Table I. Kinetic Data for $Ta_6Br_{12}^{2+}$

t, μsec	$A \times 10^5$ [a]	kC_A^0t [b]	Log k_t, M^{-1} sec^{-1}
(A) $C_A^0 = 1.0 \times 10^{-4}$ M; $\sqrt{D}/\delta$ [c] = 77.2 sec$^{-1/2}$; $N_{eff} = 9.7$			
168	7.40	0.93	7.71
378	4.82	1.95	7.72
671	2.86	5.10	7.88
1048	1.73	9.5	7.94
1306	1.35	10.0	7.88
			Av = 7.83 ± 0.10
(B) $C_A^0 = 2.7 \times 10^{-4}$ M; $\sqrt{D}/\delta = 98$ sec$^{-1/2}$; $N_{eff} = 7.0$			
297	5.46	6.6	7.91
669	3.08	12.5	7.84
1189	1.62	24.6	7.87
1858	1.08	27.0	7.76
			Av = 7.84 ± 0.06

[a] $Ta_6Br_{12}^{2+}$ monitored at 620 mμ, where $\epsilon \approx 6000$ M^{-1} cm^{-1}, $K_{eq} = 1 \times 10^5$. [b] Kinetic data evaluated from potential step beyond $E_2^{0\prime}$, 0.04 M $HClO_4$ used as supporting electrolyte. [c] $\sqrt{D}/\delta$ evaluated from potential step beyond $E_1^{0\prime}$.

any light-absorbing species within the confines of the irs optical cell during an electrochemical perturbation. High sensitivity, due to $N_{eff} \gg 1$, and signal averaging give absorbance sensitivity better than one part in 10^5 with time resolution in the microsecond range. Detailed mechanism and kinetic studies of fast homogeneous electron exchange reactions following the heterogeneous electron-transfer step at ote are now in progress.

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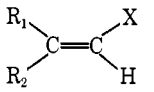
Modification of the Wittig Reaction to Permit the Stereospecific Synthesis of Certain Trisubstituted Olefins. Stereospecific Synthesis of α-Santalol

Sir:

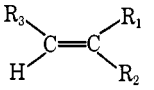
It has been shown[1] that the reaction between an aldehyde and an alkylidenetriphenylphosphorane to form a 1,2-disubstituted ethylene can be directed efficiently to the *trans* isomer by interposing a process which modifies the stereochemistry of the intermediate phosphorus betaine. The process which was described involves sequential treatment of the primary betaine (resulting from addition of the Wittig reagent to the aldehyde) with phenyllithium (at −70°) and potassium *t*-butoxide–*t*-butyl alcohol. Experiments performed in these laboratories indicated that, at least in the cases studied, the potassium *t*-butoxide–*t*-butyl alcohol reagent is *not required* for the Wittig–Schlosser synthesis.[2] This finding implied that the intermediate β-oxido phosphonium ylide (the obvious product of the reaction of a phosphorus betaine with phenyllithium) is capable of stereospecific protonation to form the *threo* betaine which is the precursor of the *trans*-1,2-disubstituted ethylene finally formed. It seemed logical to expect that only one of the isomeric betaines might be formed specifically by the reaction of electrophiles other than proton donors with β-oxido phosphonium ylides and that a useful stereospecific route to trisubstituted olefins might thereby become available. This communication describes the realization of such a synthetic process.[3] Publication of the results which have been obtained thus far is prompted by the appearance of a note describing a study of reactions of β-oxide phosphonium ylides[4] which partially overlaps the present work.

Methods which have been described previously permit the stereospecific synthesis of trisubstituted olefins of types **1a**,[3,5] **1b**,[3,5] and also **2a**,[3a,6] but not of type **2b**. We shall first describe a new approach to the synthesis of



1a, $R_1 = CH_3$; R_2 = alkyl
1b, R_1 = alkyl; $R_2 = CH_3$

(X = CH_2OH or $COOCH_3$)



