A New Reaction Sequence Leading to the Formation of Unsaturated Carbenes[1]

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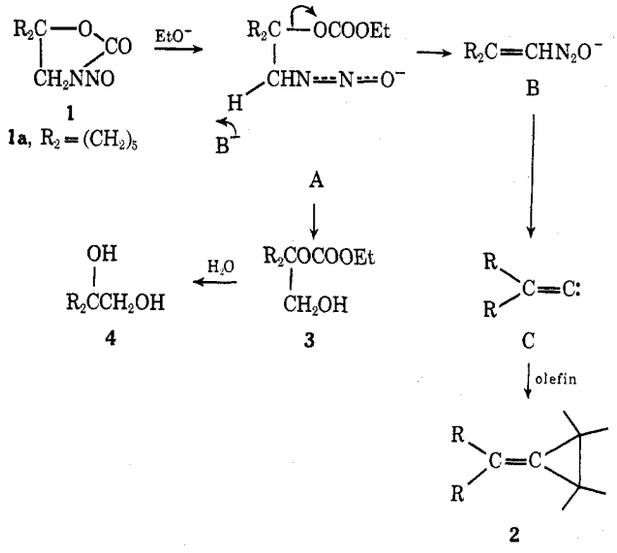
Treatment of a solution at −10 to −5° of 1-(*N*-nitrosoacetylamino)cyclohexanol in pentane containing an olefin and a tetraalkylammonium chloride with 50% sodium hydroxide initiates a series of reactions which results in the formation of cyclohexylidene carbene. The latter is trapped by olefins to yield unsaturated cyclopropane compounds in higher yields than were previously obtained by starting with *N*-nitrosooxazolidones under various conditions.

In earlier work, the formation of an unsaturated carbene was postulated to account for the formation of substituted methylenecyclopropanes (**2**) when *N*-nitrosooxazolidones (**1**) were treated with lithium ethoxide in cyclohexene.[2] A key step in the postulated mechanism is the elimination of the oxygenated carbonate function after abstraction of a proton from the carbon attached to nitrogen, as shown in the intermediate A formed by attack of a base on the carbonyl group of the substituted oxazolidone. Once the elimination has occurred the intermediate B is postulated to undergo further changes to yield the unsaturated carbene C.[2] On reaction of C with an olefin, the methylenecyclopropanes **2** result, as shown in Scheme I.

SCHEME I



In applying the above reaction, the yields of desired unsaturated cyclopropanes **2** are often below 40%. In many cases the formation of diols **4** accounts for about 40–60% of the starting materials **1**. The diols **4** are present in the reaction mixture mostly as esters of carbonic acid (**3**, cyclic or acyclic) and are isolated after alkaline hydrolysis. The diol derivatives result from loss of nitrogen from A before the elimination to B occurs. Another undesirable feature which arises on scaling up some reactions is the difficulty of controlling the exothermic reaction which sets in when base is added at room temperature[3] or above. In general the reactions do not occur in the 0–15° range.[3]

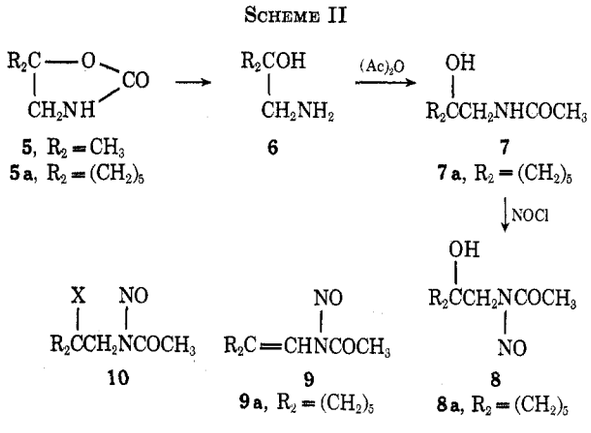
(1) This work was supported by Grant GP-12445X of the National Science Foundation.

(2) (a) M. S. Newman and T. B. Patrick, *J. Amer. Chem. Soc.*, **91**, 6461 (1970); (b) M. S. Newman and A. O. M. Okorodudu, *J. Org. Chem.*, **34**, 1220 (1969).

(3) Unpublished observations by several workers.

