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THE COURSE OF ADDITION OF BENZYNE TO <u>cis</u>- AND <u>trans</u>- ACETOXY- AND METHOXYPROPENE (1)

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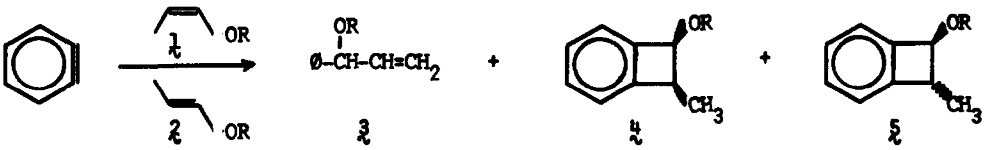
While there are many examples (2) of 2+2 cycloaddition reactions of benzyne with olefins to give benzocyclobutenes little attention has been expended on its stereochemical or mechanistic aspects. Recently, Tabushi, Oda and Okazaki reported (3) on the lack of stereospecificity of the cycloaddition of benzyne to cis- and trans-methoxypropene. Since our results and conclusions with cis- and trans-methoxy- and acetoxypropene vary from those reported (3) we now report our preliminary findings (4).



1a - 5a, R = MeO-
1b - 5b, R = AcO-

The reaction of benzyne (generated from benzenediazonium-2-carboxylate) with cis-methoxypropene [1a] under a wide variety of conditions (Table I) gave in 20-56% yield mainly cis-3-methoxy-4-methylbenzocyclobutene [4a, ~80%], along with small amounts of the trans-isomer [5a, ~10%] and the ene product, 3-phenyl-3-methoxypropene [3a, ~9%] (5). trans-Methoxypropene [2a] gave (in 33-55% yield) under comparable reaction conditions extensive amounts of the ene product 3a (~50%) and 4a and 5a in a 1:1 ratio (6). With cis- and trans-acetoxypropene [1b and 2b] qualitatively similar results were obtained although the trend was towards more ene addition. Thus, product fallout is apparently independent of reaction conditions, but markedly dependent upon the stereochemistry of the benzyne acceptor. Stereoselectivity was greatest with the cis isomers [**1a**, **1b**] and ene addition was limited; whereas, the trans isomers [**2a**, **2b**] were more, to overwhelmingly susceptible to ene addition. From preliminary competition experiments (against vinyl acetate) it appears that **2b** is about

Table I

Products From Reaction[a] of Benzyne With cis- and trans- Acetoxy- and Methoxypropene

		PRODUCTS			
			% Composition[d,e]		
RO-CH=CH-CH_3[b,c]	Solvent (ml)	% Yield	**3**	**4**+**5**	**4**:**5**
cis-Me (**1a**)	1,2-$C_2H_4Cl_2$ (50)	56	9.4	91	88:12
"	" (60)	40	9.4	91	88:12
"	" (100)	29	9.8	90	88:12
	CH_3CN (50)	38	7.8	92	90:10
	CH_3I (50)	20	10	90	88:12
trans-Me (**2a**)	1,2-$C_2H_4Cl_2$ (50)	53	44	56	49:51
"	CH_3I (50)	33	49	51	50:50
54% **1a**:46% **2a**	1,2-$C_2H_4Cl_2$ (50)	54	25	75	76:24
	[Calculated[f]	--	26	74	74:26]
cis-Ac (**1b**)	1,2-$C_2H_4Cl_2$ (50)	20	55	37	82:18
"	CH_3CN (50)	g	57	35	83:17
trans-Ac (**2b**)	1,2-$C_2H_4Cl_2$ (50)	g	85	11	33:67
"	" (100)	57	87	11	31:69
	CH_3CN (50)	g	87	9.4	31:69

