REACTION OF DIAZOALKANES WITH UNSATURATED COMPOUNDS COMMUNICATION 1. CYCLOPROPANATION OF OLEFINS WITH DIAZOMETHANE IN THE PRESENCE OF COPPER COMPOUNDS*

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Diazomethane, in spite of its high toxicity and the explosion hazard associated with its use, is still the most universal cyclopropanation reagent. The active decomposition of CH_2N_2 in the presence of catalysts allows one to prevent it from accumulating in the reaction mass and, in conjunction with the high reactivity of methylene, provides the possibility of cyclo-propanating many unsaturated compounds under mild conditions [2]. Another characteristic feature of cyclopropanation with diazomethane is the possibility of practically excluding side reactions of the initial olefins and of the products formed as the result of cyclopropanation. However, the lack of systematized data on the nature of the cyclopropanation of the double bonds of various different structural types, which substantially changes the degree of conversion of various different olefins, and the use of a large excess of CH_2N_2 indicate the need for further investigations into these reactions. On account of this, we have studied the cyclopropanation, under comparable conditions, of mono-, and diolefins of differing structure using diazomethane in the presence of CuCl.

The experiments were carried out by the continuous passage of diazomethane diluted with an inert gas into the olefin or a solution of the olefin (~1:2) in CH_2Cl_2 or hexane at -10 to 0°C. When this was done the yields of the cyclopropanation product with respect to the olefin which had entered into reaction were close to quantitative. However, the conversion of the olefins varied over wide limits depending on their structure. For instance, in the presence of 2-3 mole % of CuCl (with respect to the initial olefin) and using an equimolar amount of CH_2N_2 , the conversion of cyclohexene (CHX), cycloheptene (CHP), and cyclooctene (COC) into the corresponding bicyclo[nl.0]alkanes (I) sharply increases upon passing from CHX to CHP and then to COC.



where n = 4 (a), 5 (b), 6 (c).

When this was done the yields of the corresponding (I) were 20-25% for bicyclo-[4.1.0]heptane (Ia), 50-55% for bicyclo[5.1.0]octane (Ib), and 75-80% for bicyclo[6.1.0]nonane (Ic).

Norbornene (NB), norbornadiene (NBD), and cycloocta-1,5-diene (COD) are cyclopropanated with a high degree of conversion. At the same time, it has been established from a comparison of the physicochemical characteristics of the products with those of known samples that $tricyclo[3.2.1.0^{2,4}]$ octane (II), $tricyclo[3.2.1.0^{2,4}]$ -oct-6-ene (III), and $tetracyclo[3.3.1.0^{2,4}.0^{6,8}]$ nonane (IV) are formed exclusively in the form of the exo-isomers from the first two hydrocarbons. Cyclopropanation of COD yields cis- and trans-tricyclo [7.1.0.0^{4,6}]decanes (VI) and (VII) in approximately equal proportions

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Under similar conditions the conversion of 4-vinylcyclohexene (VCH) as well as of cyclohexene (CHX) itself is only 20-25% and moreover the cyclopropanation takes place both with respect to the endocyclic bond and with respect to the exocyclic double bond.



3-Vinylnorcarane (VIII) and 4-cyclopropylcyclohexene (IX) constitute a mixture of structural isomers which is difficult to separate. However, according to the integral intensities of the signals due to the olefinic protons in the PMR spectra, (VIII) and (IX) are formed in ratio of ~1.3:1.

The cyclopropanation of diene hydrocarbons show that, in the presence of CuCl, there is a gradual accumulation of the mono- and dicyclopropanation products as the CH₂CN is added. However, the attainment of high degrees of conversion of olefins solely by the addition of an excess of CH₂N₂ was found to be ineffective. Data obtained from a GLC analysis of the samples which were withdrawn during the passage of the CH2N2 showed that, in all cases, the yield of the cyclopropane adducts fell off appreciably from a certain moment which manifested itself initially in the appearance of a red-brown coloration, and subsequently, in the formation of a black deposit. When this occurs, the CH_2N_2 decomposes just as efficiently as it did initially but the products of the cyclopropanation of olefins are barely formed any more. The black deposit consisted of active metallic copper. The addition of an acetone solution of $CuCl_2$ to it led to the formation of a white deposit of CuCl. Hence, only a part of the CH_2N_2 was consumed in the reaction with the olefin and, from the moment when Cu(0) was formed, the remainder of it was predominantly converted into methylene oligomerization products [4]. The regeneration or addition of fresh portions of CuCl in the middle of the reaction increased, for example, the yield of the cyclopropanation products of VCH by a further 9-12% and the use of a large amount (up to 40 mole %) CuCl increases the conversion of VCH by a factor of almost three (Table 1).

