

BIPHENYL SERIES—I

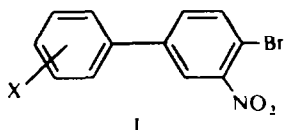
THE SYNTHESIS OF SOME 2', 3'- AND 4'-SUBSTITUTED 3-NITRO-4-BROMOBIPHENYLS

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Abstract—The synthesis of a range of 2', 3'- and 4'-substituted 3-nitro-4-bromobiphenyls and of their intermediates is described.

IN ORDER to obtain information concerning the electronic transmission of polar substituent effects in biarylic systems, we synthesized a range of 2', 3'- and 4'-substituted 3-nitro-4-bromobiphenyls (I) and investigated kinetically the piperidino-debromination of these compounds.

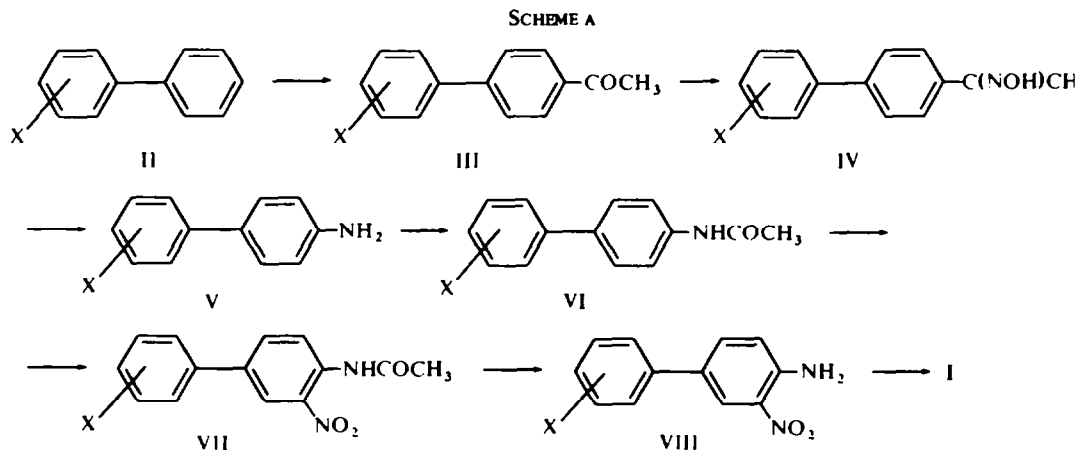


X = H, 2'-, 3'-, 4'-Hal (Hal = Cl, Br, I),
2', 3'-, 4'-SO₂CH₃, 4'-COCH₃,
2', 3'-, 4'-NO₂.

In the present paper we report the synthesis of biphenylic derivatives and the kinetic results obtained are discussed in the following papers.

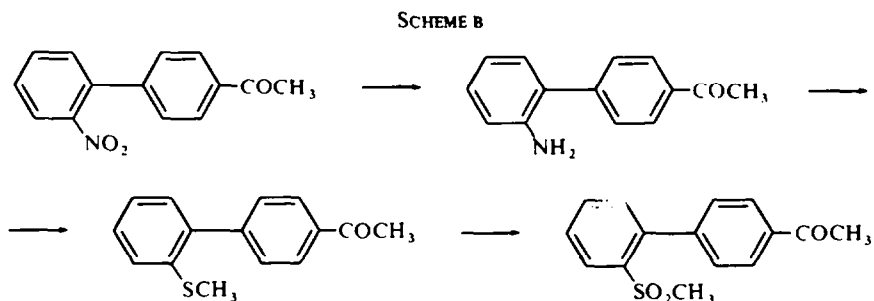
Some biphenylic substrates used (I, X = H (1a), 4'-Br (1b), 3'-NO₂ (1c), 4'-NO₂ (1a)) were known compounds and were obtained by the methods reported in the literature. The majority instead were prepared by suitable synthetic routes and are reported in this paper.

Compounds I were generally prepared using the same unambiguous synthetic Scheme a.



X = 2', 3'-, 4'-Hal, 2', 3'-, 4'-SO₂CH₃, 2'-NO₂.

