

STUDIES IN CLAISEN REARRANGEMENT—II

2-BUTYN-1,4-DIYL BIS-(ARYL ETHERS)

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Abstract—The rearrangement of 1,4-bis-aryloxybut-2-yne to 4b,9b-dihydro-4b,9b-dimethylbenzofuro(3,2-b) benzofuran is described. The compounds arising from the dehydration of 2,3-(*o*-hydroxyphenyl)-2,3-dihydroxybutane, reported earlier in the literature, are shown to possess benzofuro-(2,3-b) benzofuran system.

THE facile formation of a 6H-Benzofuro-(3,2-c)-1-6a-dihydro-11a-methylbenzopyran derivative from the thermal rearrangement of 2-butyn-1,4-diyl bis-(aryl ethers) was reported earlier.¹ The projected mechanism leading to this product (*vide* Chart I) envisaged the possibility of different modes of protonation in the ultimate step of ring closure resulting in different stereochemistry at the ring junction of the benzopyranobenzofuran system. The present investigation was undertaken to verify such a possibility.

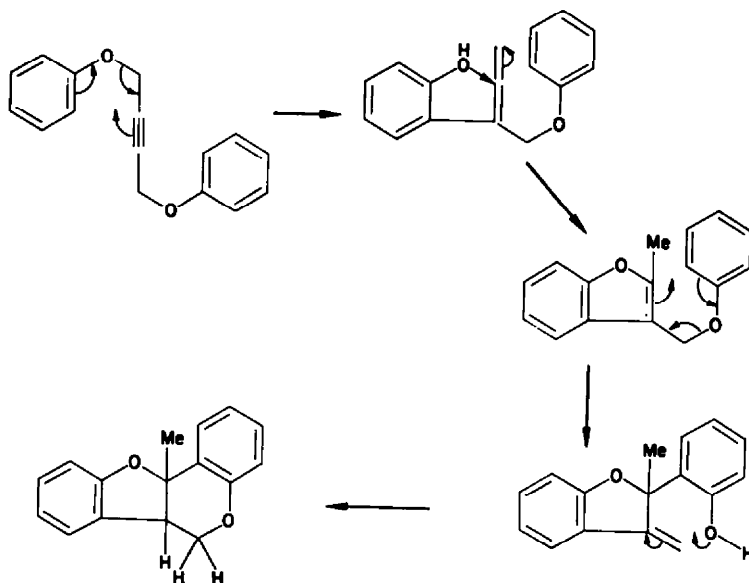


Chart I

¹ B. S. Thyagarajan, K. K. Balasubramanian and R. Bhima Rao, *Tetrahedron Letters* No. 21, 1393 (1963).

The rearrangement of the butynyl ethers was sensitive to the temperature of the reaction, as only solvents boiling above 200° were found to be effective. For this reason, while diethylaniline was effective by itself, the addition of acids like HCl or HClO₄ or such other acids which caused a lowering of the b.p. of the reaction medium, failed to effect the rearrangement. The difficulty was overcome by the addition of a solid acid like *p*-toluenesulphonic acid. Fourteen different ethers were synthesized and rearranged under these conditions. All except four of these rearranged smoothly to give crystalline products in yields as high as 60%. The product in every case was isomeric with the starting material in composition but was different from the corresponding benzopyranobenzofuran derivative.¹ They showed no unsaturation as they were unreactive towards bromine or permanganate. They were unaffected by selenium dioxide in boiling aqueous dioxan. The UV spectra were closely similar to those of the starting materials, showing no extra conjugation had been created. In every case it was also observed the products had much higher m.p. than the corresponding benzopyranobenzofuran derivative. This suggested the possibility of high symmetry in the molecule.² The NMR* spectra of all the rearranged compounds were extremely simple showing only the presence of uncoupled aliphatic methyl groups and aromatic ring protons. No other types of protons were present in the molecule. Accommodating all these facts, only two different structures are possible, as shown below:



Of the two, System A must exhibit unsplit singlet absorption for the methyl groups owing to their location on a quaternary carbon atom and the symmetry of the system. All the rearranged products, excepting XV and XXI, do show such an absorption pattern. Compounds XV and XXI also show only the methyl and aromatic protons with the difference—there are two distinct peaks for the aliphatic methyls suggesting their non-equivalence in the structure. This is easily accommodated by the Structure B postulated above.

