

SYNTHESIS AND CHEMICAL PROPERTIES OF N, N'-DIHYDROXY [2.2] PARACYCLOPHANE-4, 5, 12, 13-TETRACARBOXYLIC ACID-BISIMIDE

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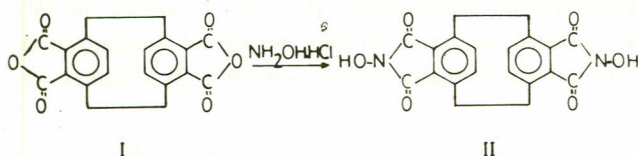
[2.2] *Paracyclophane*-4, 5, 12, 13-tetracarboxylic acid dianhydride (I) reacts with hydroxylamine hydrochloride in pyridine to give N, N'-dihydroxy [2.2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-bisimide (II). The reaction of (II) with arylsulphonyl chlorides, acid chlorides, ammonia, primary aromatic amines, amino acids, hydrazines and base hydrolysis as well as its pyrolysis have been studied.

Key words: [2.2] *Paracyclophane*; Heterocyclic [2.2] *paracyclophane*; Imides.

INTRODUCTION

It is well known that phthalic anhydride reacts with hydroxylamine hydrochloride to give the corresponding *N*-hydroxyphthalimide [1-3]. We report in this paper the synthesis of N, N'-dihydroxy [2.2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-bisimide (II) from the reaction of [2.2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid dianhydride (I) [4, 5], which may be considered as a dimer of phthalic anhydride, with hydroxylamine hydrochloride in the presence of a base such as pyridine.

It is the primary aim of this work to introduce the [2.2] *paracyclophane* nucleus into heterocyclic chemistry. Furthermore, we wish to study the effect of *transannular* electronic interaction which exists in the *paracyclophane* molecule [6, 7] as well as the steric hindrance created by ethano-bridges upon the reactivity of certain types of reactions.

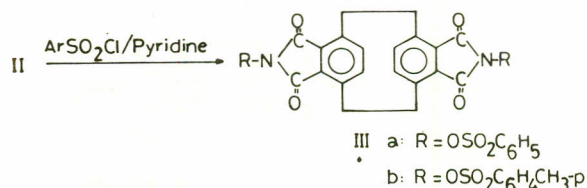


The structure of (II) was assigned on the basis of its analytical and spectroscopic properties. The infrared spectrum showed a doublet at (1760 cm^{-1}) and (1725-1710 cm^{-1}) as expected for the coupling carbonyl band of cyclic imides [8-10] and at 3520 cm^{-1} (ν OH). The n.m.r. measurement showed the following signals: $\delta = 7.40$ (s, 4H, Ar-H), 4.23-3.50 and 3.29-2.78 (m, 10 H, 2 CH_2CH_2 ,

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2 OH). The molecular ion peak in the mass spectrum of (II) was observed at $m/e = 378$ ($\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_6$) and the base peak at $m/e = 189$ ($\text{M}^+/2$, of Experimental).

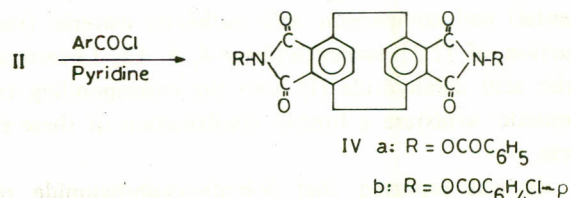
Interaction of *bis-N*-hydroxyimide (II) with arylsulphonyl chlorides in the presence of pyridine afforded *N, N'*-diarylsulphonyloxy [2.2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-bisimides (IIIa, b).



The structures of (IIIa, b) are supported by their analytical data and IR spectra, which showed an absorption band at 1785 cm^{-1} and at 1740 cm^{-1} as expected for cyclic imides [8-10].

Also the mass spectra gave a molecular ion peak at $m/e = 658$ for (IIIa) while at $m/e = 686$ for compound (IIIb).