The 2-methylsulphonyl-4'-acetylbiphenyl (III, X = 2'-SO₂CH₃) was prepared via scheme (b).



The acetylation of 3-nitro-4-bromobiphenyl (I, X = H) yielded 3-nitro-4-bromo-4'-acetylbiphenyl (I, X = 4'-COCH₃).

Satisfactory elemental analyses were obtained for all the compounds I and for the relative intermediates reported in Schemes a and b, which require no comment. The structures of compounds I, II VIII were confirmed in some cases by comparison with known samples.

EXPERIMENTAL

X-substituted biphenyls (II). 2-Chloro-,² 2-bromo-,³ 2-iodo-,⁴ 2-nitro-,² 3-chloro-,² 3-bromo-,⁵ 3-iodo-,⁶ 4-chloro-,⁷ 4-iodo-⁸ and 4-methylsulphonyl-biphenyl⁹ were prepared by known methods.

3-Methylsulphonyl-biphenyl (II, X = 3-SO₂CH₃) was obtained by oxidation of II (X = 3-SCH₃) under reflux with peracetic acid as a colourless crystalline product from MeOH, m.p. 85°. (Found: C, 67.60; H, 5.33; S, 13.70; C₁₃H₁₂O₂S requires: C, 67.24, H, 5.17; S, 13.79%).

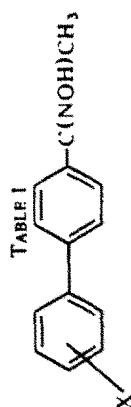
3-Xenyl-methyl-sulphide (II, X = 3-SCH₃). 3-Aminobiphenyl¹⁰ (0.152 mole) in dil HCl (1:1, v/v; 96 ml) was diazotized with NaNO₂ (11.5 g) at 5–10°. The soln obtained was added dropwise at 70° with stirring to a soln of potassium ethyl xanthate (80 g) and Na₂CO₃ (20 g) in water (200 ml) and the mixture heated at 70° for a further 3 hr and then extracted with ether. The ether was removed by distillation and the residue was warmed under reflux with EtOH (150 ml) and NaOH (18 g). The EtOH was removed by steam distillation and the residue was taken up in the minimum of water. The aqueous soln, washed with ether, was methylated at 0° with Me₂SO₄ (18.7 g) and the mixture was warmed at 40–50° for 2 hr and extracted with ether. The ether was removed by distillation and the oily residue was distilled under reduced pressure: b.p. 175°/20 mm. (Found: C, 78.81; H, 6.20; S, 16.20; C₁₃H₁₂S requires: C, 78.00; H, 6.00; S, 16.00%).

X-substituted 4-acetylbiphenyls (III). 2'-Chloro-, 2'-bromo-, 2'-iodo-, 2'-nitro-, 3'-chloro-, 3'-bromo-, 3'-iodo-, 4'-chloro- and 4'-iodo-4-acetylbiphenyl were prepared by known methods.¹¹

2'-Methylsulphonyl-4-acetylbiphenyl (III, X = 2'-SO₂CH₃) was obtained by oxidation of III (X = 2'-SCH₃) under reflux with peracetic acid as a colourless crystalline product from MeOH, m.p. 135°. (Found: C, 65.99; H, 5.31; S, 11.80; C₁₅H₁₄O₃S requires: C, 65.69; H, 5.11; S, 11.68%).

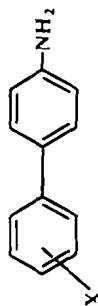
2'-Xenyl-(4-acetyl)-methyl-sulphide (III, X = 2'-SCH₃) was obtained from III (X = 2'-NH₂) by the method reported for 3-xenyl-methyl-sulphide as a colourless product from ligroin, m.p. 71°. (Found: C, 74.73; H, 5.90; S, 13.15; C₁₅H₁₄OS requires: C, 74.38; H, 5.79; S, 13.22%).