2a, $R_1 = CH_3$; R_3 = alkyl; R_2 = CH_2OH or $COOCH_3$
2b, $R_1 = CH_2OH$ or $COOCH_3$; $R_2 = CH_3$; R_3 = alkyl

olefins of type **2b**, *via* β-oxido phosphonium ylides as key intermediates, which closes this methodological gap. Reaction of a solution of ethylidenetriphenylphosphorane in tetrahydrofuran at −78° with heptanal for 5 min produced the betaine **3** which was treated with 1 equiv of *n*-butyllithium (in hexane) at −78° to form the deep red β-oxido phosphonium ylide **4**. The solution of the relatively stable ylide **4** was allowed to warm to 0° and then treated with 2 equiv of dry paraformaldehyde to generate the colorless β,β′-dioxido phosphonium derivative **5**. After a reaction time of 0.5 hr at 0° and 12 hr at 25°, the mixture was worked up in the usual way to give 2-methyl-*cis*-2-nonen-1-ol (**6**) in 73% yield. The stereochemistry of 6 is clearly indicated by analysis[7–9] of the nmr spectrum (in CCl_4) which

(1) M. Schlosser and K. F. Christmann, *Angew. Chem. Intern. Ed. Engl.*, 5, 126 (1966); *Ann. Chem.*, 708, 1 (1967).

(2) We suggest this name for the modified[1] Wittig reactions which afford *trans*-1,2-disubstituted olefins.

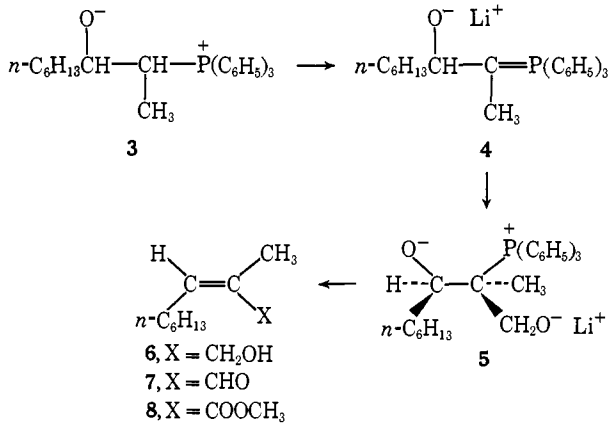
(3) For other recent contributions from this laboratory on new stereospecific routes to trisubstituted olefins, see (a) E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 4245 (1967); (b) E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson, *ibid.*, **90**, 5618 (1968); (c) E. J. Corey and J. A. Katzenellenbogen, *ibid.*, **91**, 1851 (1969).

(4) M. Schlosser and K. F. Christmann, *Synthesis*, **1**, 38 (1969), describe the reaction of certain β-oxido ylides with methyl iodide, perchloryl fluoride, iodobenzene dichloride, and bromine.

(5) E. J. Dorey, N. W. Gilman, and B. C. Ganem, *J. Amer. Chem. Soc.*, **90**, 5616 (1968).

(6) E. J. Corey, K. Achiwa, and J. A. Katzenellenbogen, *ibid.*, **91**, 4318 (1969).

(7) K. C. Chan, R. A. Jewell, W. H. Nutting, and H. Rapoport, *J. Org. Chem.*, **33**, 3382 (1968).

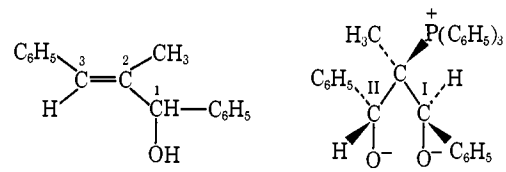


reveals peaks at 5.19 (triplet, 1 H), 3.99 (singlet, 2 H), and 1.71 (singlet, 3 H) due to a vinyl proton, =C—CH_2—O, and olefinic methyl protons, respectively.[10] These peaks occur precisely as expected for **6** and contrast with those observed for the geometrically isomeric olefin of type **2a** (for which the corresponding values would be 5.31, 3.83, and 1.59 ppm). The structure of **6** was further confirmed by oxidation to the corresponding aldehyde (**7**) (MnO_2–hexane) and methyl ester[5] (**8**), all of which showed the expected nmr, infrared, and mass spectral properties. Gas chromatographic analysis[9] of the product **6** (using a 6-ft, 5% LAC column at 100°) showed the absence of detectable (>1%) amounts of the geometrically isomeric olefin.