The higher degrees of conversion of olefins containing conjugated cyclic double bonds (NB, for example) into the corresponding cyclopropanes is also characterized by their high reactivity. For instance, in the competing reactions of NB and CHX, the rate of cyclopropanation of the first of them is 2.7 times faster than that of the second. However, the presence of NB promotes a greater degree of conversion of CHX into (Ia) as a result of which, when CH_2N_2 acts on an equimolar mixture of NB and CHX, their conversion into the corresponding cyclopropanes (II) and (Ia) is 86 and 60%, respectively, while in experiments on their individual cyclopropanation under the same conditions the corresponding figures are 88 and 20-25%.

It is interesting to note that when ~50% conversion of COD has been achieved in its reaction with CH_2N_2 in the presence of 30 mole % CuCl, i.e., up to the appearance of the black copper deposit, all the CuCl can be practically separated off in the form of the crystalline π -olefin complex C_8H_{12} •CuCl [5]. Apparently, the duration for which the catalyst operates successfully is related to the ability of the olefins to form π -olefin complexes with the copper salts which are used as catalysts. The experimental material on π -olefin complexes shows that the constants for the formation of the complexes are exceedingly sensitive to electronic and steric effects in the olefin ligand and also to conjugation in the ring in the case of cyclic ligands [6]. These differences are ascribed to the effect of conjugation on the π -acidity of the double bond and, consequently, on the strength of the coordination bond which is formed. According to this reasoning, the π -complexes of CuCl with such ligands as NB, NBD, and COD are characterized by the greatest stability. In fact, the highest yields of the corresponding cyclopropanes are observed in the case of these unsaturated hydrocarbons.

We consider that diazomethane, by complexing with the copper atom of the π -olefin complex, eliminates a molecule of nitrogen and the coordinately bound methylene which has been formed either adds across the double bond of the olefin lying within the ligand sphere of the copper atom or is inserted into the Cu...Cl bond (which apparently subsequently reacts with CH_2N_2) with the formation of organocopper compounds, the α -bond fission of which leads to the separation of exceedingly active metallic copper which now acts as a catalyst for the decomposition of CH_2N_2 . It seems that the direct bimolecular reaction between CH_2N_2 and CuCl does not lead to its reduction to Cu(0); otherwise the separation of copper would now be observed at the initial moment of the reaction independently of the nature of the olefin. An increase in the rate of addition of CH_2N_2 or a large dilution of the olefin with CH_2Cl_2 or ether promotes the dissociation of the π -olefin complexes of CuCl and reduces the conversion of the corresponding olefins into cyclopropanes. The PMR spectral data indicate that there is a reversible equilibrium in π -olefin complexes of Cu(I) in solutions. In these spectra an averaged olefin proton signal is observed and moreover its position depends on the ratio of the components. What is more, the likelihood of the formation of complexes with several olefic ligands including mixed complexes if their double bonds are nonequivalent also follows from these data.



The nature of the anion of the copper salts which are employed as the catalyst has a substantial effect on the degree of the cyclopropanation of olefins with diazomethane. The less nucleophilic the anion (BF_4 or OTf⁻, for example, the greater the extent to which the copper ion tends to be involved in selective and strong complex formation with the multiple bonds of the olefins and the greater their degree of cyclopropanation. At the same time, the regioselectivity which is observed is explained by the better ability of less substituted double bonds to form π -olefin complexes [7]. When such catalysts as CuCN and CuI are used, for which the formation of π -olefin complexes is uncharacteristic [8], cyclopropanation of olefins barely occurs. However, the introduction of n-donor ligands such as (C_6H_5O)₃P into the coordina-

TABLE 1. Degree of Cyclopropanation of 4-Vinylcyclohexene (VCH) by Diazomethane in the Presence of CuCl at -10 to 0°C as a Function of the Ratio of the Reagents