Accordingly, we sought to improve the synthetic scheme by modification of the starting materials **1** so that the elimination step as pictured for A → B would proceed more nearly to completion. We proposed to hydrolyze the oxazolidones **5** used to prepare **1** to the corresponding amino alcohols **6** which could be acetylated[4] on nitrogen to **7** and the latter nitrosated to yield *N*-nitrosoacetylamino alcohols **8**. With these new compounds in hand we hoped that conditions could be found which would permit dehydration to unsaturated *N*-nitrosoacetylamides **9** prior to treatment of the latter with base (thus ensuring elimination), or that the tertiary hydroxyl could be converted into a leaving group (X in **10**) so that the base-induced elimination would proceed more readily than in the previous examples.[2] The routes are outlined in Scheme II.

SCHEME II



The oxazolidones **5** are readily converted into the amino alcohols **6** by alkaline hydrolysis. Because of their tendency to react with carbon dioxide in the air, the amino alcohols **6** were immediately treated with 1 equiv of acetic anhydride to yield the desired acetylamino alcohols **7**, which were readily nitrosated to the nitrosoacetylamino alcohols **8**.

Attempts were made to dehydrate 1-(*N*-nitrosoacetylaminomethyl)cyclohexanol (**8a**) to the corresponding unsaturate **9** by treatment with concentrated sulfuric acid at 0° or with thionyl chloride at −5 to 0°. However, in each case only dark oils were obtained which gave no nitrogen when treated with base.

On treating a solution of **8a** and methanesulfonyl chloride in methylene chloride at 0–5° with triethylamine (or collidine)[5] vigorous evolution of nitrogen occurred. Hence we were unable to prepare the mesylate **10a**. If cyclohexene replaced methylene chloride

(4) In principle acyl groups other than acetyl could be used to advantage.

(5) Dr. Philip Hogan, Lewis College, Lockport, Ill., has informed me that he is studying the behavior of nitrosooxazolidones on treatment with amines. Hence we are not continuing this line of research here.

TABLE I

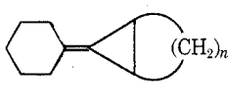
SYNTHESIS OF ALKYLIDENECYCLOPROPANES FROM 8a

Product[a]	Yield,[b] %	Bp, °C (mm)
11	78[c]	61–62
16‡	61[d]	73–74 (0.3)
17‡	60[d]	87–88 (0.2)
18, R = OC_6H_5‡	60[e]	107–108[f] (0.3)
19, R = OC_2H_5‡	83[e]	69–70 (2.5)
20, R = O-t-C_4H_9‡	60[d]	62–63 (0.5)

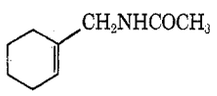
[a] All new compounds marked with ‡ gave ir, nmr, and mass spectra consistent with the assigned structures. [b] The yields represent material of >95% purity (by vpc) isolated by fractionation on a spinning band column. In all reactions there was isolated 9–10% of a mixture of about 8% of cyclohexylformaldehyde, 12% of cyclohexanone, and 80% of cycloheptanone as determined by vpc analysis. [c] Average of three runs. [d] One run. [e] Average of two runs. [f] Solidified on standing, mp 44–45°.

in a similar experiment at room temperature, 25–30% yields of bicyclo[4.1.0]hept-7-ylidenecyclohexane (**11**) were obtained.

Following the failure of these attempts to prepare **9a**, attempts were made to modify 1-(acetylaminomethyl)cyclohexanol (**7a**) prior to nitrosation. Treatment of **7a** with *p*-nitrobenzoyl or 3,5-dinitrobenzoyl chlorides in collidine or pyridine returned unchanged **7a**. On treatment of **7a** with concentrated sulfuric acid at 10° a 90% yield of 1-acetylaminomethylcyclohexene (**12**) was obtained. However, attempts to nitrosate **12** failed, as tarry materials were obtained.[6]



11, $n = 4$
16, $n = 5$
17, $n = 6$



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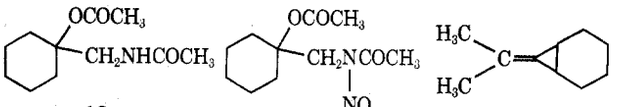
Acetylation of **7a** to the *O,N*-diacetate **13** was accomplished by treatment with excess acetic anhydride at 100–104°. Nitrosation of **13** yielded the *N*-nitrosodiacetate **14**, which, in cyclohexene solution containing Aliquat-336,[7] afforded a 59% yield of **11** on treatment with sodium hydroxide. Thus, the desired goal of improving the yields of carbenic addition products seemed at hand. However, before doing intensive work with the diacetates, **8a** in cyclohexene was treated with sodium hydroxide.[7] To our surprise 75–80% yields (isolated) of **11** were obtained. Thus, having developed a potentially useful synthetic reaction, we have explored this method and report our results[8] herein.

