Elimination Reactions. V. Steric Effects in Hofmann Elimination[1]

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Received April 2, 1974

Abstract: Earlier Hofmann elimination studies have been extended, and the percent syn eliminations in several ring systems have been correlated using cis-d_1 and trans-d_1 models. The measurements of several syn and anti k_H/k_D kinetic isotope effects are reported. Results indicate that Hofmann elimination of *N,N,N*-trimethyl-3,3-dimethylcyclopentylammonium hydroxide goes by 97% syn mechanism to give 3,3-dimethylcyclopentene and by 70 ± 6% syn mechanism to give 4,4-dimethylcyclopentene. There appears to be severe steric interactions in the anti mechanism in the 3,3-dimethylcyclopentyl system. Results indicate that, for Hofmann pyrolysis of trimethylammonium hydroxides, cyclopentene is formed by a 39 ± 7% syn mechanism, cyclohexene is formed by a 2 ± 2% syn mechanism, and cycloheptene is formed by a 30 ± 2% syn mechanism. Steric effects on isotope effects and mechanisms are discussed.

We have shown previously[2,3] by the use of cis 2-deuterium labeled cyclic ammonium hydroxides that Hofmann elimination varies in stereochemistry from almost pure syn mechanism for the four-membered ring to almost pure anti mechanism for the six-membered ring. In order to extend and corroborate this study, we have now examined the Hofmann elimination using trans deuterium labeled models. Some rather interesting steric effects on the stereochemistry of elimination have been observed.

Results

In the previous work we used, among other models, the 3,3-dimethylcyclopentylammonium hydroxide (I) as a system to obtain a syn k_H/k_D to be used in a simple ring compounds (IV, V, and VI). Specifically compound Ib was used. This kind of model kinetic isotope effect is necessary in analyzing the data from Hofmann elimination on cis and trans 2-deuterium analogs of simple ring systems in terms of a percent syn and anti mechanism. In order to test the validity of the syn k_H/k_D from Ib as a general model, we have now examined compounds Ia and Ic. The results show a rather striking steric effect.

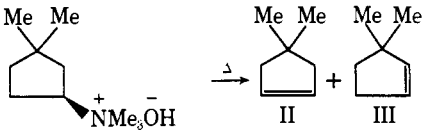
Compounds Ia and Ic (Chart I) were subjected to Hofmann elimination with the results shown in Table I. From the results on I and Ia, one can calculate[4] a syn k_H/k_D = 1.8 for the formation of III. Moreover, the formation of III from I can be calculated to proceed by a 97% syn mechanism.

The syn kinetic isotope effect found for the formation of III is in good agreement with others we have found, for example, II is formed with a syn k_H/k_D = 1.7.[3] In order to see if the 3,3-dimethyl substituents in I are unusual in their effect on the syn kinetic isotope effect, compound VII and the deuterium analog VIIa were studied. The data are given in Table I. The results indicate that compounds I and VII are very analogous in the mechanism leading to symmetrical olefins II and VIII with a syn k_H/k_D = 1.8 for the latter. This isotope effect allows one to calculate that VII gives olefin VIII by a 78% syn mechanism. This can be compared with the value of 76% syn mechanism calculated earlier[3] for I going to II (using Ib as a model).

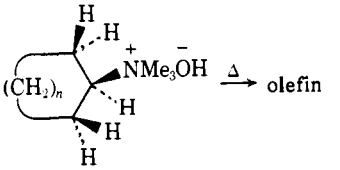
The anti k_H/k_D for the formation of II from I can be obtained from I and Ic. The results of Hofmann elimination on I and Ic are shown in Table I and indicate that II is formed from I with an anti k_H/k_D = 5.6. This isotope effect and the data in Table I allow one to calculate that I gives II by a 64% syn mechanism. The calculated values of 64% syn mechanism from trans labeled Ic and 76% syn mechanism from cis labeled Ib agree with each other to within experimental error which is probably on the order of ±5–10% (arising mainly from the mass spectral analysis of olefin-d_1 content). Thus the average value of 70 ± 6% syn mechanism for I going to II seems reasonable.

