Tetrahedron Vol 25, pp 4401 to 4407 Pergamon Press 1969 Printed in Great Britain

RELATIVE REACTIVITIES OF SUBSTITUTED OLEFINS TOWARD BENZYNE

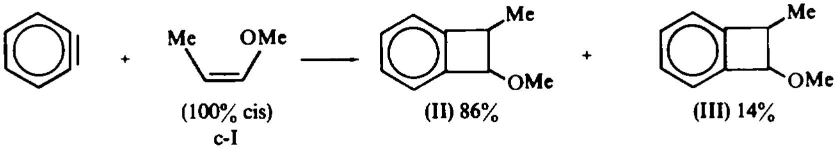
I. TABUSHI, K. OKAZAKI and R. ODA

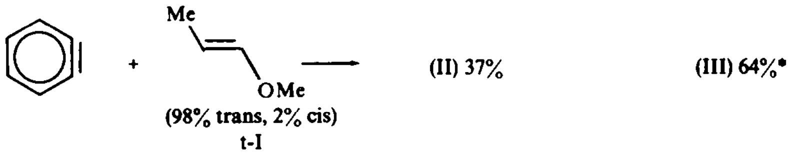
Department of Synthetic Chemistry, Kyoto University, Sakyo-ku, Kyoto, Japan

(*Received in Japan* 31 *March* 1969; *Received in the UK for publication* 9 *June* 1969)

Abstract—In the reaction of various substituted olefins with benzyne, product determination and relative reactivity measurements were carried out. The principal reaction is the addition-H migration. Orientation of the first addition (concerning with the substituent on the double bond) and acceleration with acetyl, methoxycarbonyl, aluoxyl or alkyl substituent revealed that a biradical intermediate is involved.

ALTHOUGH benzyne has been extensively investigated[1] this has not included the electronic states. Since 2 + 2 cycloaddition of benzyne with vinyl ether or vinyl ester was reported,[2,3] we have investigated the stereochemistry of the cycloaddition of propenyl ethers[4] and found the addition-cyclization of *cis*- or *trans*-propenyl methyl to be partially nonstereospecific as ascertained by others.[5,6] This indicates that the addition-cyclization proceeds in two steps i.e., addition-free rotation-addition. We are investigating benzyne-olefin reactions but here report that olefins bearing various substituents give predominantly the addition-H migration products. Relative reactivity of substituted olefins are also described.





Products. Benzyne was generated by thermolysis of benzenediazonium-2-carboxylate in methylene chloride in the presence of a substituted olefin. Substituted olefins used were: *cis*- and *trans*-propenyl methyl ethers (I), isopropenyl acetate (IV), 2-cyclopropylpropene (V), methyl methacrylate (VI), methyl crotonate (VII), 3-methyl-pent-3-ene-2-one (VIII) and isopropenyl methyl ketone (IX). The products

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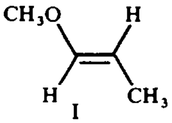
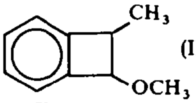
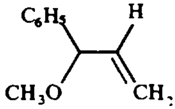
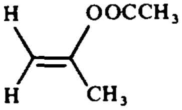
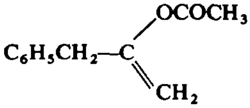
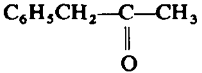
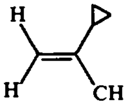
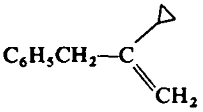
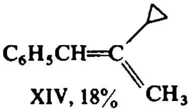
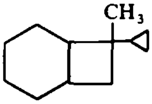
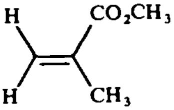
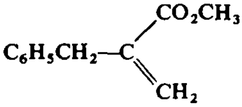
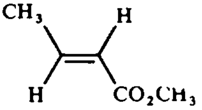
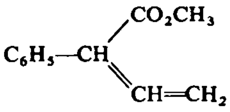
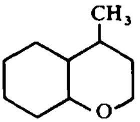
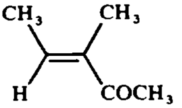
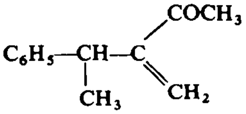
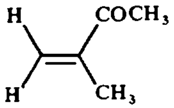
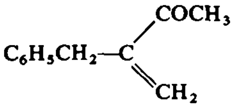
* Previous communication only described the result from the 92% *trans* olefin.

