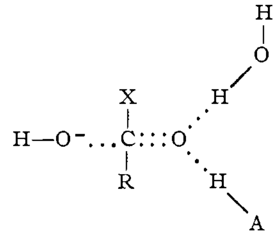
gives only N-phenyl-N′-*p*-tolylformamidine in the absence of acid, but also gives N,N′-di-(*p*-tolyl)-formamidine in the presence of traces of acid.[9] Roberts originally suggested[9a] that this reaction, in the presence of acid, proceeds by a mechanism similar to that of eq. 11, but later it was concluded that the reaction occurred by a back reaction of initially formed N-phenyl-N′-*p*-tolylformamidine.[9b] The synthesis of substituted imido esters by exchange reactions is generally carried out under slightly acidic conditions, and the use of ether–water mixtures of the base of one component and the hydrochloride of the other is presumably effective because the exchange reaction can take place in the slightly acidic aqueous phase. The over-all equilibrium will favor the products in which the hydrochloride of the strongest base is left in the aqueous phase; *i.e.*, the weaker base is incorporated into the imido ester.[7,8,10]

Carbonyl groups in hydroxylic solvents are certainly hydrogen-bonded to one or more molecules of solvent through the lone pair electrons of the oxygen atom and it is conceivable, although perhaps not likely, that the $H_2{}^{18}O$ exchange observed in ester and amide hydrolysis occurs by a displacement reaction with concerted proton transfer to the leaving oxygen atom, without passing through a discrete addition intermediate.[40] Such a concerted reaction is virtually impossible for the amine exchange reactions with imido esters, since the leaving nitrogen atom does not have the necessary available lone pair electrons for proton transfer until the double bond to carbon has been broken, *i.e.*, until an addition intermediate has been formed.



It should be noted that it is very difficult to formulate mechanisms for a number of known reactions involving displacement of the =NR group, such as the hydrolysis of imido ester hydrochlorides and the oxazoline reaction recently described by Rosnati and Misite,[41] without invoking a tetrahedral addition intermediate. Several new examples of compounds analogous to such intermediates, containing three electronegative atoms bound to a carbon atom, have recently been synthesized.[42–44]

Acknowledgments.—We are grateful to Drs. Margaret Hunter and Martha Ludwig for their generous and very helpful discussion of their experimental results before publication, to Yen Chi Nguyen for technical assistance, to Dr. Gordon Hamilton for advice on the treatment of the kinetic data and to the National Institutes of Health (Grants C-3975, CRT-5033) and the National Science Foundation for financial support.

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[41] V. Rosnati and D. Misiti, *Tetrahedron*, **9**, 175 (1960).

[42] D. H. Clemens and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 2588 (1961).

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[CONTRIBUTION FROM CENTRAL RESEARCH LABORATORIES, INTERCHEMICAL CORP., NEW YORK 36, N. Y.]

Azo-Hydrazone Conversion. I. The Japp–Klingemann Reaction

BY HSIEN CHENG YAO[1] AND PAUL RESNICK

RECEIVED AUGUST 9, 1961

Intermediate azo compounds have been isolated from the Japp–Klingemann reaction. The conditions employed for the isolation of these compounds seems to be general and excellent yields of the azo compounds may be obtained. The cleavage of these compounds with water, ethanol, phenol, aniline and acetic acid was studied. The results indicate that these reactions involve an acyl cleavage and an azo to hydrazone conversion.

An intensive review of the Japp–Klingemann reaction has been published by Phillips.[2] The reaction between a diazonium salt and an active methinyl carbon is assumed to involve formation of an unstable azo compound followed by hydrolytic cleavage of the azo compound. The isolation of these intermediates hitherto has not been accomplished.[3]

Although the cleavage products of the Japp–Klingemann reaction are considered to be hydrazones,[2] it has been difficult to establish this structure. Azo, hydrazone and ene–hydrazine[4] tautomeric forms are also possible.

The coupling of a diazonium salt to a methinyl carbon gives an unstable azo compound which cleaves to give a hydrazone, whereas the coupling product of the same diazonium salt to a methylene carbon is relatively stable. In the latter case, the coupling product is not an azo compound but a hydrazone.[5] Apparently, an azo to hydrazone

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[1] Scientific Laboratory, Ford Motor Co., Dearborn, Mich. Paper presented at 140th A.C.S. Meeting, Chicago, Ill., September 8, 1961.

