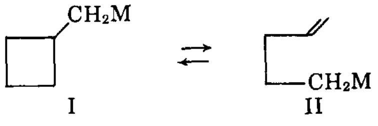
Communications TO THE EDITOR

Intramolecular Cleavages and Double Bond Additions of Polar Organometallic Compounds[1]

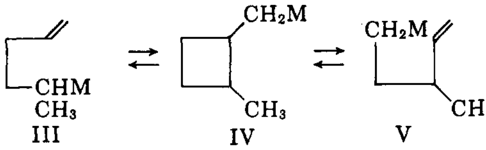
Sir:

Rearrangement of the cyclobutylmethyl organometallic compounds of sodium, lithium, and magnesium to isomeric acyclic compounds (I → II) is reported in this communication. In addition, 1-methyl-1-pent-4-enyl organometallic compounds of the same metals



M = Na, Li, or Mg

have been found to rearrange to 3-methyl-1-pent-4-enyl isomers (III → V); we propose that this rearrangement occurs by ring closure of the initially



M = Na, Li, or Mg

formed organometallic compounds III to cyclic isomers IV followed by ring opening to acyclic isomers V. These rearrangements are similar to that observed by Roberts and co-workers for the cyclopropylmethyl and 1-but-3-enyl Grignard reagents.[2]

The rates of some of these reactions can be measured and it should be possible to study the effects of different reaction conditions on these intramolecular cleavages and double bond additions. The Grignard reagents (studied in tetrahydrofuran) appear to rearrange much more slowly than the sodium and lithium reagents despite the use of less polar hydrocarbon media for the latter. The equilibration of isomeric organometallic compounds also permits estimation of their relative stabilities. For example, it appears that the equilibrium mixture of lithium compounds III and V in cyclohexane contains more than 99% of V, indicating a much greater stability for the primary than for the isomeric secondary organolithium compound.

1. **Evidence for Ring Opening.**—Treatment of cyclobutylmethyl chloride with sodium in tetradecane produced 1-pentene and methylcyclobutane in a ratio of 7:1.[3] These hydrocarbons probably arose from the action of 1-pent-4-enylsodium (II) and cyclobutylmethylsodium (I), respectively, as bases in elimination reactions.[4] Presumably cyclobutylmethylsodium (I) formed first and then underwent ring opening to form the acyclic organosodium compound II.

The lithium compound prepared at room temperature in benzene from cyclobutylmethyl bromide and lithium rearranged similarly. Samples hydrolyzed after standing for 1 or 18 hr. gave a 93:7 mixture of 1-pentene and methylcyclobutane.[5] It is likely that the rearrangement was nearly complete when the first sample was taken, since removal of the solvent under vacuum, followed by hydrolysis of the residue, reduced the methylcyclobutane to less than 0.5%. Some hydrolysis by traces of moisture presumably occurred during or shortly after formation of the reagent.

The cyclobutylmethyl Grignard reagent also was observed to rearrange at temperatures near the boiling point of tetrahydrofuran (65°).[6] This rearrangement occurs in the presence or absence of excess magnesium, with the chloride or the bromide, and with either regular Grignard reagent magnesium or sublimed magnesium. The degree of rearrangement increases with time of heating, eliminating the possibility that all of the rearrangement occurs during formation of the Grignard reagent.[7] Rearrangement to the acyclic reagent proceeds at least 99.8% to completion.

2. **Evidence for Ring Closure.**—Organolithium compound III was prepared by reaction of lithium with a mercury compound, b.p. 92° (0.6–0.7 mm.), synthesized from mercuric chloride, and the Grignard reagent prepared from 5-chloro-1-hexene.[8] Hydrolysis after 90 min. of a portion of a solution obtained from refluxing this mercury compound with lithium in cyclohexane gave a C_6 product which was at least 99% 3-methyl-1-pentene. The composition and the yield were unchanged after the solution had stood at room temperature for an additional 24 hr.[9] This rearranged olefin probably arose from hydrolysis of organolithium compound V; presumably organolithium compound III formed initially but then rearranged rapidly to V.