Additional support for the assignment for the above structures was sought from the literature. While compounds XV and XXI had been described³ as resulting from the acid catalysed dehydration of 2,3-bis(*o*-hydroxyphenyl)-2,3-dihydroxybutanes, XIX was prepared by us by an analogous procedure. Repetition of the published procedure gave the compounds identical with the corresponding compounds obtained by us by the rearrangement of butynyl ethers.

This could normally have been taken to be substantive proof for the correctness of our structures. However, in the dehydration of the di-hydroxybutanes, one has to

* The NMR spectra were taken in a 60 MC. Varian NMR Spectrometer and were measured in CDCl₃ solution with Tetramethylsilane as internal reference.

¹ D. H. R. Barton and K. H. Overton, *J. Chem. Soc.* 2644 (1955).

² G. J. Gie, *Arkiv. Kemi., Mineral Geol.* 19A, No. 11; p. 15. (1945); Keiiti Sisido, H. Nozaki and I. Iwako, *J. Amer. Chem. Soc.* 71, 2037 (1949).

consider the additional possibility of a pinacol rearrangement prior to cyclization with the phenolic groups. This could lead to the formation of the benzofuro-(2,3-b) benzofuran (Chart II). Such a possibility had been considered improbable by Sisido *et al.*³ There was little evidence offered by them in support of their proposed structures.

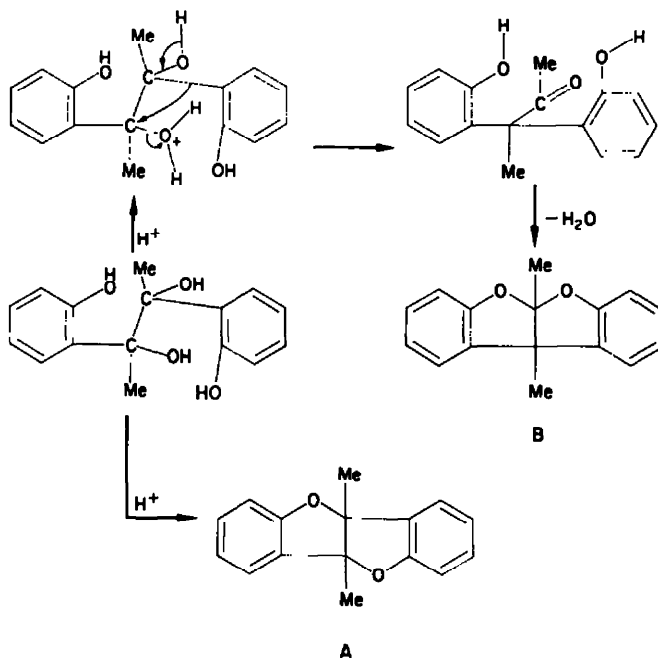


Chart II

The NMR spectra of the three compounds throw interesting light on their structures. Of the three, only XIX shows an unsplit aliphatic methyl absorption at 1.7 ppm and a multiplet of aromatic protons. The other two, XV and XXI show two peaks in the methyl region at 1.6 and 1.7 ppm with a separation of 6 c/s. That this is not due to any coupling, is borne out by the clear absence of any coupling partner in the entire spectrum. Necessarily this arises from the non-equivalence of the two methyl groups in the benzofuro-(2,3-b) benzofuran structure.

Formation of chromans or coumarans, by choice, of suitable acid reagents, from *ortho* allyl phenols is well known.⁴ In such cases, an acid was added to a preformed *ortho* allyl phenol and not to the unrearranged allyl ether. Our results are unique in the sense, the Claisen type rearrangement is carried out in a basic medium, in the presence of a proton donor, leading to the formation of coumarano-coumaran systems.