[2] R. R. Phillips, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1959, Vol. 10, Chapter 2.

[3] (a) R. P. Linstead and A. Bao-Lang Wang, *J. Chem. Soc.*, 807 (1937); (b) G. Favrel, *Bull. soc. chim. France*, [4] **47**, 1290 (1930); (c) G. Favrel, *Compt. rend.*, **189**, 335 (1927); (d) L. Kalb, F. S. Schweitzer, H. Zellner and E. Berthold, *Ber.*, **59**, 1860 (1926); (e) G. Vanags and L. Sakhar, *Doklady Akad. Nauk S.S.S.R.*, **129**, 1182 (1959).

[4] (a) A. E. Arbuzov and Yu. P. Kitaev, *ibid.*, **113**, 577 (1957); (b) Y. P. Kitaev and A. E. Arbuzov, *Izvest. Akad Nauk S.S.S.R., Otdel. Khim. Nauk*, 1037 (1957); (c) Yu. P. Kitaev and A. E. Arbuzov, *Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci.*, 1068 (1957) (English Translation); (d) R. O'Connor, *J. Org. Chem.*, **26**, 4375 (1961).

TABLE I

AZO COMPOUNDS FROM THE JAPP–KLINGEMANN REACTION

Compound	Yield, %	M.p., °C.	λ_{max}, mμ	log E_{max}	Formula	Carbon, % Calcd. Found	Hydrogen, % Calcd. Found	Nitrogen, % Calcd. Found
α-Phenylazo-α-methylacetoacetic	78	[a]	272	3.85	$C_{13}H_{16}N_2O_3$	62.80	6.46	11.28
acid ethyl ester (I)						62.75	6.41	11.17
α-Phenylazocyclopentanone-α-	92	[b]	270	4.02	$C_{14}H_{16}N_2O_3$	64.61	6.20	10.81
carboxylic acid ethyl ester (II)						64.38	6.28	10.86
α,α′-Biphenyl[4,4′]diazo-α,α′-	85	81–82[c]	315	4.28	$C_{26}H_{30}N_4O_6$	63.12	6.07	11.33
dimethyldiacetoacetic acid diethyl ester (III)						63.17	6.09	11.39
α-Phenylazo-α-methylacetoacetanilide	90	105–106[d]	280	4.07	$C_{17}H_{17}N_3O_2$	69.14	5.80	14.23
(IV)						69.08	5.87	14.28
α-Phenylazo-cyclopentanone-α-	88	104[d]	280	4.05	$C_{18}H_{17}N_3O_2$	70.33	5.57	13.67
carboxanilide (V)						70.24	5.53	13.60

[a] B.p. 138–140° (4 mm.), n^{22}D 1.5158. [b] Liquid after exhaustion of solvent *in vacuo;* decomposing at about 120° (4 mm.), n^{22}D 1.5477. [c] Recrystallized from petroleum ether (30–60°). [d] Recrystallized from 1:1 benzene–petroleum ether.

conversion occurs in both the Japp–Klingemann reaction and the coupling of a diazonium salt to a methylene carbon. On the other hand, reactions that are accompanied by a hydrazone to azo conversion have also been reported. For example, the reaction of a keto-phenylhydrazone with lead tetraacetate gives an azo-acetate[6] and the reaction of an arylaldehyde phenylhydrazone with oxygen produces an azo-hydroperoxide.[7]

The purpose of this work was to investigate the intermediate azo compounds of the Japp–Klingemann reaction and the azo-hydrazone conversion in the cleavage of these compounds.

Experimental and Results

Isolation of the Azo Compounds of the Japp–Klingemann Reaction. General Procedure. α-Phenylazo-α-methylacetoacetic Acid Ethyl Ester (I).—A solution of 14.4 g. (0.1 mole) of α-methylacetoacetic acid ethyl ester in 90 ml. of pyridine was diluted with water until the solution became cloudy and then cooled to 0°. A diazonium solution prepared by dissolving 9.5 g. of aniline in 80 ml. of 5 *N* hydrochloric acid, cooling to 0°, and adding a saturated aqueous solution of 8 g. of sodium nitrite was then added slowly with stirring. During the addition, a yellow oil separated. The mixture was treated with ice and extracted with either ether or benzene. The cold extract was washed several times with ice-water, dried over magnesium sulfate and concentrated under diminished pressure. The residue was then purified by vacuum distillation. The main fraction distilled at 138–140° (4 mm.).