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[1] Preliminary work was supported by research grant 7766 (to H. G. R.) from the National Institutes of Health and by a National Science Foundation Postdoctoral Fellowship (to E. A. H.). Recent work has been supported by grants from the Petroleum Research Fund administered by the American Chemical Society (to E. A. H. and to H. G. R.) and by equipment grants (to E. A. H.) from the Graduate School and the Institute of Technology of the University of Minnesota. Grateful acknowledgement is hereby made of this support.

[2] M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Ruchardt, and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 2646 (1960).

[3] Product analyses were by vapor phase chromatography. Identification of the separated components was by gas phase infrared spectra.

[4] Products of formula C_5H_8 also were formed. The nature of these products will be discussed elsewhere. Compare with W. Kirmse and W. von E. Doering, *Tetrahedron*, **11**, 266 (1960); L. Friedman and J. G. Berger, *J. Am. Chem. Soc.*, **83**, 492, 500 (1961); and P. S. Skell and A. P. Krapcho, *ibid.*, **83**, 754 (1961).

[5] It is assumed that hydrolyses of the organometallic compounds are considerably more rapid than their rearrangements. The assumption is valid at least with the Grignard reagents.

[6] R. C. Krug, I. W. Smith, and C. E. Fry [*J. Am. Chem. Soc.*, **76**, 3222 (1954)] previously have reported the reaction of a Grignard reagent from cyclobutylmethyl bromide with phenyl isocyanate. It appears that the anilide they obtained was that of cyclobutylacetic acid.[7]

[7] The structures of the original and rearranged Grignard reagents have been confirmed by carbonation to the corresponding carboylic acids (R. A. Doughty).

[8] Reaction of the mercury compound with hydrochloric acid gave a mixture of 98% of 1-hexene and 2% of 3-methyl-1-pentene. The rearranged group (1°) should be cleaved even more readily by acid than the unrearranged group (2°) [F. C. Whitmore and H. Bernstein, *J. Am. Chem. Soc.*, **60**, 2626 (1938)] so this per cent of 3-methyl-1-pentene represents maximum of rearranged groups.

[9] That the olefins observed had not formed prior to the hydrolyses was shown by pumping off the volatile material and then hydrolyzing the residue; little of the olefinic product was in the volatile portion.

Aliquots of a refluxing tetrahydrofuran solution of a Grignard reagent prepared from 5-chloro-1-hexene were hydrolyzed at intervals. The proportion of 3-methyl-1-pentene in the mixture of 1-hexene and 3-methyl-1-pentene increased, but at decreasing rate, to about 20% after 14 days. At that time volatile materials were removed from the solution under vacuum and the remaining solid hydrolyzed to give in poor yield a mixture containing 85% of 3-methyl-1-pentene and only 15% of 1-hexene. Apparently in this case, attack of the Grignard reagent on solvent to produce olefin is competitive with the slower rearrangement, so that with increasing time, a smaller fraction of the olefin in the samples analyzed was actually formed in the hydrolysis operation.

Reaction of 5-chloro-1-hexene with sodium in hydrocarbon solvents also gave 1-hexene and 3-methyl-1-pentene, with the rearranged olefin predominating. The reaction mixtures contained 1,5-hexadiene and smaller amounts of other compounds that must have formed by reaction of the chloride with the sodium compounds.

Reasonable possibilities for the mechanism of these rearrangements include a four-center process and either heterolytic or homolytic cleavage to the corresponding carbanion or free radical which then undergoes rearrangement. The increase in the facility of rearrangement with polarity of the carbon–metal bond supports the ionic mechanism or a highly polar four-center process. However, the free radical mechanism remains a possible alternative.[10] We currently are investigating this question kinetically and stereochemically and are exploring several extensions and variations of these elimination and intramolecular addition reactions.

(10) R. C. Lamb of the University of Georgia kindly has informed us of a similar cyclization noted in oxygenation of the Grignard reagent from 6-bromo-1-hexene, in which a free radical pathway appears likely. He also found some cyclization in the carbonation of the same Grignard reagent. This agrees with our findings that the Grignard rearrangement occurs in that system.