If the syn and anti kinetic isotope effects found for the formation of II from I are valid for other compounds, then one should be able to analyze the results of Hofmann elimination on cis and trans 2-deuterium labeled cyclic compounds of the type of IV, V, and VI. The trans 2-deuterium labeled compounds were prepared and studied and the results, along with the earlier results from the cis labeled

Chart I



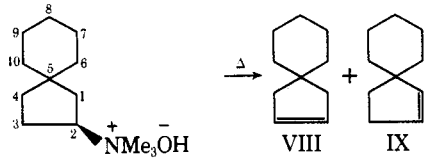
I, hydrogen analog
Ia = *cis*-3-d_1
b = *cis*-5-d_1
c = *trans*-5-d_1



IV (n = 2), hydrogen analog
IVa = *cis*-2-d_1
b = *trans*-2-d_1

V (n = 3), hydrogen analog
Va = *cis*-2-d_1
b = *trans*-2-d_1

VI (n = 4), hydrogen analog
VIa = *cis*-2-d_1
b = *trans*-2-d_1



VII, hydrogen analog
VIIa = *cis*-3-d_1

Table I. Hofmann Elimination Results

Compd	Hofmann products[a,b]
I	52.0% II; 48.0% III
Ia	65.4% II (100% d_1); 34.6% III (95% d_0; 5% d_1)
Ib	42.0% II (65% d_0; 35% d_1); 58.0% III (100% d_1)
Ic	43.0% II (9% d_0; 91% d_1); 57.0% III (100% d_1)
IVa	Cyclopentene (14% d_0; 86% d_1)
IVb	Cyclopentene (15% d_0; 85% d_1)
Va	Cyclohexene (1% d_0; 99% d_1)
Vb	Cyclohexene (24% d_0; 76% d_1)
VIa	Cycloheptene (10% d_0; 90% d_1)
VIb	Cycloheptene (18% d_0; 82% d_1)
VII	51% VIII; 49% IX
VIIa	40.5% VIII (67% d_0; 33% d_1); 59.5% IX (100% d_1)

[a] The data are corrected for the approximate 3% d_0 compound in the starting material. Some of the data in this table are taken from ref 3. [b] The gas chromatographic analyses are the average value of not less than four analyses on a given sample and are accurate to ±1.0%. The mass spectral analyses for deuterium are the average of not less than four analyses on a given sample and are probably accurate to ±1.0% deuterium. Each reaction was run at least in duplicate and the average is shown.

compounds,[3] are shown in Table I. Examination of these results, assuming the same syn and anti kinetic isotope effects found for the conversion of I to II, leads to the immediate conclusion that these two isotope effects cannot both be valid for compounds of the type IV, V, and VI. The results calculated on the basis of the cis and trans deuterium labeled model are incompatible. Examination of models of compound I give some insight as to why compound I fails as a model in some cases. Molecular models indicate that, for the syn mechanism, compound I is free of severe steric interactions and thus probably gives a syn k_H/k_D leading to II that is a valid isotope effect for syn mechanisms in most simple cyclic compounds. It is for the anti mechanism that compound I becomes an invalid model for simple cyclic systems. Molecular models indicate that, for the anti mechanism of I leading to II, one of the *gem*-dimethyl groups on the ring undergoes very severe steric interaction with the bulky trimethylammonium group. This interaction is apparently severe enough to cause an abnormal kinetic isotope effect for the anti mechanism on I.

There appears to be another system, namely the trans-2-d_1 cyclohexyl system (Vb), which potentially can be used to obtain an anti kinetic isotope effect to be used for simple cyclic compounds. Compound Va shows only 1% loss of deuterium on Hofmann elimination. This means that the cyclohexyl ring undergoes almost exclusive anti elimination. Thus an anti k_H/k_D = 3.1 can be calculated directly from the results on the trans 2-deuterium labeled Vb since it shows a 24% loss of deuterium on elimination (see Table I).

If one now uses the anti k_H/k_D of 3.1 from the cyclohexyl system leading to cyclohexene and the syn k_H/k_D of 1.8 for the best estimate of the 3,3-disubstituted system leading to the symmetrical olefin as model isotope effects to analyze the results from the cis-2-d_1 and trans-2-d_1 five-, six-, and seven-membered ring compounds, one finds excellent correlation between the results calculated from either approach (cis or trans deuterium label). The results are shown in Table II and indicate that, in Hofmann elimination, cyclopentene is formed by a 39 ± 7% syn mechanism, cyclohexene is formed by a 2 ± 2% syn mechanism, and cycloheptene is formed by a 30 ± 2% syn mechanism. The difference of ±7% for the cyclopentene case is still within experimental error.