The Cleavage of the Azo Compounds. Hydrolysis without a Catalyst.—1. Four grams of α-phenylazo-α-methylacetoacetic acid ethyl ester (I) was dissolved in 50 ml. of dioxane and diluted to 100 ml. of water. The solution was refluxed for half an hour, cooled, and further diluted with water. The oily liquid which separated crystallized when seeded with ethyl pyruvate phenylhydrazone. The solid was collected, dried and recrystallized from petroleum ether. About 1.5 g. of the ethyl pyruvate phenylhydrazone (VI) was obtained. Some unreacted azo compound was found in the filtrate.

2. One gram of α-phenylazocyclopentanone-α-carboxanilide(V) was similarly treated. After the reaction mixture was cooled, 5-ketopentanoic acid 5-carboxanilide phenylhydrazone (X) precipitated and was recrystallized from benzene and petroleum ether; yield 76%.

Hydrolysis with Acid or Base. 1. Hydrolysis of I, II, III, IV and V with Base.—One gram of the azo compound was dissolved in 50 ml. of dioxane–water (1:1). One ml. of 10% sodium hydroxide solution was added to the solution. The solution was shaken for 1 minute at room temperature and the solvent was removed under diminished pressure at room temperature. The solid was recrystallized from benzene and petroleum ether. Yields of 75–90% were obtained in each case.

2. **Hydrolysis of I and IV with Acid.**—One gram of the azo compound was dissolved in 25 ml. of dioxane and diluted to 50 ml. with water. One ml. of 70% perchloric acid was added, and the mixture allowed to stand 2 hours at room temperature. After solvent was removed, the residue was recrystallized from benzene and petroleum ether. Ethyl pyruvate phenylhydrazone (VI) from I and pyruvanilide phenylhydrazone (IX) from IV were obtained in good yield. These hydrazones were identical with the products obtained from the base-catalyzed hydrolysis of the corresponding azo compounds, as shown by mixed melting points.

Reaction of II and V with Ethanol.—One gram of the azo compound was dissolved in 40 ml. of absolute ethanol (distilled over magnesium) and then refluxed for 3 hours. After the solvent was removed, the residue was recrystallized with benzene and petroleum ether. The product from azo compound II was a yellow crystalline solid which was assumed to be diethyl α-ketoadipate phenylhydrazone (XI). The product from azo compound V was a white crystalline solid which was assumed to be ethyl 5-ketopentanoate-5-carboxanilide phenylhydrazone (XII).

The same products were also obtained by treating the ethanol solutions with 1 ml. of 2% sodium ethoxide solution at room temperature for 10 minutes. Good yields were obtained in both cases.

Reaction of V with Phenol.—One and one-half grams of V and 0.5 g. of phenol were dissolved in 40 ml. of benzene. Two drops of triethylamine were added to this solution. The solution was then concentrated to about 20 ml. and then diluted with petroleum ether. Yellow crystals precipitated. After filtration, the product was recrystallized from petroleum ether. Phenyl 5-ketopentanoate-5-carboxanilide phenylhydrazone (XIII), 0.4 g., was obtained.

Reaction of II and V with Acetic Acid.—Two grams of the azo compound was dissolved in 30 ml. of glacial acetic acid. The solution was allowed to stand overnight at room temperature and then distilled under diminished pressure. The residue was recrystallized with benzene and petroleum ether. The product from azo compound II was 5-ketopentanoic acetic anhydride-5-carboxylic acid ethyl ester phenylhydrazone (XIV), 1.2 g. The products from azo compound V were 5-ketopentanoic acid-5-carboxanilide phenylhydrazone (X), 0.9 g., and about 0.1 g. of yellow crystals, m.p. 90–91°, which probably was 5-ketopentanoic acetic anhydride-5-carboxanilide phenylhydrazone.