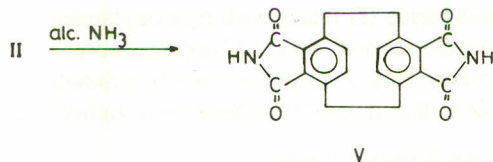
Treatment of (II) with acid chlorides in a basic solvent such as pyridine gave the corresponding *N, N'*-diaryloxy [2.2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid bisimides (IVa, b).



The structure of (IVa, b) was deduced from analytical analysis and infrared spectra, which show doublet in the

region (1790 cm^{-1}) and ($1740\text{-}1720\text{ cm}^{-1}$) characteristic of cyclic imides and another absorption band at ($1765\text{-}1760\text{ cm}^{-1}$) for the carbonyl of the ester, as well as the mass spectra, which show a molecular ion peak at $m/e = 586$ for compound (IVa) while for (IVb) the molecular ion peak is at $m/e = 654$.

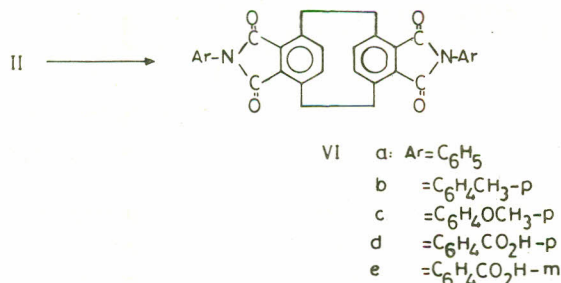
Ammonolysis of (II) with alcoholic ammonia gave the corresponding [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimide* (V).



The structure of (V) was supported by its i.r. mass spectrum and comparison with an authentic sample prepared from (I) with alcoholic ammonia [4].

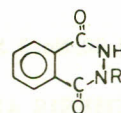
Heating of (II) above its melting point results in deoxygenation to the corresponding bisimide (V).

When (II) is allowed to react with aromatic amines and amino aromatic acids, it undergoes aminolysis to give *N,N'*-diaryl [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimides* (VIa-e).



The structures of products (VIa-c) were established through the comparison of their analytical and spectroscopic data with that reported in literature [4, 11] while the structure of (VI d, e) is supported by their analytical analysis and infrared spectra which show a doublet in the region of ($1760\text{-}1755\text{ cm}^{-1}$) and ($1740\text{-}1735\text{ cm}^{-1}$) for cyclic imides while it showed ($\nu(\text{CO})$) of the acid in the region ($1730\text{-}1710\text{ cm}^{-1}$). Also mass spectra (cf. Experimental) and comparison with authentic material (via the reaction of [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid dianhydride (I) with the corresponding amino aromatic acids) are a further confirmation of these structures.

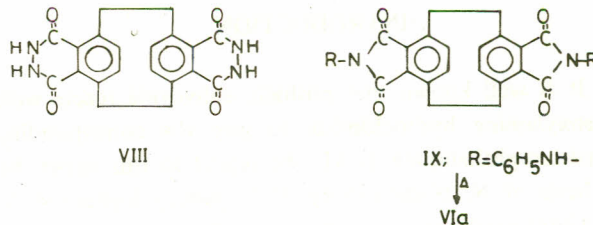
It was reported that *N*-hydroxyphthalimide reacts with hydrazines in acetic acid or ethanol to give the corresponding 1,4 pathalazinedione [12] (VII).



VII

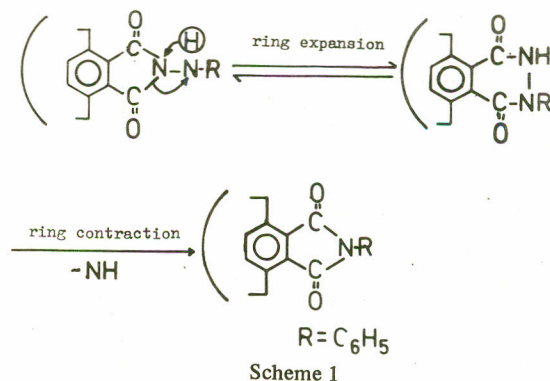
When this reaction was extended to the newly synthesized *N,N'*-dihydroxy [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimide* (II), it afforded with hydrazine hydrate the compound (VIII), while with phenylhydrazine it gave (IX).