Discussion

The present work reinforces our own earlier work[2,3] and that of Saunders and coworkers.[5,6] It is clear that under conditions normally used for preparative Hofmann eliminations, the syn mechanism is an important mode of elimination in rings other than six membered. Even in six-membered rings, steric[7] and electronic[8] factors may make syn elimination a preferred mode of elimination.

It is also apparent that, in Hofmann elimination in cyclic systems, the mechanism is quite susceptible to alteration by steric factors. One example of this is the percent syn mechanism leading to olefins II and III on pyrolysis of hydroxide I. Olefin III is formed by a 97% syn mechanism and, if one examines molecular models of this system, the reason is apparent. To achieve an anti coplanar transition state leading to olefin III, one must introduce very severe steric interactions between one of the geminal ring methyls and the very bulky trimethylammonium group. This steric interaction apparently precludes any appreciable anti mechanisms leading to III. A similar, but not as dramatic, example of steric effect of this type is apparent when comparing the percent syn mechanism of 70% leading to II compared with the percent syn mechanism of 39% leading to cyclopentene.

Another rather dramatic steric effect is the change in proportion of each olefin II and III as the base changes. Comparing the work of Brown and Saunders[5] and our own work, it is apparent that a more bulky base favors the symmetrical olefin II. Pyrolysis of the hydroxide yields nearly equal amounts of II and III, but Brown and Saunders have found that, with *tert*-butoxide as the base and a mixture of *tert*-butyl alcohol and dimethyl sulfoxide as the solvent, the ratio of II to III is 6.4. This is almost certainly not a base strength effect, because the percent syn mechanism leading to II in both cases is about 70%, and the syn k_H/k_D isotope effects for the formation of II are almost identical, 1.9 for *tert*-butoxide vs. 1.7 for hydroxide. Apparently the bulkier *tert*-butoxide base suffers steric interaction with one of the geminal ring methyls when attack is at the 2-position of I. This kind of steric effect has been found in many other systems[9] but the present study allows other factors such as base strength effects and change of mechanism to be ruled out.

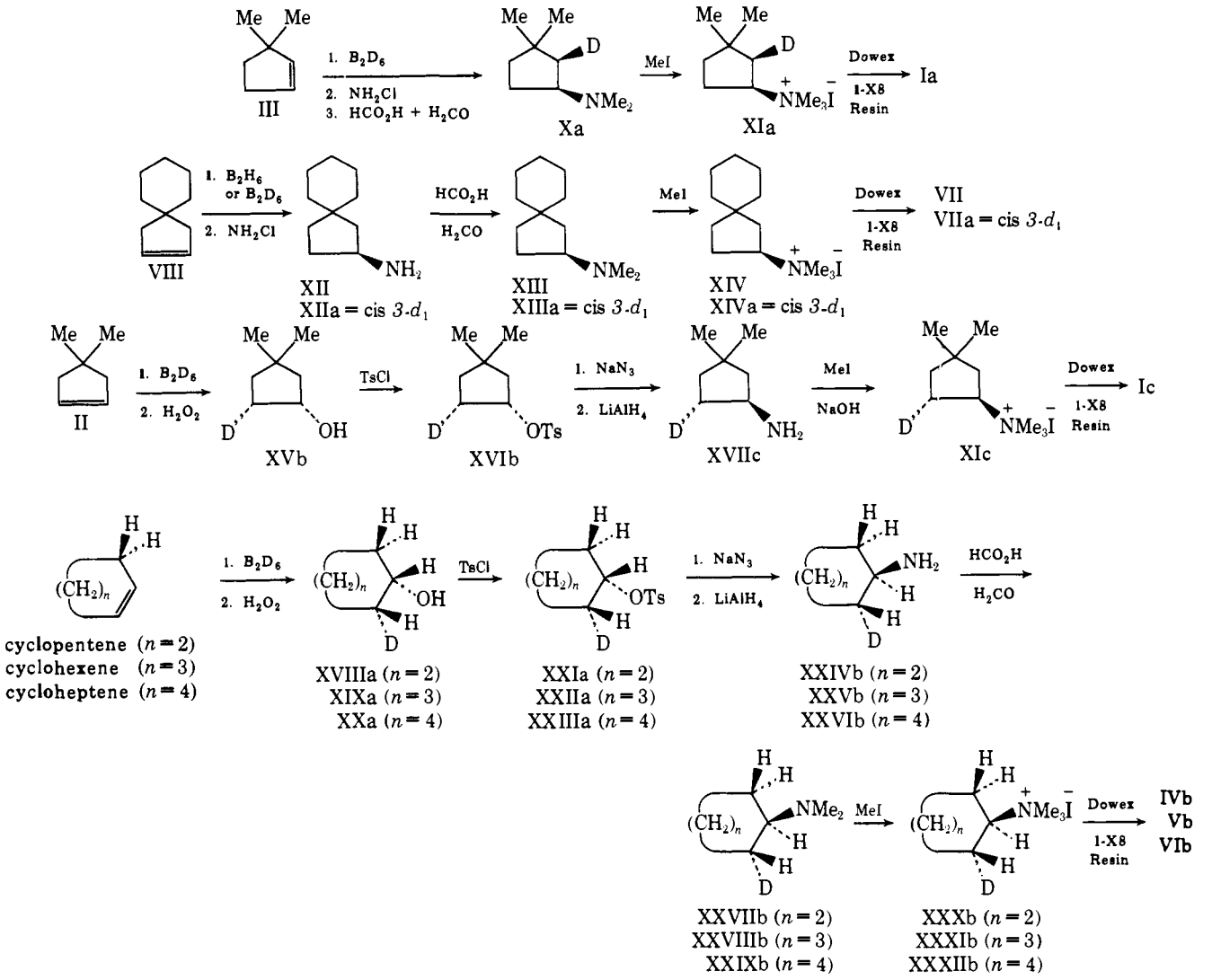
Evidence that steric effects may alter the degree of bond breakage in the transition state for Hofmann elimination

