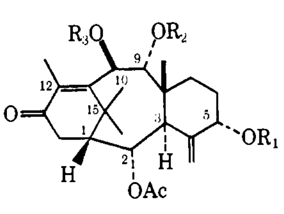
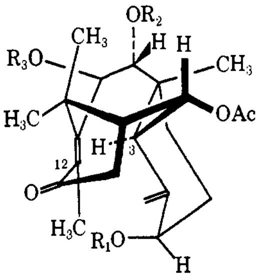


trans

1, $R_1 = COCH{=}CHPh$; $R_2 = R_3 = Ac$

2, $R_1 = Ac$; $R_2 = R_3 = H$



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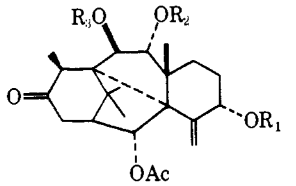


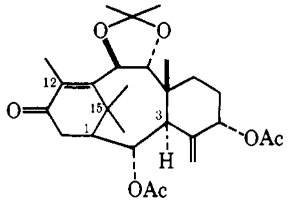
cis

4a, $R_1 = COCH{=}CHPh$; $R_2 = R_3 = Ac$

trans

b, $R_1 = COCH{=}CHPh$; $R_2 = R_3 = Ac$

5, $R_1 = Ac$; $R_2 = R_3 = H$



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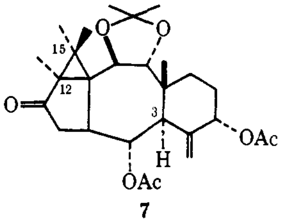

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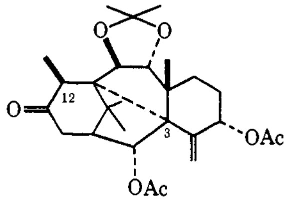

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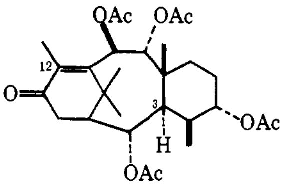

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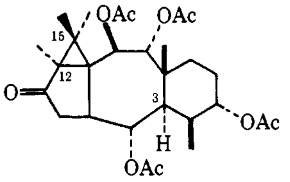

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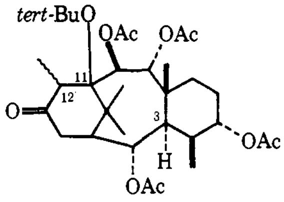

11

was both sensitized with acetophenone and quenched with piperylene and cyclohexa-1,3-diene.[10] Furthermore, the high quantum yields (disappearance) at 365 nm measured in dioxane (0.091) and *tert*-BuOH (0.078) as compared to that in nonpolar benzene (0.031), and the nonoccurrence of hydrogen transfer from the solvent *i*-PrOH, lead to the conclusion that the energy levels of T_1 and T_2 states are also close in this case and that the transformation proceeds predominantly *via* the π,π^* triplet.

In view of the extreme proximity of the H-3 to the 11-ene[1f,11] this transannular reaction can be regarded as following a concerted ${}_{\sigma}2_s + {}_{\pi}2_s$ route.[12,13] The possibility of an intermolecular hydrogen abstraction can be disregarded on the basis of kinetic studies[14] and the cage structure of 2 (see 3).

H. Azumi, Tohoku University, for his help in phosphorescence measurements.

[10] In the case of 1 the cinnamate group also absorbs light efficiently as the irradiation was carried out in a quartz tube. Thus, the intramolecular quenching of the enone moiety by the cinnamate group would be inefficient.

Acknowledgments. We acknowledge Public Health Service Grant No. CA-11572 and the Ministry of Education, Japan, for financial support.

[11] *Cf.* M. Shiro, T. Sato, H. Koyama, Y. Maki, K. Nakanishi, and S. Uyeo, *Chem. Commun.*, 98 (1966).

[12] A C-11–C-12 biradical is also conceivable but less likely.

[13] R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969).