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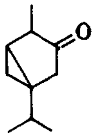
The Photolysis of Thujone

Sir:

We wish to report that the photolysis of the terpene ketone thujone (I) appears to offer an example of the participation of a cyclopropane ring in facilitating the photochemical elimination of carbon monoxide from a ketone. Thujone (I) is converted smoothly and with unusual rapidity into carbon monoxide and 2-isopropyl-1,4-hexadiene (III) on exposure to ultraviolet radiation in the wave-length region[1] 2500–3000 Å.

Infrared spectral analysis of the gaseous product showed it to be carbon monoxide (λ_{max}^{gas} 4.62, 4.73 μ), and gas–liquid chromatography of the liquid product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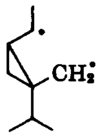
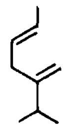


II


III

revealed only traces of products[2] other than 2-isopropyl-1,4-hexadiene (III) [λ_{max}^{film} 6.09 μ (C=C), 7.26 and 7.35 μ (CH_3CCH_3), 3.31 and 10.29 μ (*trans*—RCH=CHR), 3.25 and 11.20 μ (CR_1R_2=CH_2); n.m.r. spectrum,[3] 65 and 79 (*C*H_3CHCH_3), 99 (CH_3C=C), multiplet about 132 (CH_3C*H*CH_3), 163 (CH_2), 285 (C=CH_2), multiplet about 327 (—C*H*=C*H*—); integral, 16 protons, in accord with the foregoing assignments. *Anal.* Calcd. for C_9H_{16}: C, 87.23; H, 12.77. Found: C, 87.51; H, 12.80]. The photolyses were carried out in quartz cells using either 150-watt high pressure Hanovia (510B1) xenon–mercury arcs or General Electric (H400A33-1) 400-watt "Dark Light" arcs with the external envelope removed. Manometric measurements were made in a nitrogen-filled system using mercury-filled burets.

Under given photochemical conditions the rates of carbon monoxide evolution (first 10% of reaction) from thujone,[4] cyclopentanone, and cyclohexanone as neat liquids were respectively 0.79, 0.047, and 0.025 ml. per minute. Since the integrated absorption intensities [$\int \epsilon \, d\nu$] of thujone, cyclopentanone, and cyclohexanone for the wave-length interval 2600–3300 Å. were, respectively, 44.5, 29.2, and 27.5 in arbitrary units, the fifteen- to thirtyfold greater photolysis rate for thujone reasonably cannot be attributed to its somewhat greater absorption in the photolytic region and may, instead, be ascribed to the presence of the cyclopropane ring in the homoallylic position.

Photolysis of solutions of thujone dissolved in ten times its volume of either cyclohexene or 1-propanol proceeded at rates comparable to those found for the neat liquid; and gas–liquid chromatographic and infrared spectral analysis of the photolyzate showed only traces of products other than the diene III. These results are taken to indicate that any intermediate radical such as II is capable of at best only very brief existence, and that the transition of thujone from its photoexcited state to the diene III and carbon monoxide is made unusually efficient by participation of the neighboring cyclopropane ring system. A similar facilitation of the photolysis of the 3-cyclopentenone system by the electrons of the double bond would be predicted. The clean-cut nature of such photochemical reactions may prove useful in synthesis and in gasometric actinometry in the photochemically important 2500–3000-Å. region.[5]

Acknowledgment.—We wish to express our appreciation to the National Science Foundation (G-9476) and

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(1) The photolysis proceeded at an uninhibited rate and to the same products using a 30% solution of thujone in benzene.

(2) The ultraviolet absorption spectrum of the gas chromatographically homogeneous diene III showed weak absorption at λ_{max}^{EtOH} 231 mμ indicative of less than 5% of conjugated diene in the material.

(3) At 60 Mc., in deuteriochloroform. Chemical shifts are in cycles per second referred to tetramethylsilane as internal standard at 0 c.p.s.