2'-Amino-4-acetylbiphenyl (III, X = 2'-NH₂) was obtained by reduction of III¹¹ (X = 2'-NO₂) with tin and HCl as a colourless product from ligroin, m.p. 79°. (Found: C, 79.99; H, 6.27; N, 6.74; C₁₄H₁₃NO requires: C, 79.62; H, 6.16; N, 6.64%).



X =	Crystallization solvent	m.p.	N	Found %		S	Formula	N	Required %		S
				Hal	%				Hal	%	
2'-Cl	ligroin	136°	5.65	14.25	—	—	C ₁₄ H ₁₁ ClNO	5.70	14.46	—	—
2'-Br	ethanol	136°	4.82	27.91	—	—	C ₁₄ H ₁₁ BrNO	4.83	27.56	—	—
2'-I(11)	methanol	142°	—	—	—	—	—	—	—	—	—
2'-NO ₂	benzene	156°	11.08	—	—	—	C ₁₄ H ₁₁ N ₂ O ₃	10.94	—	—	—
2'-SO ₂ CH ₃	ethanol	191°	4.76	—	11.20	—	C ₁₃ H ₁₁ NO ₃ S	4.84	—	—	11.07
3'-Cl	ligroin	128°	5.81	14.54	—	—	C ₁₄ H ₁₁ ClNO	5.70	14.46	—	—
3'-Br	ligroin	128°	4.90	27.85	—	—	C ₁₄ H ₁₁ BrNO	4.83	27.56	—	—
3'-I	ethanol	160°	4.20	—	—	—	C ₁₄ H ₁₁ I NO	4.15	—	—	—
3'-SO ₂ CH ₃	ethanol/dioxan	190°	4.73	—	11.28	—	C ₁₃ H ₁₁ NO ₃ S	4.84	—	—	11.07
4'-Cl	ethanol/dioxan	197°	5.77	14.31	—	—	C ₁₄ H ₁₁ ClNO	5.70	14.46	—	—
4'-I	ethanol/dioxan	258°	4.24	—	—	—	C ₁₄ H ₁₁ I NO	4.15	—	—	—
4'-SO ₂ CH ₃	ethanol/dioxan	245°	4.86	—	11.18	—	C ₁₃ H ₁₁ NO ₃ S	4.83	—	—	11.07

TABLE 2



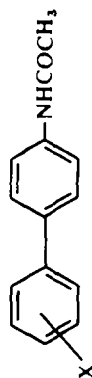
X =	Crystallization solvent	m. p.	Found % N	Formula	Required % N
2'-Cl (11)	—	42-43°	—	—	—
2'-I (11)	—	(b.p. 115-120°/0.1 mm)	—	—	—
2'-NO ₂	ligroin/benzene	94°	13.04	C ₁₂ H ₁₀ N ₂ O ₂	13.08
2'-SO ₂ CH ₃ ^a	methanol/dioxan	186°	5.71	C ₁₃ H ₁₃ NO ₂ S	5.66
3'-Cl (11)	—	47-48°	—	⊗	—
3'-I	ligroin/benzene	78-80°	4.85	C ₁₂ H ₁₀ IN	4.74
3'-SO ₂ CH ₃ ^b	—	157-158°	—	—	—
4'-Cl ^c	—	134°	—	—	—
4'-I ^c	—	166°	—	—	—
4'-SO ₂ CH ₃ ^b	—	211-212°	—	—	—

^a Found: S, 12.98; required: S, 12.95%.

^b V. A. Kopytng, T. N. Gerasimova and A. A. Tabatskaya, loc. cit.

^c P. Gelmo, Berl., 39, 4176 (1906).