The yields of products obtained by reaction of **8a** with cyclohexene, cycloheptene, cyclooctene, phenyl vinyl ether, ethyl vinyl ether, and *tert*-butyl vinyl ether, **11**, **16**, **17**, **18**, **19**, and **20**, respectively, are listed in Table I. The strained double bond exocyclic to the cyclopropane rings in **16–20** appears at about 5.58 μ, which is characteristic for such olefins.[9] In one experiment involving **8**, a 50% yield of 7-isopropylidenebicyclo[4.1.0]heptane (**15**) was obtained.



13 **14** **15**

We conclude from the above experiments that, if carbenic addition products are desired, it is preferable to use the new procedure involving nitrosoacetylamino alcohols **8** than nitrosooxazolidones **1**. However, when **8a** was treated with sodium ethoxide in ethanol, only a 50% yield of ethoxymethylenecyclohexene was obtained (together with 38% of cycloheptanone) whereas by starting with **1a** an 84% yield results.[2b] Thus, if vinyl ethers are the desired end products, the earlier reactions involving nitrosooxazolidones are preferable. It remains for further work to find out which procedure is better for the varied vinyl compounds preparable by the earlier methods.[10]

Experimental Section[11]

1-(Acetylaminomethyl)cyclohexanol (7a).[8]—A mixture of 15.5 g of **5a** and 50 ml of 50% potassium hydroxide was refluxed for 20 min. The cooled mixture was transferred under nitrogen to a small separatory funnel. The organic layer was diluted with 70 ml of methanol and treated dropwise with 10.2 g of pure acetic anhydride. After 30 min at reflux the volatile materials were removed on a rotary evaporator and the residue was recrystallized from benzene–petroleum ether (bp 60–110°) to yield 15.4 g (90%) of **7a**: mp 117–118°; ir 2.75 (OH), 2.95 (NH), 6.05 μ (C=O); nmr ($CDCl_3$ + 1 drop D_2O) δ 1.51 [s, 10 H, $-(CH_2)_5-$], 2.02 (s, 3 H, CH_3), 3.26 (s, 2 H, $-CH_2-$); *m/e* 171 (calcd 171).

1-Acetylamino-2-methyl-2-propanol (7).—The hydrolysis of 5,5-dimethyl-2-oxazolidone (**5**)[12] to 1-amino-2-methyl-2-propanol and acetylation of the latter to **7**, bp 116–117° (0.5 mm), proceeded in 82% overall yield as described for **7a**: ir 2.75 (OH), 2.94 (NH), 6.04 μ (C=O); nmr (CCl_4 + 1 drop D_2O) δ 1.17 [s, 6 H, $(CH_3)_2$], 2.00 (s, 3 H, CH_3), 3.28 (s, 2 H, $-CH_2-$); *m/e* 131 (calcd 131).

Anal. Calcd for $C_6H_{13}NO_2$: C, 55.0; H, 9.9; N, 10.7. Found: C, 55.1; H, 9.9; N, 10.5.

1-(*N*-Nitrosoacetylaminomethyl)cyclohexanol (8a).—A solution prepared at *room temperature* from 3.8 g of nitrosyl chloride in 25 ml of glacial acetic acid was added dropwise during 12–15 min to a solution of 4.0 g of **7a**, 5 g of freshly fused potassium acetate, and 0.5 g of phosphorus pentoxide in 25 ml of acetic acid *cooled so that the acetic acid is partly crystallized*. After 2 hr the mixture was allowed to come to room temperature and was then poured on ice. A cold methylene chloride extract was made rapidly and passed through a cone of magnesium sulfate. The solvent was removed at room temperature or below on a rotary evaporator to yield **8a** as a yellow oil which had no NH absorption in the ir spectrum and had the carbonyl band at 5.75 μ. Because of its instability a suitable elemental analysis was not obtained. This, and the nitroso compound obtained by a similar method from **7**, should be used rapidly or stored in the freezing compartment of a refrigerator (at best for only a few days).

1-Acetoxy-1-acetylaminomethylcyclohexane (13).—A solution of 2.0 g of **7a** in 10 ml of acetic anhydride and 2 ml of pyridine

(6) A similar failure to nitrosate $C_6H_5CH{=}CHNHCOOC_2H_5$, obtained by pyrolysis of cinnamoyl azide in ethanol, was met (unpublished observation by T. Patrick in our laboratories).

(7) Aliquat 336 is methyltricaprylammonium chloride. Our procedure is based on the principle outlined by C. M. Starks, *J. Amer. Chem. Soc.*, **93**, 195 (1971).