It was observed that the heating of *N,N'*-dianilino [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimide* (IX) above its melting point results in the formation of *N,N'*-diphenyl [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimide* (VIa).



compound (VIII) shows a strong absorption-band in the region 1690 cm^{-1} and ($1620\text{-}1600\text{ cm}^{-1}$) characteristic for this type of compounds [8], and at 3230 cm^{-1} ($\nu(\text{NH})$), while for (IX) a doublet at 1760 cm^{-1} and $1720\text{-}1710\text{ cm}^{-1}$ characteristic for cyclic imides and an absorption band at 3400 cm^{-1} ($\nu(\text{NH})$) were observed. Mass spectra of (VIII) and (IX) show a molecular ion peak at $m/e = 376$ and 528 respectively (cf. Experimental).

Pyrolysis of *N,N'*-dianilino [2,2] *paracyclophane*-4, 5, 12, 13-tetra-carboxylic acid-*bisimide* (IX) results in the formation of *N,N'*-diaryl [2,2] *paracyclophane*-4, 5, 12, 13-tetracarboxylic acid-*bisimide* (V). The formation of (V) may proceed according to this postulated mechanism as in the case of phthalic acid derivatives [12] (Scheme 1).



Treatment of (II) with aqueous sodium or alcoholic potassium hydroxide respectively, followed by acidification, results in the formation of (I) [4].

From these results, it may be concluded that the transannular electronic interaction in (II) and the steric factor have no influence on the reactions performed, so in case of hydrazinolysis with phenyl-hydrazine the formation of *bis-N*-dianilino derivative (IX) which is less sterically hindered than that of the hydrazide derivative as in the case of the reaction of (II) with hydrazine hydrate to form (VIII), may be attributed to the lesser degree of nucleophilicity in the case of phenylhydrazine (N-Ph) rather than the steric hindrance of phenyl group with ethylene bridges.

EXPERIMENTAL

Melting points are not corrected. ¹H-n.m.r spectra were measured on BrukerHFX 90 (90 MHz) using tetramethylsilane as the internal reference. (¹H-n.m.r spectra could not be carried out for all of new compounds due to their difficult solubility in the available deuterated solvents). I.R spectra were determined with a Perkin-Elmer model 157 G spectro-photometer in KBr discs. Mass spectra were carried out on MS 9 and MS 30 (AEI Manchester).

N, N'-Dihydroxy[2, 2] paracyclophane-4, 5, 12, 13-tetracarboxylic acid-bisimide (II): A mixture of 1g(2.4 mmol) I and 0.6g(4 mmol) hydroxylamine hydrochloride in 30 ml pyridine was refluxed for 1 hr. After cooling the reaction mixture was poured into ice/hydrochloric acid. The solid product was filtered off, washed with hot water and recrystallized from ethanol to give 0.97g (89 %) (II) as pale yellow crystals, m.p 300°

C₂₀H₁₄N₂O₆(378.34); calcd. C: 63.49%, H: 3.72% N: 7.42%
found C: 63.03%, H: 3.94% N: 7.35%

MS(rel.intensity) *m/e* = 378(M.40), 362(14), 361(18), 346(9), 202(11), 190(21), 189(100), 173(51), 160(19), 102(30) and 89(48).

N, N'-Diarylsulphonyloxy[2, 2] paracyclophane-4, 5, 12, 13-tetracarboxylic acid-bisimides (IIIa, b): *Bis-N*-hydroxyimide II (.38g, 1 mmol) in 20 ml chloroform was treated with 3 ml pyridine until a clear solution was obtained. Arylsulphonyl-chloride (3 mmol) dissolved in 10 ml dry chloroform were added dropwise to the solution with stirring. Chloroform was then evaporated and the solid product obtained was filtered, washed with hot water, ethanol and recrystallized from a proper solvent to give (IIIa, b) (Table 1).