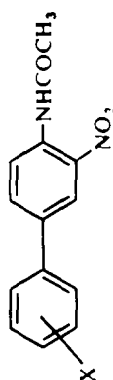
TABLE 3



X =	Crystallization solvent	m.p.	N	Found % Hal	S	Formula	N	Required % Hal	S
2'-Cl	benzene	159°	5.81	14.63	--	C ₁₄ H ₁₂ ClNO	5.70	14.46	--
2'-Br	benzene	151°	4.98	27.87	--	C ₁₄ H ₁₂ BrNO	4.83	27.56	--
2'-I	benzene	177°	4.20	--	--	C ₁₄ H ₁₂ I NO	4.15	--	--
2'-NO ₂	benzene	155°	11.11	--	--	C ₁₄ H ₁₂ N ₂ O ₃	10.94	--	--
2'-SO ₂ CH ₃	benzene	207°	4.93	--	10.94	C ₁₅ H ₁₃ NO ₃ S	4.84	--	11.07
3'-Cl	ethanol	182°	5.76	14.62	--	C ₁₄ H ₁₂ ClNO	5.70	14.46	--
3'-Br	ethanol	181°	4.77	27.79	--	C ₁₄ H ₁₂ BrNO	4.83	27.56	--
3'-I	ethanol	180°	4.18	--	--	C ₁₄ H ₁₂ I NO	4.15	--	--
3'-SO ₂ CH ₃	ethanol	173°	4.87	--	11.19	C ₁₅ H ₁₃ NO ₃ S	4.84	--	11.07
4'-Cl ^a	--	245°	--	--	--	--	--	--	--
4'-I ^a	--	245°	--	--	--	--	--	--	--
4'-SO ₂ CH ₃	ethanol/dioxan	270°	4.81	--	11.08	C ₁₅ H ₁₃ NO ₃ S	4.84	--	11.07

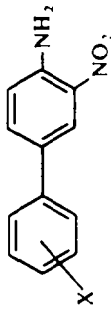
^a P. Gelmo, *Ber.* **39**, 4176 (1906).

TABLE 4



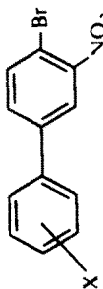
X =	Crystallization solvent	m.p.	N	Found %		S	Formula	N	Required %	
				Hal	Hal				Hal	S
2'-Cl	ethanol	137°	9.74	12.53	—	—	C ₁₄ H ₁₁ ClN ₂ O ₃	9.64	12.22	—
2'-Br	ethanol	132°	8.36	24.18	—	—	C ₁₄ H ₁₁ BrN ₂ O ₃	8.35	23.88	—
2'-I	ethanol	172°	7.27	—	—	—	C ₁₄ H ₁₁ I N ₂ O ₃	7.33	—	—
2'-NO ₂	ethanol	168°	14.04	—	—	—	C ₁₄ H ₁₁ N ₃ O ₅	13.95	—	—
2'-SO ₂ CH ₃	ethanol	183°	8.49	—	9.56	—	C ₁₅ H ₁₄ N ₂ O ₅ S	8.38	—	9.58
3'-Cl	ethanol/dioxan	180°	9.71	12.32	—	—	C ₁₄ H ₁₁ ClN ₂ O ₃	9.64	12.22	—
3'-Br	ethanol/dioxan	184°	8.47	24.01	—	—	C ₁₄ H ₁₁ BrN ₂ O ₃	8.35	23.88	—
3'-I	ethanol/dioxan	176°	7.36	—	—	—	C ₁₄ H ₁₁ I N ₂ O ₃	7.33	—	—
3'-SO ₂ CH ₃	ethanol/dioxan	188°	8.39	—	9.65	—	C ₁₅ H ₁₄ N ₂ O ₅ S	8.38	—	9.58
4'-Cl	ethanol/dioxan	205°	9.57	12.26	—	—	C ₁₄ H ₁₁ ClN ₂ O ₃	9.64	12.22	—
4'-I	ethanol/dioxan	200°	7.44	—	—	—	C ₁₄ H ₁₁ I N ₂ O ₃	7.33	—	—
4'-SO ₂ CH ₃	ethanol/dioxan	250°	8.43	—	9.71	—	C ₁₅ H ₁₄ N ₂ O ₅ S	8.38	—	9.58