(8) For a preliminary communication, see M. S. Newman and Z. ud Din, *Syn. Commun.*, **1**, 247 (1971).

(9) H. E. Simmons, E. P. Blanchard, and H. D. Hartzler, *J. Org. Chem.*, **31**, 295 (1966).

(10) See, for example, M. S. Newman and C. D. Beard, *J. Org. Chem.*, **35**, 2412 (1970); *J. Amer. Chem. Soc.*, **92**, 4309 (1970), and references cited therein.

(11) All melting points and boiling points are uncorrected. The term "worked up as usual" means that an organic solvent layer of the reaction products was washed successively with dilute acid and/or alkali and saturated salt solution and was then filtered through a cone of anhydrous magnesium sulfate. The solvents were removed and the residue was distilled to yield the products. All compounds marked ‡ had ir, nmr, and mass spectra (parent peak) consistent with the assigned structures. Analyses were by Galbraith Laboratories, Knoxville, Tenn.

(12) M. S. Newman and T. B. Patrick, *J. Amer. Chem. Soc.*, **91**, 6461 (1969). See *ibid.*, **92**, 4312 (1970), for correction of nomenclature of unsaturated carbenes (footnote 2).

was held at 100–104° for 3 hr, cooled, and poured on ice. After the usual work-up ($CHCl_3$ solvent), distillation yielded 2.0 g (83%) of **13** as a colorless oil, bp 127–129° (0.3 mm).

Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.9; H, 8.9; N, 6.6. Found: C, 61.7; H, 8.8; N, 6.5.

Reactions of 8a with Cyclic Olefins.—In a typical reaction a stirred solution held at −10 to −5° of 4.5 g of **8a** in 25 ml each of pentane and cyclohexene containing 1 g of Aliquat-336[7] was treated dropwise with 50% sodium hydroxide. The theoretical amount of nitrogen was collected during 15 min. After the solution was warmed to 40° for 5 min the organic layer was worked up as usual. After solvent was removed the residue was chromatographed over Woelm neutral alumina to remove the Aliquat-336. Distillation afforded 3.1 g (80%) of **11**,[2b] bp 61–62° (0.3 mm). The reactions of **8a** with cycloheptene and cyclooctene were carried out essentially the same way to yield bicyclo[5.1.0]oct-8-ylidenecyclohexane ± (**16**), ir 5.58 μ, *m/e* 190 (calcd 190), and bicyclo[6.1.0]non-9-ylidenecyclohexane ± (**17**), ir, 5.58 μ, *m/e* 204 (calcd 204), respectively. The results are summarized in Table I.

Anal. Calcd for $C_{14}H_{22}$: C, 88.4; H, 11.6. Found: C, 88.3; H, 11.7. Calcd for $C_{15}H_{24}$: C, 88.2; H, 11.8. Found: C, 88.2; H, 11.8.

Reactions of 8a with Vinyl Ethers.[13]—The reactions of **8a** with ethyl vinyl ether and *tert*-butyl vinyl ether were carried out as described above for the reaction of **8a** with cyclic olefins except that the pentane was omitted. However, since on cooling a solution of **8a** in phenyl vinyl ether turbidity resulted, an equal volume of pentane was added.

(13) We acknowledge with thanks generous gifts of ethyl vinyl ether, *tert*-butyl vinyl ether, and phenyl vinyl ether from the General Aniline and Film Corp.

2-Ethoxycyclohexylidenecyclopropane (**19**).—In a typical reaction 50% sodium hydroxide was slowly added dropwise to a stirred solution of 4.6 g of **8a** in 60 ml of ethyl vinyl ether and 1 ml of Aliquat 336[7] at −10 to −5°. The slow addition requires about 15 min in order that the temperature be maintained below −5°. During this time about the theoretical amount of nitrogen was collected. After 10 ml of water was added the organic layer was worked up as usual. The organic product was dissolved in pentane and chromatographed over 40 g of Woelm neutral alumina to remove the Aliquat 336. Distillation through a 12-in. Nester-Faust spinning band column afforded **19** in 80% yield: ir 5.59 μ; nmr (CCl_4) δ 3.65 (m, 1 H, $-CHOC_2H_5$), 3.52 (q, J = 6.8 cps, 2 H, OCH_2CH_3), 2.26 (m, 4 H, allylic CH_2 in cyclohexyl ring), 1.58 (m, 6 H, nonallylic CH_2 in cyclohexyl ring), 1.15 (t, J = 6.8 cps, 3 H, CH_2CH_3), 1.05 (m, 2 H, CH_2 in cyclopropyl ring); *m/e* 166 (calcd 166).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.5; H, 10.9. Found: C, 79.5; H, 10.7.

