-(N-saccharinyl)-benzoic acid chloride (**1a**) or 4-(N-saccharinyl)-benzoic acid chloride[2] (**1c**) with glycine. This showed that the reaction took place via azido group displacement. (ii) IR spectra revealed absorption bands at 1720–1710 cm^{-1}(νCO), 1620–1610 cm^{-1}(ν CN), 1750–1740 cm^{-1}(ν CO of cyclic imide) and (1340–1330 cm^{-1} and 1140–1130 cm^{-1}) ν SO_2. (iii) Mass spectra of **3b** showed molecular ion peak at m/z (relative abundance %) 342 (0.03).

On the other hand m- (N-saccharinyl) benzoic acid azide (**2b**) underwent base catalyzed decomposition with glycine under the same reaction conditions to give N-carboxymethyl -N′ (m-saccharinyl-phenyl) urea (**5b**). The structure of **5b** was supported by (i) Direct comparison (m.m.p) with authentic specimens prepared by the reaction of 3-saccharinyl- phenyl isocyanate[2] (**4b**) with glycine. This showed that the reaction took place via Curtius rearrangement (ii) IR spectra which showed bands due to ν CO of diaryl urea at 1660 cm^{-1}, ν CO of cyclic imide at 1740 cm^{-1}, ν (OH and NH) at 3450–3250 cm^{-1} and ν SO_2 at (1330 cm^{-1} and 1120 cm^{-1}). (iii) Mass spectra showed molecular ion peak at m/z (relative abundance %) 375 (0.01).

Attempts to cyclize **5b** in the presence of acetic anhydride gave 1-(m- saccharinyl-phenyl)- imidazol-2,5- dione (**6b**). The structure of **6b** was proved by (i) IR spectra which showed bands duo to ν CO of two different imides at 1750 cm^{-1}, 1710 cm^{-1}, 1690 cm^{-1}; ν CN at 1620 cm^{-1} and ν SO_2 at (1320 cm^{-1} and 1130 cm^{-1}) (ii) ^1H NMR spectrum showed signals at (δ ppm), 5.3 (s,2H, CO-CH_2-NH), 7.3–7.6 (m, 8H, ArH) and 9.2 (s, 1H, NH). (iii) Mass spectra showed molecular ion peak at m/z (relative abundance %) 357(0.01).

Also it was found that o-saccharinyl -phenyl isocyanate[2] (**4a**) or p-saccharinyl-phenyl isocyanate[2] (**4c**) reacted with glycine to give the corresponding urea derivatives **5a** and **5c**. The structures of **5a** and **5c** were proved by IR spectra which showed bands due to ν CO of N, N′- diaryl urea at 1670–1660 cm^{-1}, ν CO of cyclic imide at 1740–1730 cm^{-1}, ν (OH,NH) at 3450–3300 cm^{-1} and ν SO_2 at (1340–1330 cm^{-1} and 1130–1120 cm^{-1})

Moreover, it was found that when compound **5a** or **5c** was refluxed with acetic anhydride, it was easily cyclized to give 1-(o-saccharinyl-phenyl)-(**6a**) and 1-(p-saccharinyl-phenyl)- imidazolo- 2,5- dione (**6c**) respectively. The structures of **6a** and **6c** were supported by IR spectra which revealed absorption bands at 1750–1740 cm^{-1}, 1710–1700 cm^{-1}, 1690–1680 cm^{-1} (ν CO of two different imides), 1630–1620 cm^{-1} (ν CN) and 1320–1310 cm^{-1} and 1130–1120 cm^{-1} (ν SO_2).

Also it was found that azides **2a–c** underwent decompostion reaction with glycolic acid via Curtius rearrangement to give 3- (o-saccharinyl-phenyl)- (**7a**); 3- (m-saccharinyl-phenyl)- (**7b**) and 3-(p- saccharinyl-phenyl)-1,3 oxazolin -2,5 dione (**7c**) respectively. The structures of **7a–c** were established by: (i) Direct comparison (m.m.p) with authentic specimens prepared by the reaction of isocyanate[2] **4a–c** with glycolic acid. (ii) IR spectra showed absorption bands related to the presence of ν CO of two different imides (1740–1730 cm^{-1}, 1690–1670 cm^{-1}), ν SO_2 (1340–1320 and 1140–1120 cm^{-1}) and ν CO of lactone (1710–1700 cm^{-1}). (iii) ^1H NMR spectrum of **7c** showed signals at (δ ppm), 4.2 (s,2H, CH_2) and 7.3–7.8 (m,8H, ArH).