[14] The photoreactions described follow a first-order kinetic equation: $\ln(e^{2.303\epsilon cd} - 1) = -2.303\Phi I_0 \epsilon dt$ in which ϵ = molar extinction coefficient of starting ketone, c = concentration of starting ketone (moles/liter), d = cell length (centimeters), I_0 = total amount of incident light (einstein liter^{-1} second^{-1}), t = reaction time, Φ = quantum yield of disappearance of starting ketone. We are grateful to Professor M. Koizumi, Tohoku University, for his help in kinetic measurements, and the personnel of Japan Spectroscopic Co., Hachioji, Tokyo, for usage of the concave radiating monochromator CRM-FA.

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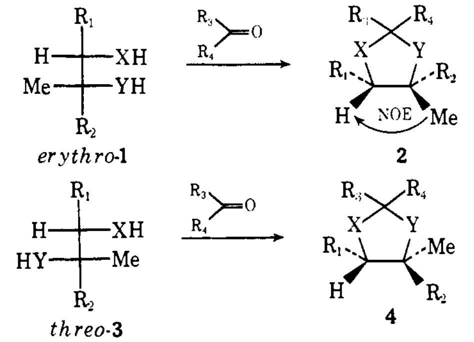
Received December 16, 1971

A General Method for Distinguishing Threo and Erythro Isomers of Certain α-Glycols and Related Compounds

Sir:

In the following we describe a method for differentiating between threo and erythro isomers. The method simply involves detection of an intramolecular nuclear Overhauser effect (NOE)[1] or W-type long-range coupling[2,3] in the nmr spectrum of an acetonide or other suitable five-membered ring derivative. Since no generalized methods seem to be known for estab-

Scheme I. Formation of Five-Membered Derivatives (X, Y:, O, NR, and S)



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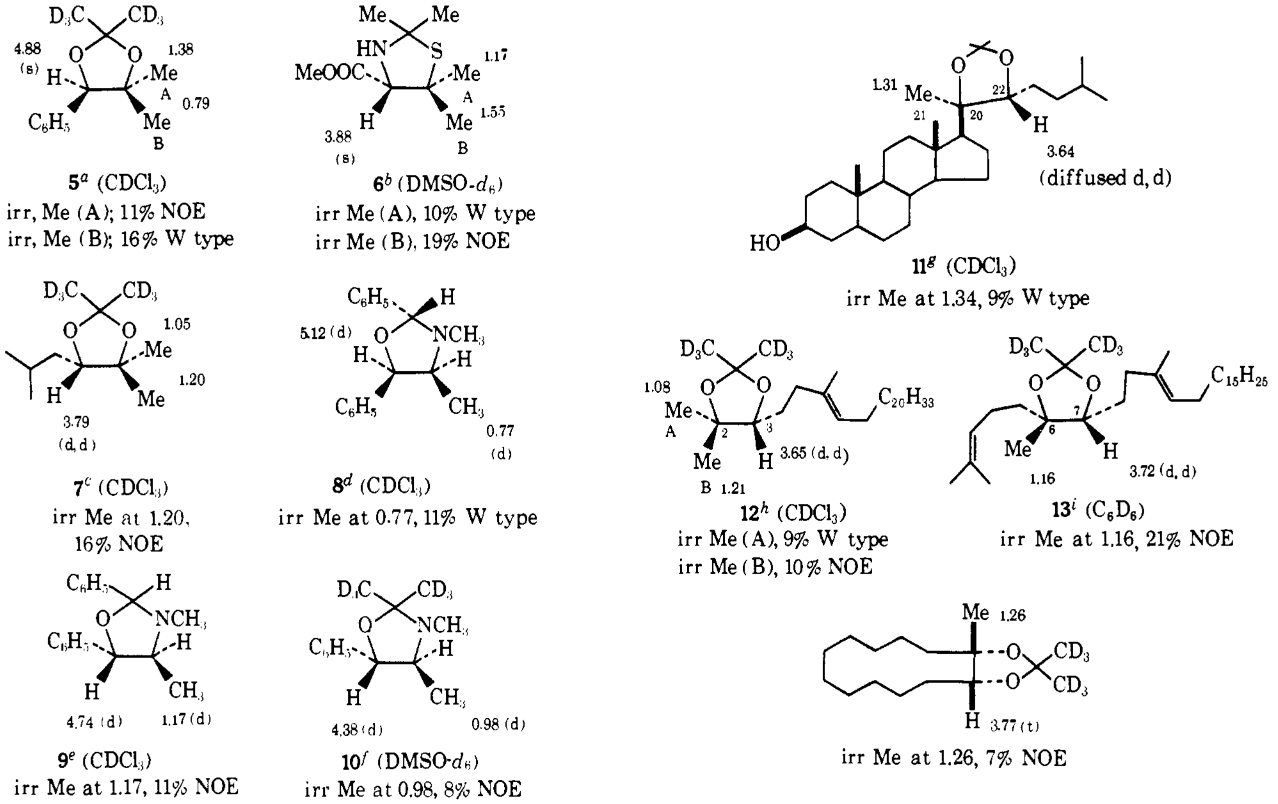
[1] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, **87**, 5250 (1965); M. C. Woods, I. Miura, Y. Nakadaira, A. Terahara, M. Maruyama, and K. Nakanishi, *Tetrahedron Lett.*, 321 (1967); J. H. Noggle and R. E. Schirmer, "The Nuclear Overhauser Effect," Academic Press, New York, N. Y., 1971.