TABLE 5



X =	Crystallization solvent	m.p.	N	Found %		S	Formula	N	Required %	
				Hal	S				Hal	S
2'-Cl	ethanol	141°	11:39	14.44	--	--	C ₁₂ H ₉ ClN ₂ O ₂	11.27	14.28	--
2'-Br	ethanol	145°	9:67	27.48	--	--	C ₁₂ H ₉ BrN ₂ O ₂	9.55	27.28	--
2'-I	ethanol	146°	8:30	--	--	--	C ₁₂ H ₉ IN ₂ O ₂	8.23	--	--
2'-NO ₂	ethanol	174°	16:34	--	--	--	C ₁₂ H ₉ N ₃ O ₄	16.21	--	--
2'-SO ₂ CH ₃	ethanol	171°	9:68	--	10.90	--	C ₁₃ H ₁₂ N ₂ O ₄ S	9.59	--	10.95
3'-Cl	ethanol	146°	11:35	14.52	--	--	C ₁₂ H ₉ ClN ₂ O ₂	11.27	14.28	--
3'-Br	ethanol	138°	9:70	27.38	--	--	C ₁₂ H ₉ BrN ₂ O ₂	9.55	27.28	--
3'-I	ethanol	140°	8:33	--	--	--	C ₁₂ H ₉ IN ₂ O ₂	8.23	--	--
3'-SO ₂ CH ₃	ethanol/dioxan	198°	9:66	--	11.17	--	C ₁₃ H ₁₂ N ₂ O ₄ S	9.59	--	10.95
4'-Cl	ethanol/dioxan	175°	11:42	14.31	--	--	C ₁₂ H ₉ ClN ₂ O ₂	11.27	14.28	--
4'-I	ethanol/dioxan	203°	8:32	--	--	--	C ₁₂ H ₉ IN ₂ O ₂	8.23	--	--
4'-SO ₂ CH ₃	ethanol/dioxan	218°	9:76	--	11.09	--	C ₁₃ H ₁₂ N ₂ O ₄ S	9.59	--	10.95

TABLE 6



X =	Crystallization solvent	m.p.	N	Found %		S	Formula	N	Required %	
				Hal	S				Hal	S
2'-Cl	ligroin	89°	4.54	37.11	—	C ₁₂ H ₇ BrClNO ₂	4.48	36.96	—	
2'-Br ^a	ligroin	90°	—	—	—	—	—	—	—	
2'-I ^b	ligroin	99°	3.35	—	—	C ₁₂ H ₇ BrINO ₂	3.47	—	—	
2'-NO ₂	ethanol	154-155°	—	—	—	—	—	—	—	
2'-SO ₂ CH ₃	ethanol	158-159°	3.89	22.61	8.99	C ₁₃ H ₁₀ BrNO ₄ S	3.93	22.47	8.98	
3'-Cl	ligroin	112°	4.79	37.37	—	C ₁₂ H ₇ BrClNO ₂	4.48	36.96	—	
3'-Br	ligroin	117°	4.05	44.81	—	C ₁₂ H ₇ Br ₂ NO ₂	3.92	44.77	—	
3'-I ^c	ligroin	109°	3.66	—	—	C ₁₂ H ₇ BrINO ₂	3.47	—	—	
3'-SO ₂ CH ₃	ethanol	147°	3.90	22.75	9.03	C ₁₃ H ₁₀ BrNO ₄ S	3.93	22.47	8.98	
4'-Cl	ligroin	94°	4.56	36.91	—	C ₁₂ H ₇ BrClNO ₂	4.48	36.96	—	
4'-I ^d	ligroin	116-118°	3.49	—	—	C ₁₂ H ₇ BrINO ₂	3.47	—	—	
4'-COCH ₃	ethanol	173°	4.41	25.29	—	C ₁₄ H ₁₀ BrNO ₃	4.38	24.96	—	
4'-SO ₂ CH ₃	ethanol	188°	4.05	22.70	8.75	C ₁₃ H ₁₀ BrNO ₄ S	3.93	22.47	8.98	

^a C. Finzi and A. Mangini, *Gazzetta*, **62**, 1193, 1197 (1932).

^b Found: C, 35.83; H, 1.79; required: C, 35.64; H, 1.73%.

^c F. H. Case, *J. Am. Chem. Soc.*, **64**, 1848, 1850 (1942).