Furthermore, azides **3a–c** reacted with benzoyl hydrazine and/or p-nitrobenzoyl hydrazine to give the corresponding N-saccharinyl-benzoic acid hydrazides (**8a–f**). The structures of **8a–f** were established from: (i) By comparison (m.m.p) with authentic samples prepared via the reaction of the corresponding acid chloride[2] **1a–c** with the same aroyl hydrazines. This showed that the reaction took place via azide group displacement.[3,4] (ii) IR spectra which showed ν NH at 3350–3200 cm^{-1}, ν CO of hydrazide at 1680–1640 cm^{-1}, ν CO of cyclic imide (1750–1730 cm^{-1}) and ν SO_2 at (1350–1310 cm^{-1} and 1140–1120 cm^{-1}). The hydrazides (**8a–f**) were used as a precursor in the synthesis of 2-aryl-5 (N-saccharinyl -phenyl)-1,3,5-oxadiazole (**9a–f**) by the action of polyphosphoric acid or acetic anhydride on (**8a–f**). The structures of (**9a–f**) were established by: (i) IR spectra which revealed absorption bands at 1750–1740 cm^{-1} (ν CO of cyclic imide), 1630–1620 cm^{-1} (ν CN), 1060–1050 cm^{-1} (ν C-O-C) and (1320–1310 cm^{-1} and 1150–1140 cm^{-1}) ν SO_2. (ii) Mass spectra, compounds **9a,9d,9e** and **9f** showed molecular ion peaks at m/z (relative abundance %) 403(0.01), 448(0.01), 403(8.73) and 448(25.33) respectively. In accordance with the ion produced under electron impact, the fragmentation of these compounds was generally found to follow the general fragmentation pattern anticipated for oxadiazoles.[5–8]

EXPERIMENTAL

All melting points are uncorrected. IR spectra in KBr were recorded on Shimadzu 470 spectrometer. ^1H NMR spectra were measured on Varion EM-390-90 MHz spectrometer using TMS as internal reference and the chemical shifts are expressed as δ(ppm). Mass spectra were recorded on HP Model: MS 5988 at 70 eV . The mass spectral data: m/z (relative abundance %) are listed in Table I. The physical data of all the synthesized compounds were given in Table II.

2- (2′-N-phenyl-saccharinyl)-1,3 -oxazolin-5-one (3a) and 2- (4′-N-phenyl Saccharinyl)-1,3-oxazolin- 5-one (3b)

Azide (**2a,c**) (0.01 mole) and/or acid chloride (**1a,c**) (0.01 mole) in dry toluene was treated with glycine (0.015 mole) and few drops of dry pyridine (0.5ml) at room temperature. The reaction mixture was refluxed for 3hr. The excess solvent was removed and the solid residue was washed with water, and then crystallized from a suitable solvent to give **3a** and **3b** respectively.

TABLE I Mass Spectra

Compd. No.	*m/z (Relative Abundance %)*
3b	342(0.03)(M^+), 284(0.11), 257(0.08), 183(100), 168(0.05), 163(0.08), 142(0.39), 141(0.69), 140(7.34), 120(37.65), 119(32), 116(0.08), 105(1.94), 104(18.39), 92(29.17), 91(5.56), 77(5.20), 76(63.89), 75(10.99), 58(0.42).
5b	375(0.01) (M^+), 342(0.02), 300(0.04), 286(100), 284(0.7), 274(0.12), 259(0.33), 183(2.16), 182(0.61), 168(0.57), 163(0.4), 141(24.37), 140(6.57), 139(76.0), 105(0.85), 104(5.26), 91(1.61), 90(10.70), 78(0.41), 76(16.65), 75(24.38), 64(3.82).
6b	357(0.31) (M^+), 342(0.14), 300(0.44), 272(0.15), 257(0.25), 183(1.98), 182(0.94), 168(2.24), 142(2.5), 141(1.91), 139(7.15), 105(20.96), 104(34.48), 91(26.0), 90(19.40), 77(41.12), 76(74.05), 75(61.64), 74(30), 69(32.22), 55(100).
9a	403(0.01) (M^+), 326(0.01), 286(0.3), 284(0.2), 270(0.1), 258(0.2), 182(0.2), 168(0.1), 140(0.31), 105(100), 103(0.26), 90(0.31), 77(65.58), 76(2.34), 63(0.55).
9d	448(0.01) (M^+), 286(81.05), 181(0.56), 186(0.65), 150(3.25), 148(0.06), 140(9.15), 139(100), 122(0.61), 104(11.39), 77(12.18), 76(55.02), 64(16.24), 63(20.19).
9e	403(8.72) (M^+), 262(4.03), 259(14.09), 182(6.60), 147(6.71), 140(10.74), 120(21.46), 105(63.09), 99(12.08), 93(18.12), 77(100), 65(15.44), 63(24.16).
9f	448(25.33) (M^+), 402(4.00), 326(12.0), 314(4.0), 284(12.0), 182(2.11), 150(17.33), 148(9.33), 140(6.67), 139(14.67), 121(10.67), 76(100), 63(18.67), 62(45.67).