(4) Whether (−)-thujone or (+)-isothujone was used made no difference in the rate.

(5) Thujone is readily available through efficient fractional distillation of thuja oil (P.R. Dreyer, Inc., New York, N.Y.). The fraction having b.p. 83.2–83.9° at 15.9 mm., $n^{25}D$ 1.4502, is suitable.

the Air Force Office of Scientific Research and Development (AFOSR-62-116) for their generous support of this investigation.

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RECEIVED APRIL 16, 1963

Substitutions by Ligands of Low Valent Transition Metals. A Preparation of Tolanes and Heterocyclics from Aryl Iodides and Cuprous Acetylides

Sir:

In the course of our studies of the reduction of multiple bonds by low valent transition metal ions,[1] we have had occasion to prepare a variety of unsymmetrical tolanes. We have found that these substances are conveniently obtained by the interaction of aryl iodides with cuprous acetylides. The reaction is best carried out in refluxing pyridine in a nitrogen atmosphere.[2]

$$\mathrm{ArI} + \mathrm{CuC{\equiv}C{-}Ph} \xrightarrow[\mathrm{N_2}]{\text{Pyridine}} \mathrm{Ar{-}C{\equiv}C{-}Ph} + \mathrm{CuI}$$

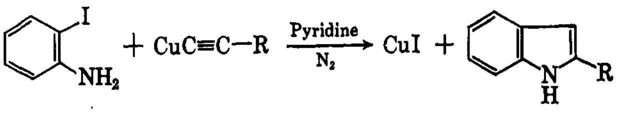
Some illustrative yields for the process are depicted (Table I).

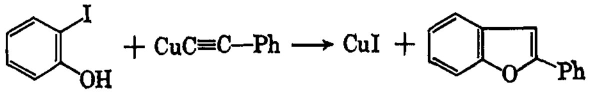
TABLE I
YIELDS OF TOLANES FROM ARYL IODIDES AND CUPROUS PHENYLACETYLIDE

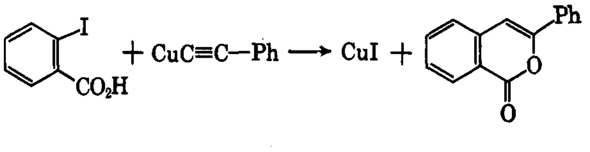
Aryl iodide	Product	Yield, %[a]
Iodobenzene	Diphenylacetylene	90
p-Methoxyiodobenzene	*p*-Methoxytolane	83
o-Methoxyiodobenzene	*o*-Methoxytolane	80
p-Nitroiodobenzene	*p*-Nitrotolane	74
o-Nitroiodobenzene	*o*-Nitrotolane	84

[a] All yields reported in this communication refer to the purified product. Microanalyses, physical constants, and spectra are correct for all substances reported herein.

When the starting halide bears an *ortho* nucleophilic substituent, cyclization to the corresponding heterocycle occurs exclusively. In a reaction typical of both the tolane and heterocyclic synthesis, 3 g. of cuprous phenylacetylide and 4.03 g. of *o*-iodophenol were placed in a flask containing 200 ml. of pyridine which had been purged thoroughly with nitrogen. The reaction solution was refluxed for six hours in a nitrogen atmosphere. During this time the color changed from yellow to a dark reddish brown. The cooled solution was diluted with water and extracted with ether. The washed and dried ether extracts were concentrated and crystallized. The crude α-phenylbenzofuran was recrystallized from hot ethanol to yield 3.2 g. of pure material.[3]

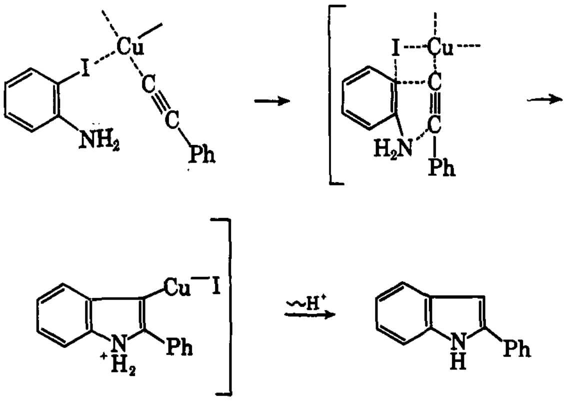






The foregoing set of transformations are indicative of the scope of the facile heterocyclic synthesis.