N, N'-Diaryloxy[2, 2] paracyclophane-4, 5, 12, 13-tetracarboxylic acidbisimides (IVa, b): 0.38g, 1 mmol (II) in 20 ml abs. chloroform was treated with 3 ml pyridine until a clear solution was obtained. Acid chlorides (3 mmol) were added dropwise to the solution at room temperature with stirring. Chloroform was evaporated and the solid product was filtered, washed with small amount of cold ethanol and recrystallized from a proper solvent to give (IVa, b) (Table 2).

Ammonolysis of II: Formation of [2,2] paracyclophane-3, 5, 12, 13-tetracarboxylic acidbisimide V. A mixture of (II) (0.76g, 2 mmol) and concentrated ethanolic ammonia (50 ml) was heated under reflux for about 6 hr. The solid product obtained was filtered off, and recrystallized from glacial acetic acid to give a colourless substance (yield 84 %), which was confirmed to be (V) by comparison of its melting point and spectroscopic data (i.r, ms) with those of an authentic sample [4].

Pyrolysis of N, N'-dihydroxy [2,2] paracyclophane-4, 5, 12, 13-tetracarboxylic acid-bisimide (II); *Formation of (V).* *N, N'*-Dihydroxy [2,2] paracyclophane-4, 5, 12, 13-tetra-

Table 1

Acid chloride	Comp. No.	mp (°C)	Yield (%)	Solvent of cryst.	Mol. form. (mol. wt.)	Analysis (%)		
						Calcd./	Found	
						C	H	N
Benzene-sulphonyl-chloride	IIIa	310	94	Ethanol	C ₃₂ H ₂₂ N ₂ O ₁₀ S ₂ (658.67)	58.35	3.37	4.25
						58.22	3.49	4.31
Toluene-sulphonyl-chloride	IIIb	306	91	Toluene	C ₃₄ H ₂₆ N ₂ O ₁₀ S ₂ (686.72)	59.47	3.92	4.08
						59.28	3.97	4.22

Table 2

Acid chloride	Comp. No.	mp (°C)	Yield (%)	Solvent of cryst.	Mol. form. (mol. wt.)	Analysis (%)		
						Calcd/Found	C	H
Benzoyl chloride	IVa	300	91	Benzene	C ₃₄ H ₂₂ N ₂ O ₈ (586.56)	69.62 69.53	3.78 3.69	4.78 4.74
	IVb	310	92	Ethanol	C ₃₄ H ₂₀ N ₂ O ₈ Cl ₂ (655.45)	62.31 62.22	3.08 3.16	4.27 4.39

Table 3

Amine or amino acid	Comp. No.	Yield (%)	MS (rel.int.) (m/e)	Mol. form. (mol.wt.)	Analysis (%)		
					Calcd. / Found	C	H
Aniline	(VIa)	90	498(M ⁺ , 83), 436 (19), 322(4), 249 (100), 221(28), 204(20), 193(42), 165(17), 118(15), 104(35), 102(44) and 90(23)	C ₃₂ H ₂₂ N ₂ O ₄ (498.54)	77.10	4.45	5.62
					76.86	4.62	5.53
<i>p</i> -Toluedine	(VIb)	92	526(M ⁺ , 9), 438(17), 366(13), 264(100), 235(71), 207(61), 191(38), 146(45), 102(22), 93(31) and 77(27)	C ₃₄ H ₂₆ N ₂ O ₄ (526.6)	77.55	4.98	5.32
					77.05	5.12	5.23
<i>p</i> -Anisidine	(VIc)	95	558(M ⁺ , 21), 454(98), 331(14), 279(100), 264(41), 227(21), 174(23), 102(19)	C ₃₄ H ₂₆ N ₂ O ₆ (558.6)	73.11	4.69	5.01
					72.82	4.86	4.81
<i>p</i> -Amino-benzoic acid	(VIId)	86	586(M ⁺ , 21), 498(21), 450(32), 422(15), 378(12), 333(28), 302(76), 293(15), 249(100), 221(48), 193(62), 146(90), and 102(89)	C ₃₄ H ₂₂ N ₂ O ₈ (586.56)	69.62	3.78	4.78
					69.13	4.01	4.62
<i>m</i> -Amino-benzoic acid	(VIe)	88	586(M ⁺ , 19), 498(13), 450(26), 302(58), 293(19), 249(100), 146(80), 102(86), and 77(63).	C ₃₄ H ₂₂ N ₂ O ₈ (586.6)	69.62	3.78	4.78
					69.21	3.99	4.60

carboxylic acid- bisimide (II) was heated above its melting point on a sand bath (400^o) for 1.5 hr. The substance melted and sublimed, and was then collected and charcolised in glacial acetic acid to give (V) in 58 % yield.