[2] S. Sternhell, *Quart. Rev., Chem. Soc.*, **23**, 236 (1969); M. Barfiels and B. Chakrabarti, *Chem. Rev.*, **69**, 757 (1969).

[3] Needless to mention, NOE is characterized by an increase in integrated intensity and a constant half-band width ($W_{1/2}$), whereas W-type coupling is characterized by an increase in peak height and a decrease in $W_{1/2}$ (no change in integrated intensity). In the present paper, we record the extent of W-type couplings in terms of height increase rather than $W_{1/2}$ decrease.

Chart I. Examples of NOE and W-Type Couplings[3]



5^a ($CDCl_3$)
irr, Me (A); 11% NOE
irr, Me (B); 16% W type

6^b (DMSO-d_6)
irr Me (A), 10% W type
irr Me (B), 19% NOE

11^g ($CDCl_3$)
irr Me at 1.34, 9% W type

7^c ($CDCl_3$)
irr Me at 1.20,
16% NOE

8^d ($CDCl_3$)
irr Me at 0.77, 11% W type

12^h ($CDCl_3$)
irr Me (A), 9% W type
irr Me (B), 10% NOE

13^i (C_6D_6)
irr Me at 1.16, 21% NOE

9^e ($CDCl_3$)
irr Me at 1.17, 11% NOE

10^f (DMSO-d_6)
irr Me at 0.98, 8% NOE

irr Me at 1.26, 7% NOE

[a] From (*R*)-(−)-mandelic acid by treatment with: (i) CH_3OH–HCl, (ii) MeMgBr, and (iii) $(CD_3)_2CO$-*p*-TsOH. [b] Acetone adduct of methyl ester of (*R*)-(−)-penicillamine. [c] From (*S*)-(−)-leucine by successive treatments with: (i) HNO_2, (ii) EtOH–HCl, (iii) MeMgBr, and (iv) $(CD_3)_2CO$-*p*-TsOH. [d] Prepared by refluxing (−)-ephedrine with benzaldehyde in EtOH: L. Neelakantan, *J. Org. Chem.*, **36**, 2256 (1971). [e] Obtained from (+)-pseudoephedrine by similar treatment as in the case of (−)-ephedrine. [f] From (+)-pseudoephedrine by treatment with $(CD_3)_2CO$. [g] 3β-(20*R*,22*R*)-Trihydroxycholestane 3,22-diacetate (gift from Dr. Mori) by treatment with: (i) $LiAlH_4$ and (ii) $(CD_3)_2CO$-*p*-TsOH. For the 20*R*,22*R* structure, see: N. K. Chaudhuri, R. Nickolson, H. Kimball, and M. Gut, *Steroids*, **15**, 525 (1970). [h] *Cf.* K. B. Sharpless, *J. Chem. Soc. D*, 1450 (1970). [i] Prepared from 7-monoacetate (given by Dr. Sharpless) by treatment with: (i) $LiAlH_4$ and (ii) $(CD_3)_2CO$-*p*-TsOH. [j] Prepared from diol (gift from Dr. Sharpless) by treatment with $(CD_3)_2CO$-*p*-TsOH.