N-acetic- N′-(3-saccharinyl Phenyl) Urea (5b)

The reaction was carried out and the reaction mixture worked-up as above to give **5b**.

Action of Glycine on Isocyanates 4a–c : Formation of 5a–c

Isocyanates **4a–c** (0.01 mole) (prepared by refluxing azides **2a–c** in dry toluene for one hour), glycine (0.01mole) and pyridine (0.5 ml) were refluxed for 2hr. The solvent was removed to leave crude solid, recrystallized from a suitable solvent to give **5a–c**.

Action of Acetic Anhydride on 5a–c: Formation of 6a–c

Compound **5a, 5b** and/or **5c** (0.01 mole) was heated in acetic anhydride (10 ml) for 1/2 hr. The reaction mixture was cooled and poured on ice-cold water. The solid product separated was filtered and recrystallized from a suitable solvent to give **6a–c**.

TABLE II Physical date of various compounds prepared

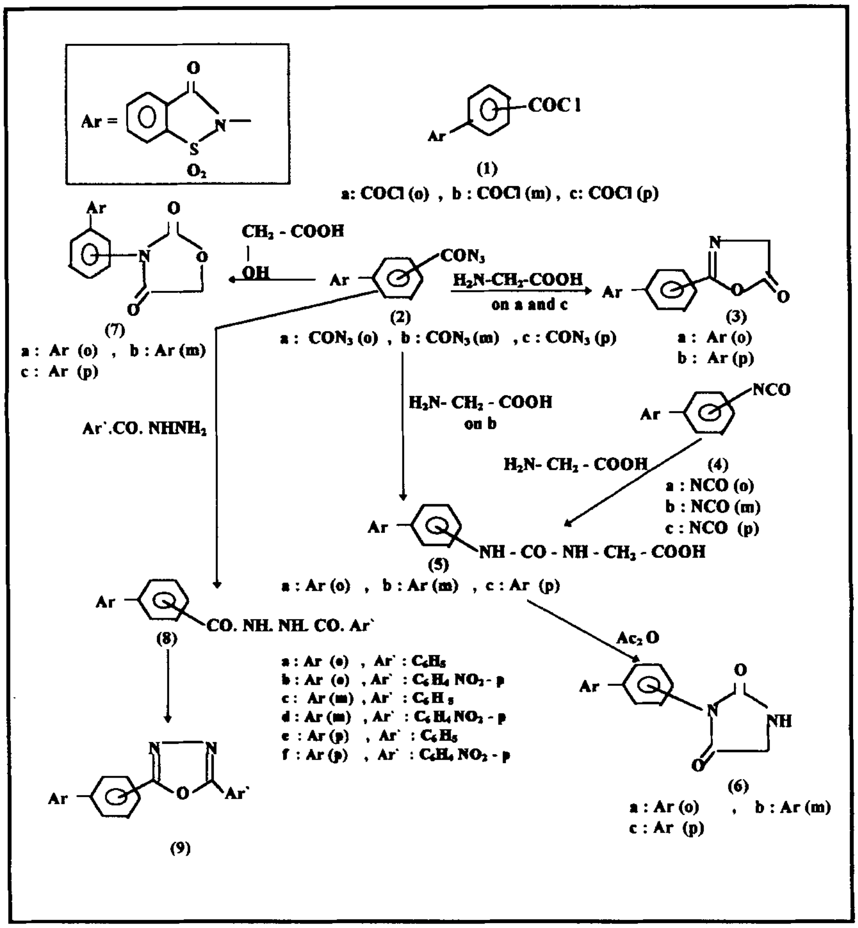
Compd. No.	*M.P.°C**	*Yield (%)*	*Mol. Formula (M.wt)*	*Analysis Calc. (%)(found)*		
				C	*H*	*N*
3a	143–145[a]	68	$C_{16}H_{10}N_2O_5S$	56.14	2.92	8.19
			(342)	(56.11	2.90	8.17)
3b	268–270[b]	62	$C_{16}H_{10}N_2O_5S$	56.14	2.92	8.19
			(342)	(56.12	2.91	8.16)
5a	225–227[c]	72	$C_{16}H_{13}N_3O_6S$	51.2	3.47	11.2
			(375)	(51.2	3.46	11.18)
5b	232–234[b]	70	$C_{16}H_{13}N_3O_6S$	51.2	3.47	11.2
			(375)	(51.08	3.45	11.17)
5c	208–210[b]	78	$C_{16}H_{13}N_3O_6S$	51.2	3.47	11.2
			(375)	(51.17	3.47	11.21)
6a	188–190[c]	80	$C_{16}H_{11}N_3O_5S$	53.78	3.08	11.76
			(357)	(53.78	3.05	11.75)
6b	201–203[c]	84	$C_{16}H_{11}N_3O_5S$	53.78	3.08	11.76
			(357)	(53.75	3.10	11.77)
6c	170–172[a]	82	$C_{16}H_{11}N_3O_5S$	53.78	2.08	11.76
			(357)	(53.79	2.10	11.79)
7a	119–121[c]	63	$C_{16}H_{10}N_2O_6S$	53.63	2.79	7.82
			(358)	(53.60	2.78	7.80)
7b	194–196[c]	68	$C_{16}H_{10}N_2O_6S$	53.63	2.79	7.82
			(358)	(53.61	2.77	7.83)
7c	197–181[c]	72	$C_{16}H_{10}N_2O_6S$	53.63	2.79	7.82
			(358)	(53.64	2.79	7.81)
8a	230–232[a]	82	$C_{21}H_{15}N_3O_5S$	59.86	3.56	9.98
			(421)	(59.82	3.55	9.97)
8b	175–177[b]	78	$C_{21}H_{14}N_4O_7S$	54.08	3.00	12.02
			(466)	(54.06	3.01	12.04)
8c	213–215[b]	62	$C_{21}H_{15}N_3O_5S$	59.86	3.56	9.98
			(421)	(59.87	3.56	9.99)
8d	201–203[b]	74	$C_{21}H_{14}N_4O_7S$	54.08	3.00	12.02
			(466)	(54.10	3.00	12.01)
8e	178–180[b]	80	$C_{21}H_{15}N_3O_5S$	59.86	3.56	9.98
			(421)	(59.85	3.55	9.96)
8f	197–199[b]	87	$C_{21}H_{14}N_4O_7S$	54.08	3.00	12.02
			(466)	(54.08	2.97	12.00)
9a	207–209[c]	79	$C_{21}H_{13}N_3O_4S$	62.53	3.23	10.42
			(403)	(62.51	3.22	10.40)
9b	152–154[c]	73	$C_{21}H_{12}N_4O_6S$	56.25	2.68	12.5
			(448)	(56.24	2.68	12.48)
9c	185–187[c]	68	$C_{21}H_{13}N_3O_4S$	62.53	3.23	10.42
			(403)	(62.53	3.21	10.41)
9d	178–180[c]	70	$C_{21}H_{12}N_4O_6S$	56.25	3.68	12.5
			(448)	(56.25	3.66	12.49)
9e	152–154[c]	86	$C_{21}H_{13}N_3O_4S$	62.53	3.23	10.42
			(403)	(62.52	3.22	10.42)
9f	163–165[c]	88	$C_{21}H_{12}N_4O_6S$	56.25	2.68	12.5
			(448)	(56.26	2.67	12.51)