TABLE 1. PRODUCTS OF THE REACTION OF BENZYNE AND SUBSTITUTED OLEFINS

Substituted Olefin	Yield of Distillable Products[a]	Structure and Composition of Products
 I	35% (54)	 (II/III = 4/6) II + III, 28% 3 others  X, 60%
 IV	40% (62)	 XI, 96·8%  $C_6H_5CH_2—\underset{\underset{O}{\parallel}}{C}—CH_3$ XII, 3·2%
 V	38% (59)	 XIII, 78%  XIV, 18%  XV, 4%
 VI	54% (83)	 XVI, 93% 4 others
 VII	30% (46)	 XVII, 47%  (tentative) XIX 2 others
 VIII	22% (34)	 XVIII, 92% 3 others
 IX	25% (39)	 XX

[a] Yield was based on anthranilic acid employed. In parentheses, the yield based on gas evolved (ca. 65%) was shown.

from propenyl acetate were also investigated. In most cases, a mixture of products was obtained in fair to good yields. These were successfully separated by small scale-preparative VPC and identified by spectral and chemical means. The products obtained and their NMR spectra are listed in Tables 1 and 2.

TABLE 2. NMR DATA OF THE PRODUCTS LISTED IN TABLE 1[a]

Compound	Pattern, chemical shift and coupling constant if available[b, c]
X	s. (6·75), 3H; two single peaks, st. (5·44), 1H; complex m. typical of end-vinyl (3·85–5·05), 3H; thin m. (c. 2·83), 5H
XI	s. (8·04), 3H; single peak, st. (6·54), 2H; two single peaks, st. (c. 5·44, c. 5·25), 1H + 1H; thin m. (c. 2·83), 5H
XIII	complex m. typical of cyclopropyl (8·60–9·05), 4H; and (9·30–9·70), 1H; single peak (6·79), 2H; m. separated into two peaks (c. 5·36, c. 5·43), 2H; thin m. (c. 2·88), 5H
XIV	complex m. typical of cyclopropyl (9·26–9·50), 4H; and (8·10–8·90), 1H; two doublets (8·29, 8·40), 3H; $J = 1·4$ cs. thin m. (3·66–3·80), 1H; m. (c. 2·84), 5H;
XV	complex and broad m. (above 8·70 up to 10·1), 5H; s. (8·52), 3H; two single peaks, st. (7·02, 7·08), 2H; m. (2·80–3·15), 4H
XVI	single peak, st. (6·43), 2H; s. (6·33), 3H; two thin m. (c. 4·65, c. 3·87), 1H + 1H; thin m. (c. 2·88), 5H
XVII	s. (6·41), 3H; two single peaks, st. (c. 5·76, c. 5·90), 1H complex m. typical of end-vinyl (3·55–5·20), 3H; thin m. (c. 2·82), 5H
XVIII	d. 8·63), 3H, $J = 6·6$ c/s; s. (7·79), 3H; q., st. (5·89), 1H, $J = 6·6$ c/s; single peak, st. (4·38), 1H; s. (4·01), 1H; thin m. (c. 2·87), 5H
XX	s. (7·80), 3H; sharp single peak (d. like) (6·53), 2H; sharp single peak (t. like) (4·50), 1H; sharp single peak (s. like) (4·08), 1H; sharp m. (2·91), 5H

[a] NMR data of the compound II or III was written in our previous paper (Ref. 1).

[b] s: singlet, d: doublet, q: quartet, m: multiplet, st: with structure, τ value (TMS in CCL_4) are listed in parentheses. c: centered at

[c] nH indicates the number of protons.

Relative reactivity of substituted olefins. The relative reactivity of each olefin was evaluated by means of analytical VPC from a competitive reaction with an appropriate reference olefin. As the reactivity does not differ much in each olefin, only isopropenyl acetate was taken as a reference throughout the competitive runs. Results are shown in Table 3.