Further work is in progress on elucidating the role of other proton donors in influencing the stereochemistry or the gross structure of the products formed in the rearrangement reported. Work is also in progress in a study of the rearrangements of aryloxymethyl coumarins, chromenes and chromones.

⁴ C. D. Hurd and W. A. Hoffman, *J. Org. Chem.* **5**, 212 (1940).

EXPERIMENTAL

The symmetrical 1,4-diaryloxy-2-butyne were prepared according to the procedure described by Johnson.⁵ The dissymmetrical ethers were prepared by a different procedure (*vide infra*). The butynyl ethers obtained are listed in Table 1. The m.p. were determined with an ordinary thermometer and were not corrected. All the ethers were recrystallized from hot EtOH or benzene-pet. ether (60–80°) mixture.

TABLE 1. 1,4-DIARYLOXY-2-BUTYNES

No.	R—O—CH ₂ —C≡C—CH ₂ —O—R'		m.p.	FORMULA	ANALYSIS %			
	R	R'			Calc.		Found	
					C	H	C	H
I	Phenyl	Phenyl*						
II	<i>o</i> -Chlorophenyl	<i>o</i> -Chlorophenyl	78°	C ₁₆ H ₁₂ O ₂ Cl ₂	62.55	3.91	62.66;	4.10
III	<i>o</i> -Methoxyphenyl	<i>o</i> -Methoxyphenyl	80°	C ₁₆ H ₁₄ O ₄	72.47	6.08	72.52;	6.18
IV	<i>o</i> -Methylphenyl	<i>o</i> -Methylphenyl	54°	C ₁₆ H ₁₆ O ₂	81.17	6.81	80.79;	6.97
V	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	88°	C ₁₆ H ₁₂ O ₂ Cl ₂	62.55	3.91	62.74;	3.94
VI	<i>p</i> -Bromophenyl	<i>p</i> -Bromophenyl	115°	C ₁₆ H ₁₂ O ₂ Br ₂	48.48	3.03	48.20;	3.02
VII	<i>p</i> -Methylphenyl	<i>p</i> -Methylphenyl	83°	C ₁₈ H ₁₈ O ₂	81.17	6.81	81.27;	6.08
VIII	<i>p</i> -Methoxyphenyl	<i>p</i> -Methoxyphenyl	101°	C ₁₈ H ₁₈ O ₄	72.47	6.08	72.71;	6.15
IX	<i>p</i> -Nitrophenyl	<i>p</i> -Nitrophenyl	192°	C ₁₆ H ₁₁ N ₂ O ₆	58.54	3.68	58.31;	3.78
X	<i>p</i> -Formylphenyl	<i>p</i> -Formylphenyl	143°	C ₁₈ H ₁₄ O ₄	73.46	4.79	73.23;	4.79
XI	<i>p</i> -Chlorophenyl	<i>p</i> -Methylphenyl	81°	C ₁₇ H ₁₄ O ₂ Cl	71.20	5.24	71.24;	5.46
XII	<i>p</i> -Chlorophenyl	<i>p</i> -Nitrophenyl	108°	C ₁₆ H ₁₁ NO ₄ Cl	60.46	3.78	60.77;	3.98
XIII	2,6-Dimethylphenyl	2,6-Dimethylphenyl	70°	C ₂₀ H ₂₂ O ₂	81.6	7.53	81.70;	7.62
XIV	β -Naphthyl	β -Naphthyl	124°	C ₂₄ H ₁₈ O ₂ *				