lishing the threo and erythro relation of isomers, we believe that this simple technique has wide applicabilities for solving problems of this nature, *e.g.*, ephedrine derivatives.[4]

In its generalized form the method can be represented as in Scheme I, namely, erythro isomers give the five-membered derivative **2**, *e.g.*, acetonides, oxazolidines, or thiazolidines, which upon irradiation of the methyl group exhibits an NOE on the adjacent methine proton. In contrast, derivative **4** prepared from threo isomer **3** shows no NOE but instead a long-range W-type coupling between the methyl group and adjacent proton. Data are summarized in Chart I.[5]

Experimental measurements were carried out with degassed *ca.* 15% solutions containing a drop of benzene in addition to TMS, and locking on the benzene signal when irradiating the methyl signals.[6] Although deuteriochloroform was generally satisfactory as the solvent, in some cases it was necessary to carry out the measurements in dimethyl-d_6 sulfoxide. Generally speaking, the latter solvent gave larger NOE values and also smaller differences between degassed and nondegassed solutions. Usage of deuterioacetone is recommended for formation of acetonides due to the obvious advantage of having less methyl peaks in the nmr spectrum. Aldehydes can be substituted for acetone when acetonide formation is slow or extremely hindered, *e.g.*, the ephedrine derivative **8**.[7]

Although it was initially suspected that intramolecular relaxations of the methine proton with an α-methylene group might impede measurements of NOE or long-range coupling, this was clearly not the case as exemplified by compounds **7**, **11**, **12**, etc. Examples **5**, **6**, **7**, and **12** show that, without exception, a distinct demarcation exists between the NOE and W-type coupling. This is of primary importance as it enables the method to be applied to instances where only one of the isomers is available.

In acetonide **7** and the squalene derivative **12** the methyl group cis to the adjacent methylene group appears at a higher magnetic field as compared to the *trans*-methyl group.[8] This anisotropic effect of the

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(4) For example, see: B. Witkop and C. M. Foltz, *J. Amer. Chem. Soc.*, 79, 197 (1957).

(5) Rather large samples (*ca.* 50 mg) were required for some compounds (*e.g.*, **11–13**) where the molecular weight is not only high but the methine proton being observed is only one out of *ca.* 50 protons; moreover, the signals are doublets of doublets. In order to obtain unambiguous results in these cases, operating conditions of the spectrometer (Varian HA-100) were carefully optimized for each sample.

(6) The benzene-lock method was used because it was not possible to lock on the TMS signal and irradiate methyl signals, especially when chemical shifts of methyl signals were less than 1 ppm.

(7) Pseudoephedrine formed the acetonide-d_6 **10** only slowly (20 days at room temperature with a 1:2 mixture of acetone-d_6–benzene in the presence of Linde 4A molecular sieves). In three times this reaction period, ephedrine gave only a small amount of the acetonide. These conditions are similar to those of H. Pfanz and G. Kirchner, *Justus Liebigs Ann. Chem.*, **614**, 149 (1958). Consequently, the acetals **8** and **9** were prepared as indicated in Chart I.

methylene group provides a further diagnostic method for differentiating the two isomers.

An application of the present method is determination of the erythro natures of compounds **13** and **14**. It was also employed in the recent determinations of the absolute configurations of ecdysone side chains[9] and the C_{18} juvenile hormone.[8]

Acknowledgments. We express our gratitude to Professor K. B. Sharpless, Massachusetts Institute of Technology, for gifts of samples and to Dr. H. Mori, Teikoku Hormone Co., for a gift of precursor to **11**. The work was supported by Public Health Service Grants AI 10187 (to K. N.) and GM 44322 (to D. A. S.), and by the Naito Foundation (to M. K.).