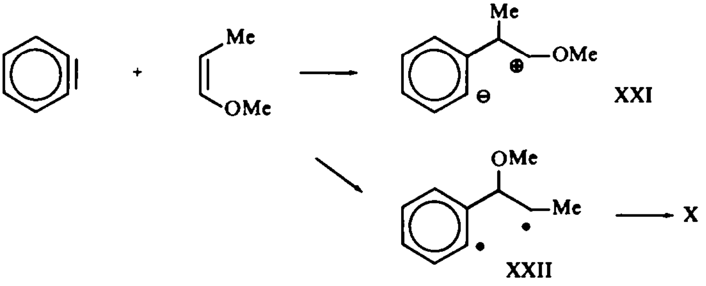
TABLE 3. RELATIVE REACTIVITY OF SUBSTITUTED OLEFINS TOWARDS BENZYNE[a]

V	VI	IX	cis-I	trans-I	IV	VIII	VII
14·1	3·4	2·8	2·0	1·3	1·0	0·30	0·01
13·8	3·1	2·6	2·0	1·5		0·31	
		3·2	1·9	1·3		0·33	
			2·0				

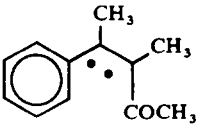
[a] From competitive experiments with isopropenyl acetate as reference compound.

It was found that the reactivity of substituted olefins is practically independent of the polar character of the substituents. Instead the reactivity seems to be correlated with the radical affinity of the olefins. Unfortunately, there is no suitable measure of this radical affinity,* but qualitatively the radical nature of the reaction is evident, for example, the greater reactivity of IX or VI than IV.† 1,2-Disubstituted olefins react more slowly than the corresponding 1,1-disubstituted olefins, probably due to steric effect (hindrance to approach) and this trend together with nonstereospecificity in the addition-cyclization and nonconcerted H-migration in the addition-migration is consistent with the proposed two-step mechanism.

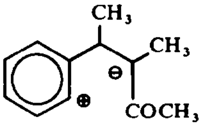
Mechanism of the reaction. If the reaction is in two steps, the substituent effect on the product orientation clarifies the nature of the first addition. The benzyne addition-migration product from I was found to be mainly X (an isomeric olefin, if any, was less than 1%) which is reversely oriented against an expected polar intermediate XXI. The formation of X was interpreted by the mechanism involving a biradical XXII.



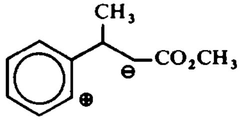
Compound VIII gives XVIII almost exclusively, which can be interpreted by the mechanism involving either a biradical XXIII or an abnormal polar intermediate XXIV which originates from nucleophilic addition of benzyne. However, the latter possibility was excluded since the more electrophilic methyl crotonate XXV makes no or only a minor contribution to the products. Our preliminary results show that the β-orienting and accelerating effect of an acetyl group toward benzyne is common in a series of methyl and acetyl substituted olefins. Thus the mechanism involving the biradical intermediate XXIII should be accepted.



XXIII



XXIV



XXV

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[*] Me affinity is often used but it does not seem suitable for the present purpose to treat the reactivity of the electron deficient radical. The carbonyl attached to the double bond enhances the reactivity of radical addition as can be qualitatively shown: Addition of Me radical with ethyl fumarate and maleate were reported to be 77 and 13 times faster, respectively, than that with ethylene.[7]

[†] Nonconcerted H-migration was shown in some cases: e.g., V gave both of 1,5- (XIII) and 1,3- (XIV) H-migration products. Isomerization of XIII to XIV occurred in the experimental condition but only to a minor extent when benzyne concentration was not very high so that the observed product ratio XIII/XIV was practically the same as the kinetically controlled ratio. α-Methylstyrene also gave 1,5- and 1,3-H-migration products.

The biradical mechanism is also supported by the observed relative reactivity of substituted olefins as already discussed. The mechanism is consistent with the previous observation that the benzyne product ratio is independent of the polar nature of the solvent.[5]

EXPERIMENTAL

Starting olefins cis- *and* trans-*Propenyl methyl ethers.* A crude mixture of propenyl methyl ethers was prepared by thermolysis of propionaldehyde dimethylacetal.[8] From the crude mixture, MeOH was removed by water extraction and propionaldehyde by NaHSO$_3$aq extraction. The mixed propenyl methyl ether was fractionally distilled by means of a spinning band, giving the initial fraction consisting mostly of *cis*-isomer and the final fraction consisting mostly of *trans*-isomer. Each isomer was further purified by preparative VPC (Apiezon Grease L).