* Reported by A. W. Johnson⁵

Preparation of 1-(p-chlorophenoxy)-4-(p-nitrophenoxy)-2-butyne (XII). *p*-Chlorophenol (12.4 g) and KOH (5.6 g) were dissolved in EtOH (350 cc) and this ethanolic solution was added slowly to a refluxing solution of 1,4-dichloro-2-butyne (18.4 g) in 50 cc EtOH during a period of 4 hr. The precipitate, after leaving the reaction mixture overnight at room temp was filtered. The filtrate was concentrated and the residue dissolved in ether. The ethereal solution was washed with 10% NaOH aq, then with water until neutral and dried (MgSO₄). The solvent was removed. The excess dichloro-2-butyne was removed by fractional distillation, b.p. 50° (8 mm). The pot residue on further distillation yielded a colourless liquid, b.p. 120° (0.7 mm), yield 6.2 g. This liquid supposed to be 1-chloro-4-(*p*-chlorophenoxy)-2-butyne was added slowly to a refluxing solution of *p*-nitrophenol (7 g) and KOH (2.8 g) in 250 cc EtOH. The mixture was refluxed for 10 hr, cooled and filtered. The yellow precipitate was washed with dil. NaOH aq, and then with water. The dry solid weighed 4 g, m.p. 108°. The ethanolic filtrate yielded 2.7 g more of the same solid upon concentration.

Preparation of 1-(p-chlorophenoxy)-4-(p-methylphenoxy)-but-2-yne (XI). *p*-Cresol (10.8 g) and *p*-chlorophenol (12.4 g) were dissolved in 250 cc EtOH containing KOH (11.2 g). To this ethanolic solution was added 1,4-dichloro-2-butyne (12.3 g) and the mixture refluxed with stirring for 12 hr. The reaction mixture was filtered hot. The filtrate upon cooling yielded a white glistening solid, yield 8 g, m.p. 81° and recrystallized from hot pet. ether (60–80°).

⁵ A. W. Johnson, *J. Chem. Soc.* 1009 (1946).

TABLE 2a. BENZOFURO (3,2-b) BENZOFURANS

No.	R	R ^I	R ^{II}	R ^{III}	R ^{IV}	m.p. °C	FORMULA	ANALYSIS %			
								Calc.		Found	
								C	H	C	H
XVI	Cl	H	H	H	H	228	C ₁₆ H ₁₃ O ₂ Cl ₂	62.55	3.91	62.46	4.18
XVII	—OCH ₃	H	H	H	H	158	C ₁₈ H ₁₄ O ₄	72.47	6.08	72.30	6.09
XVIII	—CH ₃	H	H	H	H	203	C ₁₈ H ₁₆ O ₂	81.17	6.81	81.19	6.54
XIX	H	Cl	H	Cl	H	207	C ₁₆ H ₁₃ O ₂ Cl ₂	62.55	3.91	62.87	3.97
XX	H	Br	H	Br	H	215	C ₁₆ H ₁₃ O ₂ Br ₂	48.48	3.03	48.06	3.08
XXII	H	—OCH ₃	H	—OCH ₃	H	145	C ₁₈ H ₁₆ O ₄	72.47	6.08	72.48	6.14
XXIII	H	Cl	H	—CH ₃	H	175	C ₁₇ H ₁₅ O ₂ Cl	71.20	5.24	70.92	5.54
XXIV	H					246	C ₂₄ H ₁₈ O ₂	85.18	5.36	85.31	5.45
		Phenyl	Phenyl								

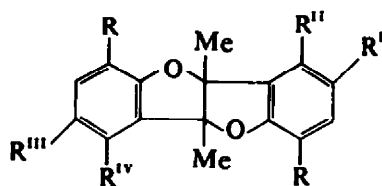
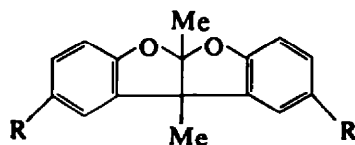


TABLE 2b. BENZOFURO (2,3-b) BENZOFURANS

No.	R	m.p. °C	FORMULA	ANALYSIS %			
				Calc.		Found	
				C	H	C	H
XV	R = H	140	C ₁₆ H ₁₄ O ₂	80.65	5.92	80.42	6.13
XXI	R = CH ₃	197	C ₁₈ H ₁₆ O ₂	81.17	6.81	81.21	6.86



General procedure for the rearrangement of butynyl ethers. The ether (1 g) was refluxed with *p*-toluenesulphonic acid (1 g) in 5 cc *N,N*-diethylaniline for 12 hr.* The reaction mixture was cooled and extracted with 100 cc ether. The ethereal solution was washed with 1:1 HCl until the solution showed no basicity and then washed with water. The ether solution was washed with dil. NaOH aq and finally with water. The neutral ethereal solution was dried (MgSO₄). The solvent was removed and the solid obtained triturated with 5 cc EtOH and filtered, yield 0.6 g. All the rearranged compounds were crystallized from EtOH or large volumes of pet. ether (60°–80°). The coumarano-coumarans obtained are listed in Tables 2-a and 2-b. The UV data of the starting ethers and the coumarano-coumarans are given in Tables 3 and 4.