[8] For another example, see K. Nakanishi, D. A. Schooley, M. Koreeda, and J. Dillon, *J. Chem. Soc. D*, 1235 (1971).

[9] M. Koreeda, D. A. Schooley, K. Nakanishi, and H. Hagiwara, *J. Amer. Chem. Soc.*, **93**, 4084 (1971).

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Received February 2, 1972

α vs. β Scission in Reactions of Alkoxy and Thiyl Radicals with Diethyl Alkylphosphonites

Sir:

Previous work has indicated that reactions of alkoxy radicals with trialkylphosphines give mostly products of *displacement* of the attached alkyl substituent (product III in Scheme I). For example, *tert*-BuO· with n-Bu_3P at 130° gives a 4/1 displacement/oxidation ratio,[1] whereas at −90° with Et_3P, only esr signals resulting from Et· are noted.[2] The alkyl group displacement predominates despite the fact that it is *thermodynamically much less favored than oxygen transfer.*[3] On the other hand, in reactions of various trivalent phosphorus derivatives with thiyl radicals (RS·), no well-established examples of displacement exist.[6] Such reactions normally give exclusively *oxidation* products, II.

Scheme I

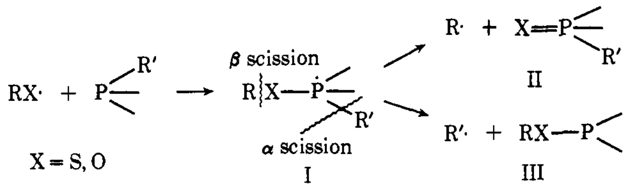
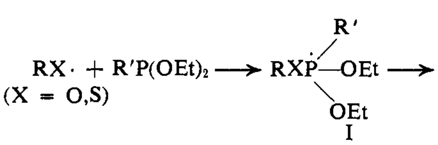


Table I. *α vs. β* Scission in the Reactions of Alkoxy and Thiyl Radicals with Diethyl Alkylphosphonites at 60° [a]



$$\mathrm{RX\cdot + R'P(OEt)_2 \longrightarrow RX\dot{P}(R')(OEt)OEt \longrightarrow}$$

(X = O,S)

I

			$\frac{R'P(X)(OEt)_2}{RXP(OEt)_2}$ [b]
1a	*tert*-BuO·	$PhCH_2$	0
1b	*tert*-BuO·	CH_3	0
1c	*tert*-BuO·	C_2H_5	0
1d	*tert*-BuO·	*tert*-C_4H_9	0
2	$PhCH_2O\cdot$	$PhCH_2$	0.3
3	*i*-PrS·	$PhCH_2$	2[c]
4	*tert*-BuS·	$PhCH_2$	5[c]
5	$PhCH_2O\cdot$	CH_3	4
6	*tert*-BuS·	C_2H_5	>20

[a] In degassed benzene except as noted. [b] Determined by vpc analysis of products (sensitivity corrected). RS· displacement products measured as $RSP(S)(OEt)_2$. [c] In *o*-dichlorobenzene. [d] From thermal decomposition of the hyponitrite, RON=NOR. [e] Azobisisobutyronitrile initiated reaction of RSH.

We present here results which show clearly that both oxidations and displacements can and do occur in reactions of RS· as well as those of RO· with alkyl-substituted trivalent phosphorus compounds. The oxidation/displacement ratio is found to be rather delicately balanced and to vary greatly with the nature of R and R′ (see Scheme I).

In Table I are compared the oxidation/displacement ratios, based on product analyses, for reactions of a series of RS· and RO· with various diethyl alkylphosphonites. Clearly, oxidation is generally more favorable with RS· than with RO·. (Compare reactions 1a and 2 with 3 and 4 as well as 5 with 6.) Further, for oxy radicals, the product ratio is dependent on the structure of RO·. Both oxidation and displacement are observed with $PhCH_2O\cdot$, but only displacement is noted with *tert*-BuO· (reactions 1 *vs.* 2 and 5). A structural effect on the oxidation/displacement ratio is also seen on comparison of *i*-PrS· with *tert*-BuS· (reactions 3 and 4).