Aminolysis of (II); Formation of N,N'-diaryl [2,2] paracyclophane-4, 5, 12, 13-tetracarboxylic acid -bismides (Va-e). A mixture of (0.2g, 0.53 mmol) (II) and (1.1 mmol) aromatic amine or amino aromatic acid in 50 ml glacial acetic acid was heated under reflux for 6 hr. The solid products were filtered off and recrystallized from acetic acid to give (VIa-e) (Table 3). All melting points are above 300^o (VIa, literature [4], mp, 290^o).

Hydrazinolysis of (II): (i) Action of hydrazine hydrate on (II); Formation of (VIII): A mixture of 0.5 g (1.3 mmol) II and hydrazine hydrate 0.43 g (13 mmol) in 30 ml glacial acetic acid was refluxed for 6 hr. The solid product was filtered off, washed with ethanol and recrystallized from acetic acid to give 0.46 g (92%) which was identified to be (VIII); mp, over 300^o

C₂₀H₁₆N₄O₄ (376.38), calcd. C: 63.82%,
H: 4.29%, N: 14.89%
found C: 63.51%, H: 4.48%, N: 14.57%

MS (rel. int.) *m/e* = 376(M⁺, 42), 360(47),
346(33), 188(98), 133(50), 102(62), 77(34),
76(26), and 43(100).

(ii) Action of phenylhydrazine on (II); Formation of N,N'-dianilino [2,2]-paracyclophane-4, 5, 12, 13-tetracarboxylic acid-bisimide (IX). A mixture of 0.378g (1 mmol) (II) and phenylhydrazine 1g (9.3 mmol) in 30 ml glacial acetic acid was refluxed for 7 hr. The solid product was filtered off, washed with ethanol and recrystallized from ethanol to give 0.44g (83%) (IX); mp, 345^o

C₃₂H₂₄N₄O₄ (528.57) calcd. C: 72.72%,
H: 58%, N: 10.60%
found C: 72.43%, H: 4.71%, N: 10.49%

¹H-n.m.r (DMSO-d₆/TMS) δ = 7.43-6.66 (m, 14H, Ar-H),
3.93-3.3 (m, 10H, 2CH₂CH₂, 2H-N).

MS(rel.int.) *m/e* = 528(M⁺, 88), 437 (54), 265
(100), 103(91), 92(99), 77(99), and 65(92).

Pyrolysis of (IX); Formation of N,N'-diphenyl [2,2] paracyclophane-4,5, 12, 13-tetracarboxylic acid-bisimide (VIa). 0.2g of (IX) was heated at 400-450^o on a sand bath for 2 hr. The solid product obtained was charcooled and recrystallized from acetic acid to give 140 mg (74%) from a

substance, which was identified to be (VIa [4, 11] through the comparison of its spectra with that of an authentic sample prepared by the reaction of (I) with aniline in acetic acid.

Base Hydrolysis of (II); Formation of [2,2] Paracyclophane-4, 5, 12, 13-tetracarboxylic acid dianhydride (I). (i) With aqueous sodium hydroxide: A solution of II(0.38g, 1 mmol) in aqueous sodium hydroxide (50 %, 20 ml) was refluxed for 2 hr, cooled and acidified with dilute hydrochloric acid. The solid product was filtered off, washed with water and purified by sublimation (200^o, 10⁻³ torr) to give a white substance which identified to be (I).

(ii) With alcoholic potassium hydroxide: A mixture of 0.225 g (0.6 mmol) (II) in 15 ml Aryl alcohol and 0.17 g (3 mmol) potassium hydroxide dissolved in 2 ml water was refluxed for 3 hr. The solvent was evaporated and the solid product obtained was dissolved in hot water and acidified, washed with water, dried to give 0.178 g (91%) of dianhydride (I).

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