Table II. Isotope Effects and Mechanisms on Hydrogen Analogs

Compd	Ring size	Syn k_H/k_D	% syn[a]	Average % syn	% syn[b]	Anti k_H/k_D
I → II	5	1.7 ± 0.15	76	70 ± 6	64	5.6 ± 1.4
I → III	5	1.8 ± 0.10	97			
IV, n = 2	5	1.8[c]	46	39 ± 7	32	3.1[f]
V, n = 3	6	1.8[c]	4	2 ± 2	0[d]	3.1 ± 0.15[e]
VI, n = 4	7	1.8[c]	31	30 ± 2	28	3.1[f]
VII → VIII	5	1.8 ± 0.15	78			

[a] Calculated on the basis of the syn k_H/k_D shown from the cis deuterium labeled model. [b] Calculated on the basis of the anti k_H/k_D shown from the trans deuterium labeled model. [c] This syn isotope effect is an average value from a number of standards. [d] An assumed value for the purpose of calculating the anti k_H/k_D for the cyclohexane ring. [e] A value for the cyclohexane ring if the mechanism is nearly pure anti. [f] Value taken from the cyclohexyl model.

Chart II



comes from comparing the anti k_H/k_D of 3.1 for the cyclohexyl system and the anti k_H/k_D of 5.6 for the formation of 4,4-dimethylcyclopentene (II). Although a final interpretation of this difference must be put off until rate studies on the two systems can be compared and until the transition state for the cyclohexyl system is better understood, two things seem clear. The difference in isotope effects is large enough to be real, and models of both systems indicate that the difference is largely of steric origin. The 3,3-dimethylcyclopentyl system I suffers severe steric interactions in the anti mechanism leading to olefin II. The isotope effects seem to indicate that there is less carbon-hydrogen bond breakage in the anti transition state leading to II than in the anti transition state leading to cyclohexene.[5] This would be in line with the suggestion by Saunders and Ashe[6] that steric strain might aid in carbon-nitrogen bond breakage with concurrent decrease in extent of carbon-hydrogen bond breakage in the transition state.

In the pyrolysis of hydroxide I, olefin III is calculated to form by an almost exclusive syn mechanism, while II is calculated to form by only a 70% syn mechanism, and yet each olefin is formed in almost equal amounts. This indicates that syn elimination to the 2-position of I is slightly faster than syn elimination to the 5-position. The reason for this is not clear.