TABLE 3. UV OF 1,4 DIARYLOXY-2-BUTYNES

No.	R—O—CH ₂ —C≡C—CH ₂ —O—R'		$\lambda_{\text{max}}^{\text{EtOH}}$ m μ	log ϵ
	R	R'		
I	Phenyl	Phenyl	270	3.3977
II	<i>o</i> -Chlorophenyl	<i>o</i> -Chlorophenyl	281	3.4755
			274	3.5016
			204	4.4995
III	<i>o</i> -Methoxyphenyl	<i>o</i> -Methoxyphenyl	272	3.5915
			225	3.9563
			273	3.3792
IV	<i>o</i> -Methylphenyl	<i>o</i> -Methylphenyl		
V	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl		
VI	<i>p</i> -Bromophenyl	<i>p</i> -Bromophenyl	278	3.3042
VII	<i>p</i> -Methylphenyl	<i>p</i> -Methylphenyl		
VIII	<i>p</i> -Methoxyphenyl	<i>p</i> -Methoxyphenyl	286	3.7655
IX	<i>p</i> -Formylphenyl	<i>p</i> -Formylphenyl	273	4.4796
XI	<i>p</i> -Chlorophenyl	<i>p</i> -Methylphenyl	276	3.4808
XII	<i>p</i> -Chlorophenyl	<i>p</i> -Nitrophenyl	301	4.0011
XIII	2,6-dimethylphenyl	2,6-dimethylphenyl	262	2.8051

All the UV spectra were taken in EtOH.

TABLE 4. UV OF COUMARANO-COUMARANS

No.	$\lambda_{\text{max}}^{\text{EtOH}}$ m μ	log ϵ	No.	$\lambda_{\text{max}}^{\text{EtOH}}$ m μ	log ϵ
XV	283	3.7976		(shoulder) (<i>cont'd.</i>)	
	203	4.2378	XXI	288	3.8387
XVI	292	3.8299	XXII	304	3.9323
	(shoulder)			226	4.2103
	286	3.8598	XXIII	290	3.8061
XVII	205	4.7473		226	4.2187
	282	3.6151		206	4.2810
	230	4.1128	XXIV	340	3.7191
XVIII	210	4.2288		326	3.6966
	280	3.7556		289	3.8240
XIX	293	3.7935		278	3.9766
	226	4.2500		266	3.9378
	203	4.5860		234	5.0608
XX	292	3.7573			
	226	4.3166			
	206	4.4494			

* Use of more than 5 cc *N,N*-diethylaniline for 1 g of the ether did not give pure product in the case of I and VII. When lower boiling *N,N*-dimethylaniline (b.p. 193°) was used in the place of diethylaniline, the rearrangement did not give any pure product. Ethers IX, X and XII gave only tarry material. XIII did not yield any solid compound.

Preparation of 2,3-bis(2-hydroxy-4-chlorophenyl)-2,3-dihydroxybutane. This compound was prepared from 2-acetyl-4-chloro phenol⁶ by the method of Baker.⁷

Preparation of 4b,9b-dihydro-4b,9b-dimethyl-3,8-dichlorobenzofuro (3, 2-b) benzofuran. The crude pinacol obtained in the above reaction was cyclized according to the procedure of Sisido *et al.*⁸ Recrystallization from pet. ether (60°–80°) gave white crystals, m.p. 207–209°, undepressed on admixture with an authentic specimen of XIX.

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⁶ K. V. Auwers and Wittig, *Ber. Dtsch. Chem. Ges.* **57**, 1270 (1924).

⁷ W. Baker and J. C. McGown, *J. Chem. Soc.* 559 (1937).