Reaction of I, II, III, IV and V with Aniline.—One gram of azo compound was dissolved in 10 ml. of benzene. One ml. of aniline was added at room temperature. After 5 minutes, the solvent was removed under diminished pressure. The residue was extracted with hot water and then recrystallized with benzene and petroleum ether. Acetanilide was obtained from the water extract in the reactions of I, III

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(5) (a) R. H. Wiley and C. H. Jarboe, Jr., *J. Am. Chem. Soc.*, **77**, 403 (1955); (b) C. H. DePuy and P. R. Wells, *ibid.*, **82**, 2909 (1960); (c) S. M. Parmerter, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1959, Vol. 10, Chapter 1.

(6) D. C. Iffland, L. Salisbury and W. R. Schafer, *J. Am. Chem. Soc.*, **83**, 747 (1961).

(7) K. H. Pausacker, *J. Chem. Soc.*, 3478 (1950).

TABLE II

REACTION PRODUCTS OF AZO-COMPOUNDS

Reactants	Main product, phenylhydrazone	M.p., °C.	λ_{max} 1,[a] mμ	log E_{m_1}	λ_{max} 2, mμ	log E_{m_2}	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I + H_2O	Ethyl pyruvate (VI)	118–119[b]	290	4.193	312	4.326	$C_{11}H_{14}N_2O_2$	64.14	64.30	6.82	6.90	13.62	13.57
II + H_2O	Ethyl hydrogen-α-keto-adipate (VII)	127[c]	295	4.007	326	4.320	$C_{14}H_{18}N_2O_4$	60.40	60.46	6.53	6.48	10.11	9.97
III + H_2O	Diethyl dipyruvate bi- (VIII)	234	..	...	355	4.713	$C_{22}H_{26}N_4O_4$	64.41	63.78	6.30	6.32	13.74	13.52
IV + H_2O	Pyruvanilide (IX)	172–173	285	4.170	323	4.274	$C_{15}H_{15}N_3O$	71.13	71.60	5.92	6.00	16.63	16.50
V + H_2O	5-Ketopentanoic acid-5-carboxanilide (X)	187	286	4.274	340	4.435	$C_{18}H_{19}N_3O_3$	66.53	67.02	5.91	5.91	12.90	12.78
II + C_2H_5OH	Diethyl α-ketoadipate (XI)	77	294	4.076	322	4.344	$C_{16}H_{22}N_3O_3$	62.74	62.90	7.20	7.30	9.14	9.02
V + C_2H_5OH	Ethyl 5-ketopentanoate-5-carboxanilide (XII)	117–118	..	...	348	4.163	$C_{20}H_{23}N_3O_3$	67.91	67.65	6.50	6.10	11.90	11.70
V + C_6H_5OH	Phenyl 5-ketopentanoate-5-carboxanilide (XIII)	137–138	285	4.090	334	4.272	$C_{24}H_{23}N_3O_3$	71.75	71.62	5.73	5.49	10.47	10.40
II + CH_3COOH	5-Ketopentanoic acetic anhydride-5-carboxylic acid ethyl ester (XIV)	80–81	298	3.654	350	4.330	$C_{16}H_{20}N_2O_5$	60.04	60.80	6.29	6.05	8.80	9.73
II + $C_6H_5NH_2$	Ethyl 2-ketopentanoate-5-carboxanilide (XV)	131–132	294	4.013	322	4.288	$C_{20}H_{23}N_3O_3$	...	...	..	..	11.91	11.69
V + $C_6H_5NH_2$	α-Ketodipanilide (XVI)	230–231	287	4.137	340	4.339	$C_{24}H_{24}N_4O_3$	...	...	..	..	14.02	13.88

[a] VII and VIII are in chloroform and cyclohexane (1:1) solution, the others in cyclohexane. [b] Reported[8] m.p. 117°. [c] Reported[3a] m.p. 120°.

and V with aniline. The yield is generally good (70 to 80%).

Preparation of Phenylhydrazones.—2,3-Butanedione mono-N-methylphenylhydrazone (XVII), benzil mono-N-methylphenylhydrazone (XVIII), ethyl pyruvate-N-methylphenylhydrazone (XIX) and pyruvanilide N-methylphenylhydrazone (XX) were prepared by the conventional method of condensing α-methylphenylhydrazine with the corresponding ketone. XVII and XIX were purified by vacuum distillation. The former was distilled at 128–130° (5 mm.) $n^{22}D$ 1.5477; the latter, at 144–146° (4 mm.), $n^{22}D$ 1.5208. Compounds XVIII and XX were purified by recrystallization from petroleum ether.