The remarkably stereospecific and simple synthesis of **6** provided the crucial information leading to a stereospecific synthesis of the important essential oil α-santalol (**10**). Starting with the readily available aldehyde **9**[8,11] and using the same procedure as described above for the conversion of heptanal to **6**, α-santalol was obtained in a single step stereospecifically and efficiently. The spectra (and the odors) of synthetic and natural α-santalols were identical. Previously α-santalol has

been synthesized in *ca.* 2% yield from the aldehyde **9** by a process involving a conventional Wittig reaction which was stereoselective for the undesired isomer of **10**,[8] and by a multistep, conventional nonstereoselective chain extension sequence (<2% yield).[12]

Sequential treatment of ethylidenetriphenylphosphorane with benzaldehyde (1 equiv), *n*-butyllithium (1 equiv), and (again) benzaldehyde (1 equiv) following the procedure used for the synthesis of the primary alcohol **6** afforded as major product a secondary alcohol which was shown to be **11**, since it underwent oxidation with active manganese dioxide in hexane to form α-methyl-*trans*-chalcone[13] and since it was formed by the reduction of α-methyl-*trans*-chalcone by alcoholic sodium borohydride. Small amounts (*ca.* 2%) of the geometric isomer of **11** were also produced along with **11** in the synthesis from benzaldehyde. The stereochemical course of the synthesis of **11** from benzaldehyde was elucidated as follows. Reaction of ethylidenetriphenylphosphorane sequentially with 1-deuteriobenzaldehyde, *n*-butyllithium, and unlabeled benzaldehyde proceeded to form 1-deuterated **11** (74%) *exclusively*.[14] In contrast, the treatment of ethylidenetriphenylphosphorane sequentially with unlabeled benzaldehyde, *n*-butyllithium, and 1-deuteriobenzaldehyde afforded alcohol **11** (74%) with deuterium *exclusively* at C-3.[15] This striking observation demonstrates unequivocally that the intermediate β,β′-dioxido phosphonium ion is the *racemate* **12** rather than a stereoisomeric *meso* structure (of which two are possible). Further, the chiral centers labeled I and II in expression **12** originate, respectively, from the first and second aldehyde molecule used in the synthetic sequence. In addition, Wittig elimination from **12** involves highly selective loss of that oxygen which originated in the second aldehyde molecule used in the sequence. The stereochemistry of the formation of the β,β′-dioxido phosphonium ion **5** from **3** using



formaldehyde is strictly analogous to that demonstrated with benzaldehyde at the two corresponding asymmetric centers of **12**, carbon I and the carbon bearing the phosphonium group. Thus a critical stereochemical regularity can be discerned in the formation of the β,β′-dioxido phosphonium ion intermediates. However, it is clear that other factors control the direction of the final Wittig elimination, including relative thermodynamic stability of the olefins.

A considerable number of experimental findings are in accord with predictions based on the above results. Reaction of ethylidenetriphenylphosphorane first with acetaldehyde and then (after ylide formation) with heptanal affords **13** specifically (67%), whereas the inverse order of aldehyde addition (heptanal first, acetaldehyde second) yields **14** specifically (67%).[16]

In a similar experiment, sequential treatment of ethylidenetriphenylphosphorane with heptanal (1 equiv), *n*-butyllithium (1 equiv), and heptanal (1 equiv)[16] produced a mixture of olefins **15** and **16** in a ratio of *ca.* 9 to 1. The assignment of olefinic geometry to these products followed from correlation of the minor isomer

(8) R. G. Lewis, D. H. Gustafson, and W. F. Erman, *Tetrahedron Lett.*, 401 (1967).

(9) J. A. Katzenellenbogen, Ph.D. Thesis, Harvard University, 1969, pp 128–136, also gives extensive data on the characteristic differences in chemical shift of the C=C—CH_3, C=C—CH_2OH, and C=C—H protons in the isomeric olefins of type **2a** and **2b**, and gas chromatographic data.

(10) Chemical shifts are expressed as parts per million downfield from tetramethylsilane as internal standard.