2-*Cyclopropylpropene.* The olefin was prepared according to the reported procedure.[9] *Isopropenyl methyl ketone* was prepared from ethyl methyl ketone and paraformaldehyde.[10] (the fraction 95·5°–96° at 760 mmHg was used).

3-*Methyl-pent*-3-*en*-2-*one.* The keto-olefin was prepared by the acid catalyzed condensation of methyl ethyl ketone with acetaldehyde.[11] Other olefins were commercially available and were employed after appropriate purification.

General procedure of benzyne reaction. Anthranilic acid (3·0 g; 22 mmoles) and a small amount of trifluoroacetic acid were dissolved in 30 ml dry THF and isoamyl nitrite (5 g; 42 mmole) dissolved in 17 ml dry THF was added dropwise at room temp. The soln was further stirred for 20 min and the ppt was very quickly filtered off.[*] While the solid was still wet with solvent, it was suspended in 50 ml dry CH$_2$Cl$_2$ and 80–85 mmole of a substituted olefin was added. The suspension was heated at 43° until no appreciable N$_2$ was evolved (ca. 3). The unreacted diazonium carboxylate, if any, was removed by water extraction and the organic layer was dried (Na$_2$SO$_4$).[†] Distillation gave the corresponding products. The following b.p. ranges are for products from various substituted olefins: I, 48–50°, 6 mmHg; IV, ca. 83°, 8–9 mmHg; V, 58–59°, 7 mmHg; VI, 92–95°, 7–9 mmHg; VII, 73–75°, 5–6 mmHg; VIII, 58–59°, 7 mmHg; IX, 76–82°, 3–4 mmHg.

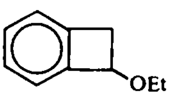
Competitive experiments. The experimental procedure was similar to the general procedure except using an appropriately composed mixture of an olefin and isopropenyl acetate (the mixture was used in considerable excess) instead of single olefin. Determination of the product composition of a crude mixture was made by analytical VPC. Calibration was made by using every isolated product. Some unknown minor products were not isolated so that the assumption was made that such a minor isomer held the same relative VPC area as the major isomer. The combined molar amount of products from an olefin was thus estimated and compared with that of isopropenyl acetate. The correction was made for the initial olefin composition.

Products from I. Distilled products were separated by small scale (10–50 μl) preparative VPC packed with PEG 20,000, where five peaks appeared. The third peak was major, which was isolated and found to be the mixture of II and III. (Found: C, 81·01; H, 8·29. $C_{10}H_{12}O$ requires: C, 81·08; H, 8·11%); electronic spectrum in EtOH: λ_{max} 272·6 mμ (log ε = 2·975), 266·3 (2·974) and 260·2 (3·000). This spectrum was similar to that of XXIV (λ_{max} reported were: 260, 266 and 272 mμ)[‡]; mass spectrum: *m/e* 148 (parent), 133 (parent minus Me) and 117 (parent minus MeO); I.R. spectrum: 3040, 2990, 2915, 2800, 1600, 1455, 1372, 1356, 1207, 1100, 1093, 1079, 1048, 996, 967, 743 and 698 cm^{-1}; The NMR spectrum showed the absorption of the *cis*-isomer

[*] In a large-scale preparation (the maximum amount employed by us was as five times as large as described), filtration should not be applied because of explosiveness of diazoanthranilate. Instead, repeated decantation and methylene chloride washing was applied. Addition of a Ag salt may increase the stability of diazoanthranilate but in the case of benzyene–benzene reaction the product composition of benzyne reaction was reported to be affected considerably by the presence of a Ag salt.[12] Therefore, the Ag stabilization procedure was not adopted in our experiments.

[†] The procedure was essentially the same as that of Friedman[12] with minor modifications.

[‡]



XXIV[13]

superimposed by that of the *trans*-isomer (the assignment of every absorption was ascertained from comparison of various samples of different stereoismer-compositions). The second major peak was X: analyses of which were satisfactory (Found C: 80·80 and H, 8·41%) and it was identical with an authentic specimen.[†] Other very minor peaks were not isolated in sufficient amounts.