^d Found: C, 35.59; H, 1.77; required: C, 35.64; H, 1.73%.

^e Found: C, 35.78; H, 1.80; required: C, 35.64; H, 1.73%.

3-Methylsulphonyl-4-acetylbiphenyl (III, X = 3'-SO₂CH₃). Crushed anhyd AlCl₃ (1.18 mole) was suspended in dry CS₂ (160 ml). Acetyl chloride (0.5 mole) and II (X = 3-SO₂CH₃; 0.47 mole) were dissolved in CS₂ (160 ml) and added to the rapidly stirred suspension during 20 min. Stirring was continued for 30 min, and the mixture was then heated under reflux, with stirring, for a further 4 hr. CS₂ was removed by distillation at reduced pressure and the residue was added to ice-water. The ketone was separated by filtration and crystallized from MeOH as a colourless crystalline product, m.p. 124°. (Found: C, 66.10; H, 5.36; S, 11.64; C₁₅H₁₄O₃S requires: C, 65.69; H, 5.11; S, 11.68%).

4'-Methylsulphonyl-4-acetylbiphenyl (III, X = 4'-SO₂CH₃). Anhyd AlCl₃ (0.2 mole) and II (X = 4-SO₂CH₃; 0.08 mole) were dissolved in dry nitrobenzene (85 ml). Acetyl chloride (0.1 mole) was added at 20° and the dark soln was stirred at room temp for 12 hr and at 50° for 6 hr. The soln was poured onto a mixture of ice, water and conc HCl. The organic layer was separated and the nitrobenzene removed by steam distillation. The residue was cooled and the separated ketone was filtered and crystallized from dioxan/EtOH as a colourless product, m.p. 199°. (Found: C, 65.98; H, 5.29; S, 11.82; C₁₅H₁₄O₃S requires: C, 65.69; H, 5.11; S, 11.68%).

Oximes of substituted 4-acetylbiphenyls (IV) were prepared according to the method reported for the oxime of 2'-iodo-4-acetylbiphenyl.¹¹ The crystallization details and the analytical data are reported in Table I.

Substituted 4-aminobiphenyls (V) (Table 2) were obtained by the Beckmann rearrangement from the corresponding oximes according to the method reported for 2'-iodo-4-aminobiphenyl.¹¹ The crude 2'-bromo- and 3'-bromo-4-aminobiphenyl (V, X = 2'-Br and 3'-Br) were oily products which were used in the next stage without purification.

Substituted 4-acetylaminobiphenyls (VI) (Table 3) were prepared by acetylation of corresponding 4-aminobiphenyls (V) with Ac₂O in benzene.

Substituted 3-nitro-4-acetylaminobiphenyls (VII) (Table 4) were obtained by nitration with conc HNO₃ (d = 1.42) in Ac₂O of the corresponding VI according to the method reported for VII (X = H)^{1b}

Substituted 3-nitro-4-aminobiphenyls (VIII) (Table 5) were obtained by refluxing for a few min a soln of substituted VII (0.08 mole) in EtOH (100 ml) with KOH (10 g) and H₂O (12.5 ml). The ppt was separated by filtration and crystallized.

Substituted 3-nitro-4-bromobiphenyls (I) (Table 6) were prepared by the Sandmeyer reaction from the corresponding 3-nitro-4-aminobiphenyls according to the method of Hodgson and Walker.¹²

3-Nitro-4-bromo-4'-acetylbiphenyl (I, X = 4'-COCH₃) was obtained by acetylation of I (X = H; 0.47 mole) with AlCl₃ (0.59 mole) and CH₃COCl (0.5 mole) in CS₂ (320 ml) according to the method reported for 3'-methylsulphonyl-4-acetylbiphenyl. The crude product (m.p. 165–170°) was purified by chromatography on silica column using benzene as eluent. After the initial fractions (containing unreacted 3-nitro-4-bromobiphenyl) 3-nitro-4-bromo-4'-acetylbiphenyl was obtained which was crystallized from EtOH: m.p. 173°.

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