a) Reaction conditions: 30-50 mmoles of **1** or **2**, ∿10 mmoles benzenediazonium-2-carboxylate at 41°. b) Recovered **1a** and **2a** were ∿97% isomerically pure. c) Purity of **1a** and **2a** determined via nmr and glpc (15' 15% Carbowax 20M on 60/80 Chromosorb P, 25°), **1b** and **2b** analyzed via glpc (15' 20% Carbowax 20M on Aeropak 30, 85°). d) Analyzed via glpc (12' 5% diisodecyl phthalate–5% Bentone 34 on 80/100 Chromosorb W, 110-130°). e) 100% - %(**3** + **4** + **5**) constitute the amount (2-8%) of two presently unidentified products formed in the reaction of benzyne with 1b and 2b. f) Assuming that **1a** is 1.5 times more reactive than **2a**. g) Not determined.

4-5 times more reactive than **1b** as a benzyne acceptor. A meaningful discussion of all of these results must await more experimental data on the factors favoring ene and/or cycloaddition pathways (7). However, from the cycloaddition data reported herein it it apparent that 2 + 2 cycloaddition reactions of benzyne can either be "highly" stereospecific or be almost lacking in stereospecificity. The lack of stereospecificity has been attributed (3) to triplet benzyne, however, this is not required to explain the results. The 2 + 2 cycloaddition reaction of benzyne can be explained as proceeding via a non-concerted cycloaddition in which limited or extensive bond rotation may occur before closure of the second bond (9). These reactions may be considered to be analogous to the 2 + 2 cycloaddition reaction of 1,1-dichloro-2,2-difluoroethylene (11).

REFERENCES AND NOTES

1. This investigation was supported in part by Public Health Service Research Grant No. CA 07909-03 from The National Cancer Institute.
2. a) H. Simmons, *J. Am. Chem. Soc.*, **83**, 1657 (1961); b) G. Wittig and H. Dürr, *Ann.*, **672**, 55 (1964); c) H. H. Wasserman and J. Solodar, *J. Am. Chem. Soc.*, **87**, 4002 (1965); d) T. Matsuda, T. Mitsuyasu, *Bull. Chem. Soc. Japan*, **39**, 1342 (1966); e) H. Heaney and J. M. Jablonski, *Tetrahedron Letters*, 2733 (1967).
3. I. Tabushi, R. Oda and K. Okazaki, *ibid.*, 3743 (1968).
4. See also: A. J. Solodar, Ph.D. Thesis, Yale University, 1967. *Dissertation Abstracts*, **28**, 4511-B (1968).
5. The composition of the reaction mixtures was determined by glpc and corroborated by nmr. All new compounds gave satisfactory elemental analysis.
6. The results of Tabushi et. al. differ in that the ene product, **3a** was not detected by them and that its nmr spectrum [δ 3.28 (singlet 3 methoxy protons), 4.50 (doublet, 1 proton), 4.95-5.9 (multiplet, 3 vinylic protons), 7.23 (singlet, 5 aromatic protons)] is such that it interferes in the nmr analysis of **4a** and **5a**. Our nmr structural assignments for **4a** and **5a** agree with that reported (3).
7. For example, the ene product may arise via a different precursor than the cycloaddition products. In the case of **1** and **2** the formation of **3** is best rationalized by initial attack on the carbon bearing the methoxy or acetoxy substituent. This is not a requirement to get to **4** and **5**. However, 2-acetoxypropene which only yields an ene product (8) with benzyne must undergo initial attack at the unsubstituted vinyl carbon.
8. L. Friedman and R. H. Levin, unpublished data.
9. This intermediate may be either diradical or dipolar. The small effect of reaction conditions on the ratio of **4** to **5** and the fact that only 3-*tert*-butylbenzocyclobutene [no rearrangement products detected] is obtained(10) from *tert*-butylethylene and benzyne suggests but by no means requires a diradical intermediate.
10. L. Friedman and G.L. Cooper, unpublished data.
11. J.S. Swenton and P.D. Bartlett, *J. Am. Chem. Soc.*, **90**, 2056 (1968), and references contained therein.