The anti kinetic isotope effect of $k_H/k_D = 4.8$, calculated by Saunders and coworkers[5,6] for Hofmann elimination to give cyclopentene in *tert*-butyl alcohol with *tert*-butoxide, is larger than the value of 3.1 which we use for pyrolysis of IVb. Whether the difference is caused by a difference in conditions or just reflects the magnitude of error in the roundabout way in which both isotope effects were obtained is not clear.

Syntheses

The syntheses of all the compounds used in this study are shown in Chart II. The preparation of amines and cis-d_1 amines directly from olefins were carried out by Brown's method and were done as described earlier.[3] In order to prepare the trans-d_1 labeled amines, the cis-d_1 labeled alcohols were prepared,[10] converted to the corresponding *p*-toluenesulfonates, and these were then subjected to substitution with inversion using sodium azide.[11] The trans-d_1 labeled azides were reduced with lithium aluminum hydride to the corresponding trans-d_1 labeled primary amines, and these were converted on to the quaternary ammonium compounds by standard means.

Experimental Section

All mass spectral analyses were performed on a Hitachi Perkin-Elmer RMU-6E mass spectrometer at low chamber potentials (13 eV or less) to minimize M − 1 fragmentation and facilitate deuterium analyses.[3] Gas chromatographic analyses and separations were done on a Hewlett-Packard Model 5750 gas chromatograph.

The sodium borohydride-d_4 was purchased from Merck Sharpe and Dohme Limited of Canada and was shown to contain greater than 96% deuterium by analysis of acetamide derivatives of primary amines derived from it. A correction in the final olefin analysis was made for the 3–4% d_0 compound in the starting material whenever it was a significant factor. Starting materials were purchased commercially, and olefins that were used were purified by distillation. Melting and boiling points are uncorrected. Deuterium-containing compounds were compared with the hydrogen analog in all cases, and no distinction in physical constants between the two is made.

Spiro[4.5]dec-1-ene (IX). This olefin was prepared in an 80% yield by the procedure of Krapcho and Donn,[12] except that butyllithium was used in place of methoxide.[13] The product had: bp 64° (18 mm) [lit.[12] bp 177° (740 mm)]; n^{20}D 1.4780.

***N,N*-Dimethyl-3,3-dimethylcyclopentylamine-*cis*-2-d_1 (Xa).** Olefin III[3] was converted to a mixture of isomeric primary amines using diborane-d_6 and chloramine as described in earlier work.[3] This mixture was converted by the method of Icke[14] to a mixture of isomeric *N,N*-dimethylamines, of which compound Xa (retention time 7.6 min) made up 66%, and the isomeric *N,N*-dimethyl-2,2-dimethylcyclopentenylamine-*cis*-5-d_1 (retention time 9.0 min) made up 34%. The isomers were separated by gas chromatography on a 20-ft column of 30% SE-30 silicone rubber on Chromosorb W at 70° and a flow rate of 100 ml/min of helium. Compound Xa was compared with an authentic sample of the hydrogen analog which had bp 160–161°.

Anal. Calcd for $C_9H_{19}N$: C, 76.59; H, 13.48; N, 9.93. Found: C, 76.64; H, 13.53; N, 9.81.

2-Spiro[4.5]decylamine (XII). The procedure for diborane and chloramine reaction used earlier[3] was used. Olefin VIII [bp 104–109° (95 mm)], prepared by Wolff-Kishner reduction[15] of 6-ketospiro[4.5]dec-2-ene,[16] gave a 40% yield of product (XII): bp 110° (35 mm); n^{25}D 1.4821.

Anal. Calcd for $C_{10}H_{19}N$: C, 78.2; H, 12.4; N, 9.2. Found: C, 78.1; H, 12.4; N, 9.0.

2-Spiro[4.5]decylamine-*cis*-3-d_1 (XIIa). A procedure identical with the preceding one using diborane-d_6 gave XIIa in a 46% yield [bp 110–112° (35 mm); n^{25}D 1.4868].

***N,N,N*-Trimethyl-2,3-dimethylcyclopentylammonium-*trans*-5-d_1 Iodide (XIc).** Using the procedure of Willstätter,[17] amine XVIIc was converted to XIc in 99% yield, mp 289–290° (lit.[3] mp 289–291°).