Products from IV. Two of the three peaks were isolated by preparative VPC (Apiezon Grease L). The peak of the shorter retention time was identical with benzyl methyl ketone. The major peak of the longer retention time was XI.[*] (Found: C, 74·82; H, 7·11. $C_{11}H_{22}O_2$ requires: C, 75·00; H, 6·82%. The acetate (3 g) was heated overnight with 20 ml 5% Na_2CO_3aq and 20 ml MeOH. After cooling and addition of water, the mixture was extracted with ether and the ether layer was dried Na_2SO_4. After distilling off the solvent, benzyl methyl ketone was obtained almost quantitatively.

Products from V. Three compounds were obtained by VPC separation (PEG 20,000). The major peak of the shortest retention time was shown to be XIII. (Found: C, 91·34; H, 9·05. $C_{12}H_{14}$ requires: C, 91·14; H, 8·86%). The second major peak of moderate retention time was due to XIV. (Found: C, 90·88; H, 9·08%); electronic spectrum: 278 mμ (log ε, 3·57), 267 (4·00), 253 (4·18), 238 (4·01), 227 (3·79). XIII and XIV were identical with authentic specimens prepared by the addition of benzylmagnesium bromide to methyl cyclopropyl ketone and dehydration of the resulting alcohol[‡] at 210° in the presence of $KHSO_4$. VPC separation of the distillate gave XIII in 26% and XIV in 74% yields. The third minor peak was due to XV. (Found: C, 90·58; H, 8·96%). Further purification was not tried because of poor yield.

Products from VI. Only the major product was isolated and shown to be XVI.[**] (Found: C, 75·14; H, 7·03. $C_{11}H_{12}O_2$ requires: C, 75·00; H, 6·82%); IR spectrum: 3030, 2860, 2840, ca. 1720, 1630, 1600, 1496, ca. 1430, many peaks in the range 1350–1120, 990, 945, 925, 825, 810, 745, 695.

Products from VII. Four peaks were separated by VPC (PEG 20,000). The second major peak of the shortest retention time was not completely determined but was considered to be XIX (NMR and IR spectra). The major peak of the third retention time was XVII. (Found: C, 75·07; H, 6·81. $C_{11}H_{12}O_2$ requires: C, 75·00; H, 6·82%). Other minor peaks were not sufficient to identify.

Products from VIII. Four peaks were separated by VPC (PEG 20,000). The peak of the second retention time was major, and due to XVIII.[||] (Found: C, 81·68; H, 8·09 (very unsatisfactory because of its hygroscopic nature). $C_{12}H_{14}O$ requires: C, 82·76; H, 8·06%); IR spectrum: 1675, 1622, 1600, 1493, ca. 1360, ca. 1250, 1123, 1060, 1015, 960, 936, 778, 755 and 690 cm^{-1}. Analysis of the corresponding semicarbazone, (Found: C, 67·73; H, 7·25; N, 18·02. $C_{13}H_{17}ON_3$ requires: C, 67·53; H, 7·36; N, 18·18%).

Products from IX. The distilled products consisted of four peaks by VPC (Apiezon L). Only the major peak (75%) was isolated by the small scale preparative VPC and was identified as XX;[19] electronic spectrum in EtOH: λ_{max} = 213 mμ (log ε, 4·79). Analysis of the corresponding semicarbazone; (Found: C, 66·51; H, 6·89; N, 19·48. $C_{12}H_{15}N_3O$ requires: C, 66·34; H, 6·96; N, 19·34%), m.p. of the semicarbazone, 143° (lit 144–145°[19]); IR spectrum; 3025, 2930, 1680, 1625, 1600, 1495, 1363, 1265, 1104, 968, 934, 745, 720, 685 cm^{-1}.

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[6] H. H. Wasserman, A. J. Soldar and L. S. Keller, *Ibid.* 5597 (1968).

[7] W. A. Pryor, *Free Radicals* p. 223. McGraw-Hill, New York (1960).

[†] The compound was prepared from phenyl-β-chlorethylcarbinyl methyl ether[14] and also obtained by us from acrolein and phenylmagnesium bromide followed by methyl iodide-sodium hydride methylation.

[*] Formation of the compound was also observed by Friedman.[15]

[‡] Benzylcyclopropylmethylcarbinol has been reported.[16]

[**] Methyl α-benzylacrylate has been reported.[17]

[||] 2-Phenyl-but-3-en-1-oic acid has been reported.[18]

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