In terms of phosphoranyl radical intermediate I,[7] these results seem best interpreted by referral to Figure 1. Reactions of RO· and RS· with PXYZ are generally very rapid with activation energies in the range 1–4 kcal/mol.[10] Both oxidation and displacement, as shown for *tert*-BuO· in Figure 1, are very exothermic processes overall,[3b] and it is quite likely that the α and β scissions are also highly favorable

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[1] S. A. Buckler, *J. Amer. Chem. Soc.*, **84**, 3093 (1962).

[2] J. K. Kochi and P. J. Krusic, *ibid.*, **91**, 3944 (1969).

[3] (a) Based on $\Delta H_f°$ (g, 298) for $(C_2H_5O)_3P$ and $(C_2H_5O)_3PO$ of −195.9 and −284.5 kcal/mol[4] and $D(tert\text{-BuO}\cdot \rightarrow tert\text{-Bu}\cdot + O)$ of 90.5 kcal/mol,[5] $\Delta H_r°$ for *tert*-BuO· + $P(OC_2H_5)_3 \rightarrow$ *tert*-Bu· + $OP(OC_2H_5)_3$ of −57 kcal/mol is calculated. For the reaction *tert*-BuO· + $P(CH_3)_3 \rightarrow$ *tert*-$BuOP(CH_3)_2$ + $CH_3\cdot$, $\Delta H_r°$ of −17 kcal/mol can be estimated. Such a value is based on $\bar{D}_{PC}$ for $(CH_3)_3P$ of 67 kcal/mol and $\bar{D}_{PO}$ of 84 kcal/mol. These values can be calculated from the standard heats of formation of trimethylphosphine[4] and triethyl phosphite[4] and those[5] for $CH_3\cdot$, $C_2H_5O\cdot$, and P. (b) The above $\Delta H_r°$ values are used as estimates for the reactions depicted in Figure 1.

[4] J. D. Cox and G. Pilcher, "Thermochemistry of Organic and Organometallic Compounds," Academic Press, New York, N. Y., 1970.

[5] From $\Delta H_f°$ data in J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966).

[6] A possible exception is the photochemically induced reaction of Et_2PPEt_2 with MeSSMe to give Et_2PSMe (identified as $Et_2P(S)Me$): Yu. N. Shlyk, G. M. Bogolyubov, and A. A. Petrov, *J. Gen. Chem. USSR*, **38**, 194 (1968). However, the mechanistic details of this reaction have not been established.

[7] Considerable esr[2,8] and chemical[9] evidence for the intermediacy of phosphoranyl radicals of the type $(RO)_xPR'_{4-x}$ has been recently presented.

[8] (a) A. G. Davies, D. Griller, and B. P. Roberts, *Angew. Chem.*, **83**, 800 (1971); (b) P. J. Krusic, W. Mahler, and J. K. Kochi, private communication.

[9] W. G. Bentrude and R. A. Wielesek, *J. Amer. Chem. Soc.*, **91**, 2406 (1969); W. G. Bentrude and T. B. Min, *ibid.*, **94**, 1025 (1972).

[10] *E.g.*, in ref 8a for the reaction of *tert*-BuO· with $(C_2H_5)_3P$, E_a for the overall rate constant is estimated to be 2.2 kcal/mol. E_a for the β scission is estimated to be 9 kcal/mol. For the reaction[11] of Ph· with $(CH_3O)_3P$ to yield $PhP(O)(OCH_3)_2$ + $CH_3\cdot$, E_a is about 3–4 kcal/mol (W. G. Bentrude, J.-j. L. Fu, and C. E. Griffin, paper submitted for publication).

[11] W. G. Bentrude, J.-j. L. Fu, and C. E. Griffin, *Tetrahedron Lett.*, 6033 (1968).