General Procedure for Preparation of Cis-d_1 Labeled Alcohols. The following general procedure was followed.[10] Into a 500-ml three-necked flask, flame dried, was placed 0.10 mol of olefin, 0.026 mol of sodium borohydride-d_4 and 60 ml of dry tetrahydrofuran. The flask was cooled to 0° and stirred vigorously with a nitrogen atmosphere, while 4.88 ml of boron trifluoride etherate in 30 ml of dry tetrahydrofuran was added over a 2-hr period. The resulting mixture was stirred at 0° for 6 hr. Then 1.5 g of ice was added, followed by 20 ml of 30% sodium hydroxide. With efficient cooling and stirring, a total of 20 ml of 30% hydrogen peroxide was added over 0.5 hr. The mixture was stirred overnight at 25°. The mixture was diluted with 300 ml of water and extracted several times with ether. The ether layers were combined, dried, and evaporated, and the product was distilled.

3,3-Dimethylcyclopentanol-*cis*-5-d_1 (XVb). Olefin II[3] was converted in 64% yield to XVb: bp 158–159°; n^{25}D 1.4520. Compound XVb was compared with a sample of the hydrogen analog XV: bp 159–161°; n^{20}D 1.4528.

Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36; O, 14.01. Found: C, 73.80; H, 12.50; O, 13.95.

Cyclopentanol-*cis*-2-d_1 (XVIIIa). Cyclopentene was converted in 65% yield to XVIIIa: bp 139–141°; n^{25}D 1.4499 (lit.[18] bp 138°; n^{20}D 1.4529).

Cyclohexanol-*cis*-2-d_1 (XIXa). Cyclohexene was converted in 70% yield to XIXa: bp 159–161°; n^{25}D 1.4628 (lit.[18] bp 160.5–161°; n^{20}D 1.4647).

Cycloheptanol-*cis*-2-d_1 (XXa). Cycloheptene was converted in 51% yield to XXa: bp 106–107° (40 mm); n^{25}D 1.4741 [lit.[18] bp 86° (20 mm); n^{20}D 1.4770].

General Procedure for Preparation of Cis-d_1 Labeled *p*-Toluenesulfonates. The following general procedure was followed.[19] To a mixture of 0.020 mol of alcohol and 2.7 ml of pyridine at 0° was added 0.022 mol of *p*-toluenesulfonyl chloride. The mixture was stirred and allowed to come slowly to 25° and was stirred at 25° overnight under a nitrogen atmosphere. The mixture was cooled as 9 ml of ice-water was added. The aqueous mixture was extracted with 3 × 25 ml portions of ether, and the ether layers were combined, washed successively with cold dilute sulfuric acid, sodium bicarbonate solution, and water. The ether solution was dried over sodium sulfate, and the solvent was removed under vacuum. The product was recrystallized from ether–pentane if it was a solid or was dried to constant weight under vacuum if it was a liquid.

3,3-Dimethylcyclopentyl-*cis*-5-d_1 *p*-Toluenesulfonate (XVIb). Alcohol XVb was converted in 79% yield to XVIb which proved to be an oil. Comparison was made to the hydrogen analog (n^{20}D 1.5080) on which an analysis was performed.

Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51; O, 17.89; S, 11.95. Found: C, 62.98; H, 6.98; O, 18.20; S, 12.13.

Cyclopentyl-*cis*-2-d_1 *p*-Toluenesulfonate (XXIa). Alcohol XVIIIa was converted in 81% yield to XXIa, mp 27–28° (lit.[18] mp 28.5–29°).

Cyclohexyl-*cis*-2-d_1 *p*-Toluenesulfonate (XXIIa). Alcohol XIXa was converted in 90% yield to XXIIa, mp 41–42° (lit.[18] mp 44.5–45°).

Cycloheptyl-*cis*-2-d_1 *p*-Toluenesulfonate (XXIIIa). Alcohol XXa was converted in 71% yield to XXIIIa, mp 20° (lit.[18] mp 19–19.6°).