In a similar way 2-phenoxycyclohexylidenecyclopropane (**18**) and 2-*tert*-butoxycyclohexylidenecyclopropane (**20**) were isolated (see Table I). The nmr spectra of **18** and **20** were almost identical with that of **19** except for the number of methylene hydrogens in the bicyclic rings.

Anal. Calcd for $C_{15}H_{18}O$: C, 84.1; H, 8.5. Found: C, 83.9; H, 8.4. Calcd for $C_{13}H_{22}O$: C, 80.3; H, 11.3. Found: C, 80.1; H, 11.5.

Registry No.—**7** (R = Me), 37150-62-2; **7a**, 37150-63-3; **8a**, 37150-64-4; **11**, 19690-02-9; **13**, 37150-66-6; **16**, 37150-67-7; **17**, 37150-68-8; **18**, 37150-69-9; **19**, 37150-70-2; **20**, 37150-71-3.

Cyclooctatetraene Derivatives from Bromocyclooctatetraene[1]

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N,N-Dimethylaminocyclooctatetraene, cyclopropylcyclooctatetraene, and cyclooctatetraenenitrile have been prepared for the first time. *N,N*-Diethylaminocyclooctatetraene has also been prepared, but was found to rearrange to α-*N,N*-diethylaminostyrene. In addition, *p*-anisylcyclooctatetraene, cyclooctatetraenealdehyde, and vinylcyclooctatetraene have been prepared in greatly improved yields over previously described procedures.

Since the Reppe synthesis of cyclooctatetraene in 1948 from acetylene,[2] numerous substituted cyclooctatetraenes have been prepared,[3] but for the most part the yields of these preparations have been at best fair. Recent work, however, has provided several cyclooctatetraenes[4] in good yield from the reaction of bromocyclooctatetraene[5] with organocopper(I) lithium reagents.[6]

In our continuing study of derivatives of bis(cyclooctatetraene)uranium(IV),[7] the need arose for preparing various substituted cyclooctatetraenes. Because of the lack of good general synthetic procedures, it was necessary to develop alternate routes to such compounds. We report the preparation of several substituted cyclooctatetraenes that were previously difficult to prepare. In addition, the syntheses of three new derivatives of cyclooctatetraene are described.

During the 1950's, Cope reported that substituted COT's could be prepared from the reaction of organolithiums with cyclooctatetraene.[8] Yields from these reactions were generally low (less than 25%) and gave side products which were difficult to separate from the desired material. In an extension of Cope's work, Paquette found that *p*-anisylcyclooctatetraene could be prepared from cyclooctatetraene and *p*-anisyllithium, but only in 3% yield.[9] We have found that the reaction of bromocyclooctatetraene with a fourfold excess of lithium di-*p*-anisylcopper(I) at −50° gives *p*-anisylcyclooctatetraene cleanly in 80% yield.

Cope and Fenton in 1951 reported the isolation of vinylcyclooctatetraene from accumulated residues of cyclooctatetraene preparations.[10] The procedure was tedious and gave only miniscule amounts of the derivative. When excess lithium divinylcopper(I) is allowed to react with bromocyclooctatetraene, the same product is obtained in 88% yield. Similarly, it was found

(1) This research was supported in part by National Science Foundation Grant No. GP-31803X.

(2) W. Reppe, O. Schlichting, and H. Meister, *Justus Liebigs Ann. Chem.*, **560**, 93 (1948).

(3) G. Schroder, "Cyclooctatetraen," Verlag Chemie, Wienheim, Germany, 1965.

(4) J. Gasteiger, G. Gream, R. Huisgen, W. Konz, and U. Schnegg, *Chem. Ber.*, **104**, 2412 (1971).

(5) W. Konz, Ph.D. Thesis, University of Munich, 1970.

(6) G. Whitesides, W. Fischer, Jr., J. San Filippo, Jr., R. Bashe, and H. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969).

(7) A. Streitwieser and U. Müller-Westerhoff, *ibid.*, **90**, 7364 (1968); A. Streitwieser and C. Harmon, *Inorg. Chem.*, in press.

(8) A. Cope and M. Kinter, *J. Amer. Chem. Soc.*, **73**, 3424 (1951); A. Cope and H. van Orden, *ibid.*, **74**, 175 (1952).

(9) L. Paquette, J. Malpass, and T. Barton, *ibid.*, **91**, 4714 (1969).

(10) L. Craig and C. Larrabee, *ibid.*, **73**, 1191 (1951); A. Cope and S. Fenton, *ibid.*, **73**, 1195 (1951).