Moreover, *o*-aninotolane when exposed to cuprous iodide and cuprous phenylacetylide in pyridine *was not* cyclized but recovered quantitatively. This finding suggests that the substitution of halide and the cyclization take place within the same copper complex.



Under proper conditions both the tolane and heterocyclic syntheses should be catalytic in copper. This point, as well as the scope and mechanism of these reactions, is under scrutiny.[4]

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(1) C. E. Castro and R. D. Stephens, Abstracts of Papers, Organic Division, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962, p. 23 Q.

(2) In the presence of oxygen, coupling of the acetylene occurs.

(3) This conversion has been effected in pyridine, dimethylsulfoxide, dimethylformamide, and acetic acid; in all solvents yields of better than 80% were obtained.

(4) The authors are indebted to the National Science Foundation for a grant (G19145) in support of this work.

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The Synthesis of Isothiazoles from Disalts of Dimercaptomethylenemalononitrile

Sir:

Mononuclear isothiazoles have been unknown until recently and few syntheses of this ring system have been described.[1-5]

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(1) A. Adams and R. Slack, *J. Chem. Soc.*, 3061 (1959).

(2) (a) J. Goerdeler, *Angew. Chem.*, **74**, 498 (1962); (b) J. Goerdeler and H. W. Pohland, *Chem. Ber.*, **94**, 2950 (1961); (c) J. Goerdeler, *Angew. Chem.*, **72**, 77 (1960).

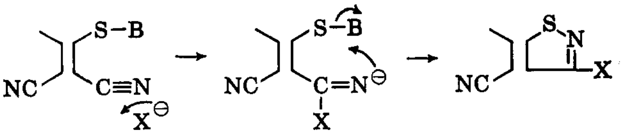
(3) F. Willie, *ibid.*, **74**, 467 (1962).

(4) F. Hubenett, F. H. Flock, and H. Hoffman, *ibid.*, **74**, 653 (1962).

(5) D. Leaver and W. A. H. Robertson, *Proc. Chem. Soc.*, 252 (1960).

Only one general synthetic method is available for the synthesis of mononuclear isothiazoles having other than hydrocarbon substituents (the ring closure of β-iminothioamides described independently by A. Adams and R. Slack and by J. Goerdeler).

We wish to report the novel synthesis of substituted isothiazoles by the ring closure of di(sodiomercapto)-methylenemalononitrile (**1**) under oxidizing conditions. This reaction appears to occur by an addition of a nucleophilic agent to the nitrile group and ring closure on sulfur with elimination of an anion.

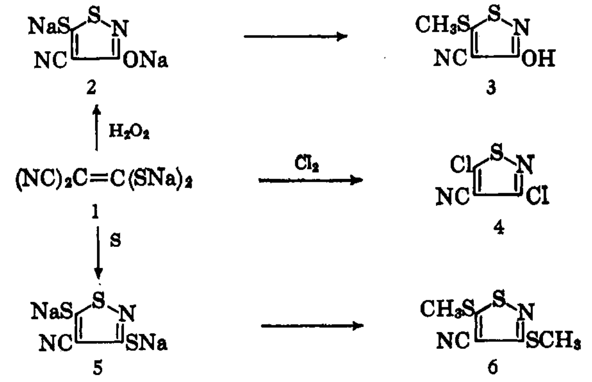


Cyclizations to form two condensed ring isothiazoles have earlier been reported from this laboratory.[6–7]