*The compounds recrystallized from

(a) benzene

(b) toluene

(c) benzene–ethanol.



Action of Glycolic Acid on Azides 2a–c and/or Isocyanates 4a–c: Formation of 7a–c

A mixture of azides **2a–c** (0.01 mole) and/or isocyanates **4a–c** (0.01 mole) in dry benzene (20 ml) were treated with glycolic acid (0.015 mole). The reaction mixture was refluxed for one houre, and the solid precipitated on cooling was filtered and recrystallized from benzene-ethanol mixture to give **7a–c**.

Decomposition of Azides 2a–c with Aroyl Hydrazines: Formation of 8a–f

To a solution of azides **2a–c** (0.01 mole) in dry benzene, the appropriate aroyl hydrazine (0.015 mole) was added and the reaction mixture was refluxed for 2 hr. The ppt. was recrystallized from a suitable solvent to give **8a–f**.

Reaction of Acid Chlorides 1a–c with Aroyl-hydrazine: Formation of 8a–f

To a solution of acid chlorides **1a–c** (0.01 mole) in dry benzene, (0.015) of aroyl hydrazine was added and the reaction mixture was refluxed for 2hr. The solid product was filtered and recrystallized from a suitable solvent to give **8a–f**.

Cyclisation of 8a–f to 1,3,5- oxadiazole Derivatives 9a–f

Method A

A solution of **8a–f** (0.01 mole) in acetic acid (10 ml) and polyphosphoric acid (20 ml) was heated to 150–180°C for one hour, then added to ice cold water. The solid product filtered and recrystallized from benzene-ethanol mixture to give **9a–f**.

Method B

A solution of **8a–f** (0.01 mole) in acetic anhydride (10 ml) was heated for half hour. The reaction mixture was cooled and poured on ice cold water. The solid product separated was filtered and recrystallized from benzene -ethonol mixture to give **9a–f**.

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