(11) E. J. Corey, S. W. Chow, and R. A. Sherrer, *J. Amer. Chem. Soc.*, **79**, 5773 (1957).

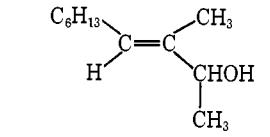
(12) J. Colonge, D. Descotes, Y. Bahurel, and A. Menet, *Bull. Soc. Chim. Fr.*, 374 (1966).

(13) (a) W. B. Black and R. E. Lutz, *J. Amer. Chem. Soc.*, 77, 5134 (1955); (b) N. H. Cromwell and R. P. Rebman, *J. Org. Chem.*, 32, 3830 (1967).

(14) The position of deuterium was determined in two ways: (1) nmr analysis and (2) oxidation by manganese dioxide to give undeuterated α-methyl-*trans*-chalcone.

(15) The position of deuterium was indicated by nmr analysis and also by oxidation with manganese dioxide to form β-deuterio-α-methyl-*trans*-chalcone.

(16) The reaction of the β-oxido phosphonium ylide with the second molecule of aldehyde was carried out at −78° (2 hr) to maximize specificity.



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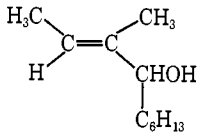

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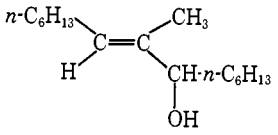

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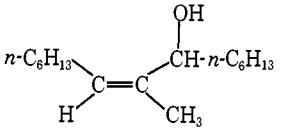

16

with the unsaturated secondary alcohol formed by the carbonyl addition of hexyllithium to the aldehyde **7** which was derived as outlined above.[17] In this instance it would seem that elimination from intermediate racemic β,β'-dioxido phosphonium ion can follow the two possible directional modes if higher temperatures (0–20°) are used in the last step of the reaction, since under these conditions **15** and **16** are produced in a ratio of 3 to 1.

We have also studied the alkylation of β-oxido phosphonium ylides as a possible stereospecific route to trisubstituted olefins. However, we find that this reaction fails completely with most alkyl halides and proceeds moderately well only with methyl iodide. In addition, the alkylation is *not stereospecific* (*cf.* ref 4) as is shown by the reaction of **4** with trideuteriomethyl iodide which produces a mixture of *cis* and *trans* isomers of 2-trideuteriomethyl-2-nonene (50% yield) in ratios of 1:1 to 3:1 depending on reaction conditions.[18]

(17) The nmr spectrum of the major isomer (**15**) (in CCl_4) manifested peaks due to olefinic proton, the proton of the -CH-O unit, and the olefinic methyl group at 5.29, 4.87, and 1.55 ppm, respectively, whereas the corresponding protons in the minor isomer (**16**) (in CCl_4) exhibited peaks at 5.14, *ca.* 4.47, and 1.62 ppm, respectively.

(18) This work was assisted by a grant from the Hoffmann-La Roche Co.

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Kinetically Linear Vinyl Cations in the Solvolysis of Stereoisomeric 1-Iodo-1-cyclopropylpropenes

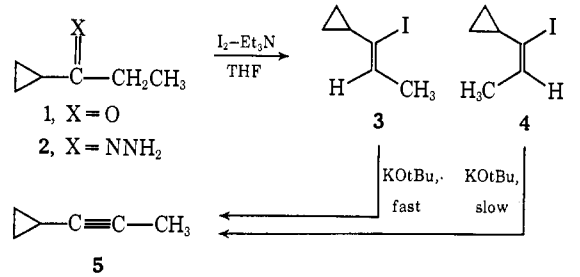
Sir:

Strong evidence now exists that vinyl cations intervene as discrete intermediates in the solvolysis of certain ethylenic derivatives.[1] Despite active recent interest in such reactions, however, a fundamental problem has remained unsolved—the stereochemistry of SN1 substitution at the vinyl center. This has been due in many cases to an inability to synthesize or separate stereoisomers of starting sulfonates, or to the fact that stereochemically distinct enol products are often rapidly converted to ketones in aqueous media.[1]

Ionization of appropriately substituted 1-cyclopropylvinyl halides[1a] provides a system ideally suited to investigation of this stereochemical question. We now report a study of such an ionization which shows that in at least this case, vinyl halides undergo silver-catalyzed substitution with complete randomization of stereochemistry. Our study provides further evidence that vinyl cations intervene in the ionization of both 1-cyclopropyl-1-haloethylenes and "homoallenic" derivatives, and that the vinyl cation intermediates attain an effectively linear structure before they are trapped by solvent acetic acid at room temperature.