VCH	CH_2N_2 ,	CuCl,	Yield, %		VCH	CH ₂ N ₂ ,	CuCl,	Yield, %	
mmoles			(VIII)+ (IX)	(X)	mmoles			(VIII)+ (IX)	(X)
10 10	20 10	0,3 0,3	22-24 17-19	3 2–3	10 10	10+10 20	0,3+0,5 4,0	27-29 46-49	46 1920

tion sphere of the copper ion apparently increases the stability of the complex (XII) which therefore up to its conversion into an organocopper compound succeeds in reacting with the olefin. The use of triphenylphosphite cuprous chloride $(C_6H_5O)_3P$ •CuCl as the catalyst for the cyclopropanation of olefins with diazomethane increases their conversion in comparison with CuCl. In the presence of 2 mole % of $(C_6H_5O)_3P$ •CuCl, the corresponding monocyclopropanation products (VIII) and (IX) and the dicyclo-propanation product (X) areformed from equivalent amounts of VCH and CH_2N_2 with yields of 49 and 22% respectively, while, in the presence of CuCl, the yields are ~23 and 3%.

Apparently, inner complex salts of copper also catalyze the cyclopropanation of olefins in a similar manner. An example of this is copper acetoacetonate $(AcAc)_2Cu$. It is obvious that during this process the $(AcAc)_2Cu$ is initially reduced to (AcAc)Cu which then yields a reactive complex similar to (XII). Hence, the addition of CH_2N_2 to an equimolar mixture of NB and CHX in the presence of 1-2 mole % $(AcAc)_2Cu$ at -5°C leads to the hydrocarbons (Ia) and (II) in approximately equal amounts (unlike in the case of CuCl). A gradual decolorization of the solution is observed during this process which is apparently due to the conversion of Cu(II) into Cu(I) and, when about 50% conversion of the olefins has been achieved, a black precipitate of metallic copper is observed to be formed.

EXPERIMENTAL

The reaction mixtures were analyzed using GLC on an LKhM-8MD chromatograph with a flame ionization detector and an I-O2 integrator (300×0.3 cm columns with 5% SE-30 or 15% Carbowax 20M on Chromaton N-AW-DMCS, helium carrier gas, 30 ml/min). The preparative separation was carried out on an LKhP-7I chromatograph (nitrogen carrier gas, 200 ml/min, a 200 \times 1.2 cm column with 15% Carbowax 20M on Chromaton N-AW-DMCS, 0.25-0.36 mm). The PMR spectra were recorded on a Tesla BS-467 (60 MHz) and Bruker WP-60 (15.08 MHz) spectrometers using CDCl₃ as a solvent and TMS as the internal standard.

Before use, the initial olefins were distilled in a stream of argon (>98.5% pure). CuCl was precipitated from hydrochloric acid solution by the addition of distilled water, washed with acetone and CH_2Cl_2 , and dried in a current of argon. The cyclopropanation products were identified by comparison with known compounds prepared by other methods, reduction of the corresponding gem-dichlorocyclopropanes [9] or the reaction of the same olefins with CH_2I_2 in the presence of a Zn-Cu couple [10].

<u>Preparation of Diazomethane.</u> A 45-50% solution of KOH (100 ml) and 25 ml of dodecane were placed in a round-bottom flask without ground glass joints. The central aperture of this flask was connected to a (glass and Teflon) screw conveyer and was fitted with inlet and outlet gas tubes through which inert gas (Ar or N₂) was blown in at a rate of ~80 ml/min. N-nitroso-N-methylurea (NMU) was added via the screw conveyer at a rate of 6-7 g/h. The CH_2N_2 which was formed was transported by the stream of gas through a drying tube filled with solid KOH into the reactor containing a mixture of the olefin, solvent, and catalyst. The reactor was equipped with a reflux condenser which operated at temperatures down to -70°C. The yield of CH_2N_2 (according to the data obtained by titration with MeCOOH) was 60-65%.

<u>Bicyclo[4.1.0]heptane (Ia)</u>. A 0.05-g sample (0.5 mmole) of CuCl cooled down to -10 to 0°C was added to a solution containing 1.65 g (20 mmole) of cyclohexane (CHX) in 3 ml of CH₂-Cl₂ and the CH₂N₂ generated from 3.5 g of NMU was passed through the solution. The reaction mixture which had turned black was filtered and the hydrocarbon fraction with bp 80-115° separated by distillation. A yield of 1.7 g of a mixture of (Ia) and CHX was obtained. Yield of (Ia) ~25%.

<u>Bicyclo[5.1.0]octane (Ib).</u> Compound (Ib) was prepared with a yield of ~55% (GLC) from 1.0 g of cycloheptene (CHP) in the presence of 0.02 g CuCl and CH_2N_2 generated from 2.0 g NMU.