General Procedure for Preparation of Trans-d_1 Labeled Amines. The following general procedure for inversion with sodium azide followed by lithium aluminum hydride reduction was followed.[11] To a stirred solution of 0.120 mol of sodium azide in 50 ml of dimethyl sulfoxide and 10 ml of water at 70° was added 0.022 mol of cis-d_1 labeled *p*-toluenesulfonate in 30 ml of dimethyl sulfoxide. The resulting solution was maintained at 70° for 18 hr and was then cooled and diluted with 300 ml of cold water. The mixture was extracted with 4 × 100 ml portions of ether, and the ether solutions were combined, washed with saturated sodium chloride solution, and dried over magnesium sulfate to yield an ether solution of crude trans-d_1 labeled azide. The ether solution of azide was added slowly with stirring to 0.216 mol of lithium aluminum hydride in 100 ml of ether. The resulting mixture was stirred at 25° for 24 hr and was then decomposed by successive addition of 9 ml of water, 6.5 ml of 20% sodium hydroxide solution, and 31 ml of water. The ether layer was separated from the solids which were rinsed with ether. The ether solutions were combined, dried over magnesium sulfate, and concentrated. The trans-d_1 labeled amines were distilled.

3,3-Dimethylcyclopentylamine-*trans*-5-d_1 (XVIIc). Tosylate XVIb was converted in 46% to amine XVIIc, bp 138–140°. Because of the small amount of material, this compound was converted directly on to the quaternary methiodide XIc without further characterization.

Cyclopentylamine-*trans*-2-d_1 (XXIVb). Tosylate XXIa was converted in 46% yield to amine XXIVb: bp 106°; n^{25}D 1.4469 (lit.[20,21] bp 108°; n^{20}D 1.4515).

Cyclohexylamine-*trans*-2-d_1 (XXVb). Tosylate XXIIa was converted in 29% yield to amine XXVb: bp 133°; n^{25}D 1.4555 (lit.[20,22] bp 133.7°; n^{25}D 1.4539).

Cycloheptylamine-*trans*-2-d_1 (XXVIb). Tosylate XXIIIa was converted in 33% yield to amine XXVIb: bp 101–106° (80 mm); n^{25}D 1.4565 [lit.[23] bp 60° (18 mm)].

General Preparation of *N,N*-Dimethylamines. The general procedure used for dimethylation of the primary amines was that of Icke and Wisegarver.[14]

***N,N*-Dimethyl-2-spiro[4.5]decylamine (XIII).** Amine XII was converted in 60% yield to XIII: bp 135° (35 mm); n^{25}D 1.4783.

Anal. Calcd for $C_{12}H_{23}N$: C, 79.5; H, 12.7; N, 7.7. Found: C, 79.3; H, 12.5; N, 7.6.

***N,N*-Dimethyl-2-spiro[4.5]decylamine-*cis*-3-d_1 (XIIIa).** Amine XIIa was converted in 65% yield to XIIIa: bp 135–137° (35 mm); n^{25}D 1.4766. This compound was compared with the hydrogen analog XIII.

***N,N*-Dimethylcyclopentylamine-*trans*-2-d_1 (XXVIIb).** Amine XXIVb was converted in 61% yield to XXVIIb: 131–134°; n^{25}D 1.4416 [lit.[20] bp 65° (84 mm); n^{25}D 1.4379].

***N,N*-Dimethylcyclohexylamine-*trans*-2-d_1 (XXVIIIb).** Amine XXVb was converted in 47% yield to XXVIIIb: bp 91–93° (60 mm); n^{25}D 1.4500 [lit.[20] bp 75° (47 mm); n^{25}D 1.4517].

***N,N*-Dimethylcycloheptylamine-*trans*-2-d_1 (XXIXb).** Amine

XXVIb was converted in 53% yield to XXIXb: bp 82–84° (20 mm); n^{25}D 1.4621 [lit.[23] bp 78° (20 mm)].

General Preparation of Quaternary Ammonium Iodides. The general procedure used was to dissolve the amine in ether and add an excess of methyl iodide. The resulting mixture was stirred overnight at 25°, and the solid product which had precipitated was collected by filtration and was recrystallized from ethanol.

***N,N,N*-Trimethyl-2,3-dimethylcyclopentylammonium-*cis*-2-d_1 Iodide (XIa).** Amine Xa was converted in 90% yield to XIa, mp 288–290° (lit.[3] mp 289–291°).

***N,N,N*-Trimethyl-2-spiro[4.5]decylammonium Iodide (XIV).** Amine XIII was converted in 80% yield to XIV, mp 222°.

Anal. Calcd for $C_{13}H_{26}NI$: C, 48.3; H, 8.1; N, 4.3; I, 39.3. Found: C, 48.0; H, 8.3; N, 4.4; I, 39.9.