Treatment of the hydrazone (**2**) of cyclopropyl ethyl ketone[2a,b] (**1**) with iodine and triethylamine (dried over NaOH and distilled from phenyl isocyanate) in tetrahydrofuran at room temperature[2c] produces compounds **3** and **4** (ratio 62:38) in 40% yield. These materials are separable by preparative vapor chromatography (vpc) and were shown to have the gross structure 1-iodo-1-cyclopropylpropene on the basis of spectral and analytical data. That the major product (**3**) is the *trans* isomer (and the minor product, **4**, its *cis* relative) was indicated by a downfield shift of the vinyl hydrogen signal of **4** in the nmr relative to **3** (**3**, δ 5.62 ppm; **4**, δ 6.25 ppm). The stereochemical assignments were confirmed by the observation that **3** reacts at least 10 times faster than **4** with KO-*t*-Bu in DMSO at room temperature[3] to produce cyclopropylmethylacetylene (**5**).

Scheme I



Ionization of *trans*-iodide **3** proceeded rapidly at room temperature when carried out in silver acetate–acetic acid. The mixture of products produced (>95% yield) contained the components illustrated in Scheme II and listed in Table I. Analytical vpc of this mixture was carried out using two 12 ft × 1/8 in. columns, one packed with 20% Carbowax 20M on Chromosorb P and the other 15% tris-β-(cyanoethoxy)propane (TCEP) on Chromosorb W. Every one of the solvolysis products was obtained in pure form by preparative gas chromatography on a 10 ft × 1/4 in. diethylene glycol succinate (DEGS) column (followed in some cases by single or double chromatography on 10 ft × 1/4 in. 20% TCEP) and identified by spectral and analytical techniques.

Ionization of *cis*-iodide **4** under identical conditions gave a distribution of products (Table I) essentially iden-

(1) (a) S. A. Sherrod and R. G. Bergman, *J. Amer. Chem. Soc.*, **91**, 2115 (1969); (b) M. Hanack and T. Bässler, *ibid.*, **91**, 2117 (1969); (c) P. J. Stang and R. Summerville, *ibid.*, **91**, 4600 (1969); (d) W. M. Jones and D. D. Maness, *ibid.*, **91**, 4314 (1969); (e) L. L. Miller and D. A. Kaufman, *ibid.*, **90**, 7282 (1968); (f) P. E. Peterson and J. M. Indelicato, *ibid.*, **90**, 6515 (1968); (g) C. A. Grob and R. Spaar, *Tetrahedron Lett.*, 1439 (1969); (h) W. M. Jones and F. W. Miller, *J. Amer. Chem. Soc.*, **89**, 1960 (1967); (i) G. Modena and U. Tonellato, *Chem. Commun.*, 1676 (1968); (j) Z. Rappoport and A. Gal, *J. Amer. Chem. Soc.*, **91**, 5246 (1969); (k) P. E. Peterson and J. M. Indelicato, *ibid.*, **91**, 6194 (1969).

(2) (a) M. Julia, S. Julia, and S.-Y. Tchen, *Bull. Soc. Chim. Fr.*, 1849 (1961); (b) V. A. Slabey and P. H. Wise, *J. Amer. Chem. Soc.*, **74**, 1473 (1952); (c) D. H. R. Barton, R. E. O'Brien, and S. Sternhell, *J. Chem. Soc.*, 470 (1962); (d) S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964).

(3) *trans* elimination of vinyl halides under E2 conditions has been shown to occur more rapidly than *cis* elimination in a number of cases. See, for example, G. Köbrich, *Angew. Chem. Intern. Ed. Engl.*, **4**, 49 (1965).