With one equivalent of hydrogen peroxide, the disodium salt[7,8] (**1**) in aqueous solution was converted to the disodium salt of 3-hydroxy-5-mercapto-4-isothiazole (**2**) in 97% yield. *Anal.* Calcd. for $C_4S_2N_2ONa_2$: C, 23.7; S, 31.7; Na, 22.8. Found: C, 22.4; H, 1.02; S, 31.3; Na, 21.1 ± 2%. $\lambda_{max}^{methanol}$ 320 $m\mu$ (ϵ 13,300), 290 (9800), 213 (11,000). The infrared spectrum (Nujol) showed strong bands at 4.55, 6.65, and 7.6 μ. Alkylation of **2** with one equivalent of methyl iodide followed by acidification yielded the methylthio derivative **3** (71%), m.p. 237–242°. *Anal.* Calcd. for $C_5H_4N_2OS_2$: C, 34.9; H, 2.34; S, 37.3; N, 16.3. Found: C, 34.9; H, 2.43; S, 37.3; N, 16.2. λ_{max}^{alc} 277 $m\mu$ (ϵ 11,500). The infrared spectrum (Nujol) showed strong bands at 3.4, 3.65, 3.75, 3.85, 4.50, 6.10, 6.45, 6.65, and 7.7 μ. Compound **3** readily dissolved in sodium carbonate solution and was recovered unchanged by acidification.

A second method, involving the reaction of the anhydrous sodium salt **1** with chlorine in boiling carbon tetrachloride, gave a 57% yield of 3,5-dichloro-4-isothiazolecarbonitrile (**4**), m.p. 65–66°. *Anal.* Calcd. for $C_4N_2Cl_2S$: C, 26.8; Cl, 39.6; S, 17.9; mol. wt., 179. Found: C, 27.1; Cl, 39.4; S, 17.8; mol. wt., 196 (Rast, acetone). The infrared spectrum showed major bands at 4.5, 6.65, and 7.52 μ.

Sulfur, as the oxidizing agent, dissolved in a boiling methanol solution of **1** to give a quantitative yield of the disodium salt of 3,5-dimercapto-4-isothiazolecarbonitrile (**5**). *Anal.* Calcd. for $C_4N_2S_3Na_2$: C, 22.0; N, 12.8; S, 44.1. Found: C, 22.3; N, 12.7; S, 42.8. $\lambda_{max}^{H_2O}$ 330 $m\mu$ (ϵ 7070), 303 (12,900), 260 (10,500), 240 (sh) (9250), and 218 (14,300). With two moles of methyl iodide, **5** was converted to 3,5-bis-(methylthio)-4-isothiazolecarbonitrile (**6**), m.p. 131–131.5°, in 80% yield. *Anal.* Calcd. for $C_6H_6N_2S_3$: C, 35.6; H, 2.9; S, 47.5. Found: C, 35.8; H, 2.9; S, 47.9. λ_{max}^{alc} 284 $m\mu$ (ϵ 13,300) 230 (11,700), 215 (11,100). The infrared spectrum showed strong bands at 4.50, 6.65, 6.79, and 7.6 μ.



The ultraviolet and infrared absorption spectra of these compounds are consistent with the proposed structures and with the meager published information on spectra of isothiazole derivatives.[2b] The ultraviolet spectra differ considerably from those of the starting di(sodiomercapto)methylenemalononitrile (**1**) [λ_{max}^{alc} 342 $m\mu$ (ϵ 18,600), 272 (5400)] and the corresponding di(methylthio)methylenemalononitrile[8] [λ_{max}^{alk} 330 $m\mu$ (ϵ 13,200), 290 (sh) (6800)]. The infrared spectra show characteristic absorption bands between 6.6–6.85 and 7.5–7.7 μ, that have been attributed to the isothiazole ring.[2b]

Further details of these reaction products and of a variety of their derivatives will be described in future papers.

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RECEIVED MARCH 6, 1963

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(6) H. E. Simmons, R. D. Vest, D. C. Blomstrom, J. R. Roland, and T. L. Cairns, *J. Am. Chem. Soc.*, **84**, 4746 (1962).

(7) W. R. Hatchard, U. S. Patent 3,048,596 (1962).

(8) J. D. Kendall and H. D. Edwards, U. S. Patent 2,493,071 (1950).