***N,N,N*-Trimethyl-2-spiro[4.5]decylammonium-*cis*-3-d_1 Iodide (XIVa).** Amine XIIIa was converted in 85% yield to XIVa, mp 213°. This compound was compared with the hydrogen analog XIV.

***N,N,N*-Trimethylcyclopentylammonium-*trans*-2-d_1 Iodide (XXXb).** Amine XXVIIb was converted in 94% yield to XXXb, mp 249–253° dec (lit.[24] mp 260°).

***N,N,N*-Trimethylcyclohexylammonium-*trans*-2-d_1 Iodide (XXXIb).** Amine XXVIIIb was converted in 94% yield to XXXIb, mp 276–277° dec (lit.[25] mp 278–278.2°).

***N,N,N*-Trimethylcycloheptylammonium-*trans*-2-d_1 Iodide (XXXIIb).** Amine XXIXb was converted in 91% yield to XXXIIb, mp 252° dec (lit.[17] mp 259°).

Quaternary Ammonium Hydroxides and Hofmann Pyrolysis. The conversion of the quaternary iodides to the corresponding hydroxides was accomplished by passage of an aqueous solution of the iodide over a column of Dowex 1-X8 basic resin and elution with water. The water was evaporated under vacuum from the hydroxide, keeping the temperature below 40°. The hydroxide was then pyrolyzed at 130–150° (50 mm). The olefin was collected, washed with a small amount of cold dilute sulfuric acid, followed by several washings with water, and was then dried. Each olefin was then analyzed and collected by gas chromatography on a 2-ft silicone rubber column or a 6-ft column of 40% ethylene glycol saturated with silver nitrate on Chromosorb W (60–80 mesh). Each olefin was analyzed for deuterium in a mass spectrometer at low voltage.

References and Notes

(1) Paper IV in this series: J. L. Coke and M. C. Mourning, *J. Am. Chem. Soc.*, **90**, 5561 (1968). These results were presented in part at the 14th Conference on Reaction Mechanisms, Burlington, Vt., June 1972.
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Stereochemical Control in Wittig Olefin Synthesis. Preparation of the Pink Bollworm Sex Pheromone Mixture, Gossyplure[1]

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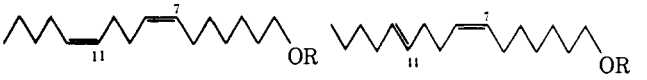
Received January 20, 1975

Abstract: Stereochemical control of the Wittig reaction of the primary aldehyde **6** with the nonstabilized alkylide, triphenylphosphonium *n*-pentylide **7**, is achieved by controlled partial equilibration of the intermediate adducts. These conditions are applied to the direct synthesis of the mixture of insect sex pheromones, "gossyplure", which is a 1:1 mixture of (7*Z*,11*Z*)- and (7*Z*,11*E*)-7,11-hexadecadien-1-yl acetate (**1a** and **2a**, respectively). The difunctionalized intermediate ethyl (*Z*)-8-oxo-4-octenoate (**6**) is conveniently prepared from (*Z*,*Z*)-1,5-cyclooctadiene (**3**). Simple Wittig reaction conditions are also outlined which give predominantly the cis olefin product **8a**.

The sex pheromone of the female pink bollworm moth, *Pectinophora gossypiella* (Saunders), has been recently identified as a ca. 1:1 mixture of (7*Z*,11*Z*)- and (7*Z*,11*E*)-7,11-hexadecadien-1-yl acetate (gossyplure).[2-5] The 1:1 mixture of the isomers **1a** and **2a** was by far the most attractive to males in the field.[2,3] Addition of as little as 10% of either the 7*E*,11*Z* or the 7*E*,11*E* isomer greatly diminished the attraction of the 1:1 mixture of 7*Z*,11*Z* (**1a**) and 7*Z*,11*E* (**2a**) isomers.[3]



1a, R = Ac
b, R = CH(Me)OEt
c, R = H

2a, R = Ac
b, R = CH(Me)OEt
c, R = H

Although **1a** and **2a** have now been prepared separately by conventional routes via acetylenic intermediates,[3,5-7] we