<u>Bicyclo[6.1.0.]nonane (Ic)</u>. Compound (Ic) was prepared in a yield of 78% (GLC) from 1.1 g of cis-cyclooctene (COC) in the presence of 0.02 g of CuCl and the CH_2N_2 generated from 2.0 g of NMU.

 $\frac{\text{exo-Tricyclo}[3.2.1.0^2, ^4]\text{octane (II).}}{0.95 \text{ g of norbornene (NB) in the presence of 0.02 g CuCl and the CH₂N₂ generated from 2 g of NMU. 0.8 g of (II) with a purity of ~98% was isolated by distillation, bp 134-136°C, n_D²⁰ 1.4790 (compare with [11]). PMR spectrum (<math>\delta$, ppm): -0.1 doublet of triplets (1H, J_{gem} = 5.9 Hz, J_{vic} = 6.9 Hz, H-anti), 0.3 doublet of triplets (1H, J_{gem} = 5.9 Hz, J_{vic} = 3.0 Hz), 2.2 multiplet (2H, CH), 0.5-1.5 (8H).

<u>Cyclopropanation of Norbornadiene (NBD)</u>. About 40 mmoles of CH_2N_2 prepared from 7 g of NMU was passed into a mixture of 1.9 g (20 mmoles) of NBD, 3 ml of CH_2Cl_2 , and 0.06 g CuCl at -10 to 0°C. According to the GLC data, the mixture contained 23% of tricyclo[3.2.1.0²,⁴]-oct-6-ene (III), 68% of tetracyclo[3.3.1.0²,⁴.0⁶,⁸] nonane (IV), and ~9% of the initial NBD. 0.3 g of (III) was isolated by distillation, bp 46-48°C (20 mm). There was also ~15% yield of (IV) with bp 60-61°C (20 mm), yield ~63%. The PMR spectra were identical to those shown in [3].

<u>Cyclopropanation of Cyclooct-1,5-diene (COD)</u>. About 60 mmoles of CH_2N_2 prepared from 10.5 g of NMU was passed into a solution of 3.3 g (30 mmole) of COD in 3 ml of CH_2Cl_2 to which 0.08 g CuCl had been added. The reaction mixture was filtered, the solvent removed from the filtrate, and the fraction with bp 50-85°C (20 mm) was separated from the residue by distillation (practically the whole of the residue distilled over). A mixture was obtained (3.8 g) which, according to the GLC data, contained ~14% of the initial COD, 35% of (V), 27% of (VI) and 24% of (VII). All the components were isolated as separate compounds using preparative GLC (180°C).

Bicyclo[6.1.0]non-4-ene (V): yield 1.1 g (30%), n_D²⁰ 1.4945, PMR spectrum (δ , ppm): 5.6 (2H, HC=CH), 2.2 (4H, =C-CH₂), 0.8 (2H, HC-CH), -0.1 (1H, CH-anti), 2.1-0.9 (5H).

cis-Tricyclo[7.1.0.0⁴, ⁶]decane (VI): yield 0.9 g (22%), n_D^{20} 1.4898, ¹³C NMR spectrum (δ , ppm): 26.4 (CH₂), 14.1 (CH), 12.7 (CH₂).

trans-Tricyclo[7.1.0.0^{4,6}]decane (VII): yield 0.8 g (20%), mp 40-41°C, ¹³C NMR spectrum (δ , ppm): 29.3 (CH₂), 18.4 (CH), 12.6 (CH₂). The isomers were assigned in accordance with [12].

<u>Cyclopropanation of 4-Vinylcyclohexene (VCH).</u> 1) About 20 mmole of CH_2N_2 prepared from 3.5 g of NMU was passed into a mixture of 1.1 g (10 mmoles) of VCH, 3 ml of CH_2Cl_2 , and 0.03 g of CuCl at -10 to 0°C. The mixture contained 22-24% of 3-vinylnorcarane (VIII) and 4-cy-clopropylcyclohexene (IX), which are difficult to isolate by GLC on the phases used in this work, ~3% of 3-cyclopropylnorcarane (X), and ~72% of the initial diene. The ratio of the isomers (VIII) and (IX), which is equal to 1.3:1, was established from the PMR spectrum of the mixture isolated by means of preparative GLC (180°C), yield 0.24 g (20%). The signals due to the olefinic protons in the HC=CH fragment of (IX) and the C=CH₂ fragment of (VIII) appear in nonoverlapping regions of the spectrum at 5.58 (narrow multiplet) and 5.05-4.7 ppm.