Ethyl pyruvate phenylhydrazone and pyruvanilide phenylhydrazone were prepared by condensing phenylhydrazine with ethyl pyruvate and pyruvanilide. The former was purified by recrystallization from petroleum ether; m.p. 118°. The ultraviolet spectra and the mixed melting point indicate that this hydrazone is the same as the hydrolytic product of azo compound I. Pyruvanilide phenylhydrazone was purified by recrystallization from benzene; m.p. 171–172°. This compound is identical with the hydrolytic product of azo compound IV.

Discussion

These experimental results indicate that the azo compounds which are intermediates in the Japp–Klingemann reaction can generally be isolated. The ultraviolet spectroscopic data of such isolated azo compounds (I, II, IV and V) indicate that the characteristic absorption maxima of these phenylazo groups fall in the region 270 to 280 mμ. Such spectra resemble those of *p*-methoxybenzylazobenzene-α-hydroperoxide (λ_{max} 272 mμ, log E_m = 4.11),[9] benzylazobenzene-α-hydroperoxide (λ_{max} 270 mμ; log E_m = 4.05)[9] and α-phenyl-α-acetoxybenzylazobenzene (λ_{max} 280 mμ, log E_m 3.70).[6]

All the azo compounds studied react with functional groups containing an active hydrogen with resulting acyl cleavage. The azo compounds react readily with aniline at room temperature without a catalyst. With water, acetic acid, ethanol and phenol the reactions are slow at room temperature. The presence of a base greatly accelerates the reactions of the azo compounds toward water, ethanol and phenol. Cleavage by water is accelerated by strong acid.

The reaction products of all the azo compounds appear to be the corresponding hydrazones. In the ultraviolet spectra of these compounds, the characteristic absorption band of the phenylazo group in the region 270 to 280 mμ disappears. Instead, two new bands appear in the regions 285 to 295 mμ and 312 to 335 mμ. The characteristic absorption maxima and molar extinction coefficient, E_m, are affected by the substituent on the carbon of $-\overset{H}{\overset{|}{N}}-N=\overset{|}{C}-$ group. These spectra resemble those of 2,3-butanedione mono-N-methylphenylhydrazone, benzil mono-N-methylphenylhydrazone, ethyl pyruvate N-methylphenylhydrazone and pyruvanilide N-methylphenylhydrazone.

Additional evidence to verify the assumption of the hydrazone structure was sought from the authentic preparations of some of the cleavage products of the azo compounds. The results show that the same product was obtained from the acyl cleavage of the azo compound and the con-

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(8) F. R. Japp and F. Klingemann, *Ber.*, **20**, 2942 (1889).

(9) H. C. Yao and P. Resnick, Interchemical Corp., unpublished work.

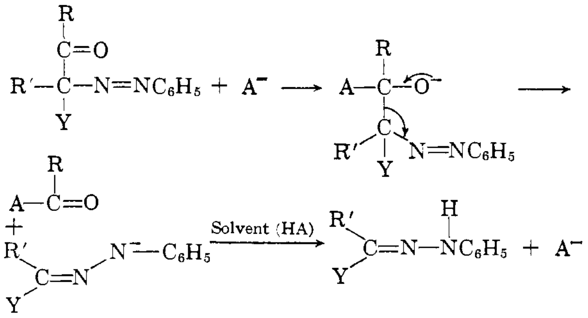
TABLE III

N-METHYLPHENYLHYDRAZONES

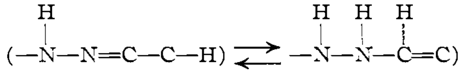
Compound prepared	B.p., °C. (mm.)	λ_{max} 1, mμ	log E_{m_1}	λ_{max} 2, mμ	log E_{m_2}	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
2,3-Butanedione mono-N-methylphenylhydrazone (XVII)	128–130 (5)	298	3.62	335	3.86	$C_{11}H_{14}N_2O$	14.74	14.91
Benzil mono-N-methylphenylhydrazone (XVIII)	59–60 (m.p.)	..	..	335	4.06	$C_{21}H_{18}N_2O$	8.93	9.01
Ethyl pyruvate N-methylphenylhydrazone (XIX)	144–146 (4)	293	3.97	315	3.80	$C_{12}H_{16}N_2O_2$	12.70	12.66
Pyruvanilide N-methylphenylhydrazone (XX)	99 (m.p.)	285	3.95	334	3.89	$C_{16}H_{17}N_3O$	15.71	15.90

densation of phenylhydrazine with the corresponding ketone.

That the hydrazone form is more stable than the azo form has been demonstrated in many coupling reactions of a diazonium salt to a methyl or methylene carbon.[5] A possible course, analogous to that customarily assumed for the cleavage of β-dicarbonyl compounds, for the conversion of azo to hydrazone in the cleavage of azo-compound is depicted as



While not germane to the acyl cleavage, the possibility of ene–hydrazine tautomerism



$$(\overset{H}{\overset{|}{—N}}—N{=}C—C—H) \rightleftarrows \overset{H}{\overset{|}{—N}}—\overset{H}{\overset{|}{N}}—\overset{H}{\overset{|}{C}}{=}C)$$

exists in the cleavage products.[4] Such isomerization has not been excluded by the evidence. The spectroscopic data may actually indicate this isomerization, since in a few cases no absorption was noted in the 285 to 295 mμ region. This is particularly noteworthy with the spectrum of the benzil derivative XVIII where ene–hydrazine tautomerism cannot occur. The possibility of ene–hydrazine tautomerism in these cleavage products is being studied with the hope that a correlation with spectral data may be obtained.

Acknowledgment.—The authors are greatly indebted to Edward Ferlauto for the spectroscopic data, Ronald Mangravite, Mrs. Barbara Artman and Mrs. Constance Morris for the microanalyses and to Professor N. Kornblum of Purdue University for his encouragement and guidance.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY, TALLAHASSEE, FLA.]

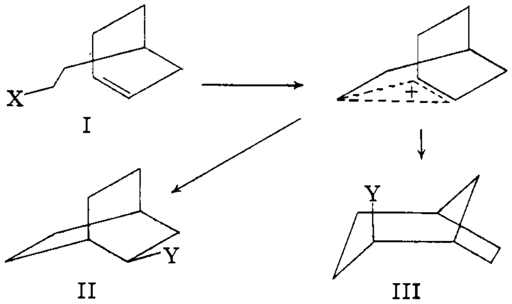
A Remarkably Facile Ring Closure Through Double Bond Participation[1]

BY WERNER HERZ AND GERALD CAPLE

RECEIVED MARCH 16, 1962

The conversion of the mesylate of 1-methyl-1-(2-hydroxyethyl)-1,2-dihydronaphthalene (VIIc) to *exo*-1-methyl-2,3-benzbicyclo(3,2,1)-4-octanol on treatment with alumina and wet benzene is reported.

Participation of the double bond, with formation of non-classical ions, has been invoked to explain rates and products observed during the solvolysis of Δ^3-cyclopentenylethyl arenesulfonates[2,3] and cycloheptenylmethyl bromobenzenesulfonate.[4] In a recent communication[5] Winstein and Carter have summarized these results and provided evidence for the participation of the double bond in the solvolysis of Δ^3-cyclohexenyl bromobenzenesulfonate (I) which leads to bicyclo(2,2,2)octanol (II) and *trans*-bicyclo(3,2,1)octanol-2 (III), presumably through intervention of the non-classical ion.



We have independently observed an instance of double bond participation in a system analogous to I, but under unprecedentedly mild conditions, and hereby report our results.

For reasons which need not be detailed here we undertook the synthesis of 1-methyl-1-vinyl-1,2-

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[1] Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant in partial support of this research.

[2] R. G. Lawton, *J. Am. Chem. Soc.*, **83**, 2299 (1961).

[3] P. D. Bartlett and S. Bank, *ibid.*, **83**, 2591 (1961).

[4] G. Le Ny, *Compt. rend.*, **251**, 1526 (1960).

[5] S. Winstein and P. Carter, *J. Am. Chem. Soc.*, **83**, 4485 (1961).