2) The experiment was carried out in a similar manner but using 1.7 g of NMU for the preparation of the CH_2N_2 . The reaction mixture contained 17-19% of a mixture of (VIII) and (IX), ~3% of (X), and the initial VCH. After the addition of 0.05 g of CuCl, the CH_2N_2 generated from 1.8 g NMU was again passed through the solution. The product obtained contained 28-29% of a mixture of (VIII) and (IX), 6-8% of (X), and 62-64% of the initial diene. The black residue was separated by decantation, a solution of 0.1 g of CuCl₂ in 3 ml acetone was added, and the white precipitate of CuCl (0.13 g) separated.

3) The CH_2N_2 generated from 3.5 g of NMU was passed into a mixture of 1.1 g of VCH, 0.5 g CuCl in 3 ml of CH_2Cl_2 , and 2 ml of hexane at $-15^{\circ}C$. The dark brown reaction mass was diluted with hexane and filtered through a small layer of silica gel. A residue weighing 1.3 g was obtained after the removal of the solvent. According to the GLC data, the yield of the mixture of (VIII) and (IX) was 48% and that of (X) was 20%.

4) A mixture of 49% (VIII) and (IX), 22% (X), and ~29% of the initial diene, which was seprated with the help of preparative GLC ($180^{\circ}C$), was obtained in a similar way to the first experiment from 1.1 g of VCH in the presence of ~0.1 g of (C_6H_5O)₃P•CuCl and the CH₂N₂ generated from 3.5 g of NMU.

3-Vinylnorcarane (VIII) and 4-cyclopropylcyclohexene (IX): yield of 0.51 g (42%), ratio 1.3:1, bp 157-160°C (in a capillary).

3-Cyclopropylcyclopropane (X): yield 0.26 g (19%), bp 175-176°C (in a capillary), $n_{\rm D}^{~20}$ 1.4750 [10].

<u>Cyclopropanation of a Mixture of Norbornene (NB) and Cyclohexene (CHX)</u>. 1) The CH_2N_2 (~1.5 mmole) generated from 0.3 g of NMU was passed into a mixture of 0.47 g (5 mmole) of NB, 0.41 g (5 mmole) of CHX, and 0.03 g of CuCl in 3 ml CH_2Cl_2 at $-5^{\circ}C$. The (II):(Ia) ratio in the reaction mixture was ~2.7:1 (GLC). A further amount of CH_2N_2 (~9 mmole) was then passed through the solution. The total amount of NMU used was 1.8 g. The conversion of CHX and the

yield of norcarane (Ia) was $\sim 60\%$ while the conversion of NB and the yield of tricyclooctane (II) was ~86\%.

2) The CH_2N_2 generated from 1.8 g of NMU was passed into a solution of 0.47 g of NB, 0.41 g of CHX, 0.03 g of copper acetoacetonate, 2 ml of hexane and 3 ml of CH_2Cl_2 at $-5^{\circ}C$. The slow decolorization of the solution was observed which became colorless after the addition of 4-5 mmole of CH_2N_2 . A black mirror of metallic copper with a reddish hue was then initially formed on the walls of the flask. The conversion of each of the olefins and, correspondingly, theyields of (Ia) and (II) were ~50%. When the duration of the whole experiment was prolonged, the ratio of (Ia):(II) in the reaction mixture was ~1.05:1.

<u>Complex of Cycloocta-1,5-diene with CuCl(C₈H₁₂•CuCl)</u>. The CH₂N₂ obtained from 1.7 g of NMU was passed into a weakly violet colored solution of 1.1 g of COD, 0.3 g of CuCl, 2 ml of hexane, and 2-3 ml CH₂Cl₂ at -5°C. The solution was left to evaporate for 24 h. The large colorless crystals of the π -complex C₈H₁₂•CuCl were washed with cold hexane (0°C) and dried for 5 min in a vacuum at 100 torr and 20°C. The yield was 0.6 g (96-97%), the composition ~1:1, according to the data obtained from the regeneration of COD under the action of NH₄OH.

CONCLUSIONS

In the presence of CuCl or (PhO)₃P•CuCl diazomethane cyclopropanates cycloalkenes and cyclodienes with various different structures. When this is done the yields of the cyclopropane compounds increase as the size of the ring and its degree of conjugation increases. This is in accord with the change in the stability of the copper complexes of these olefins which are formed under the reaction conditions.

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