Study of the Addition of Monoalkylphosphonic Acids onto Trialkyl-Substituted Epoxides

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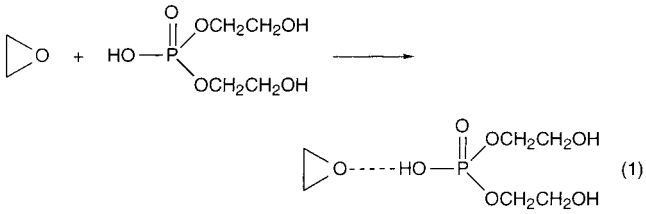
The addition of 2-chloroethylphosphonic acid (or ethephon), a well-known stimulating molecule for the production of latex by *Hevea brasiliensis*, onto 2,3-epoxy-2-methylbutane was investigated to enhance the understandings on the addition mechanisms of reagents of alkylphosphonic acid type onto trialkyl-substituted epoxides. It was demonstrated that the addition occurs according to a three-step mechanism including a rapid nucleophilic attack of the phosphorated anion on the most alkyl-substituted carbon of the oxirane, followed by formation of a dioxaphospholane structure with release of water, and finally a hydrolytic cleavage of the dioxaphospholane cycle to generate the regioisomer 1:1 adduct where the phosphorated group is on the less alkyl-substituted carbon of the initial oxirane.

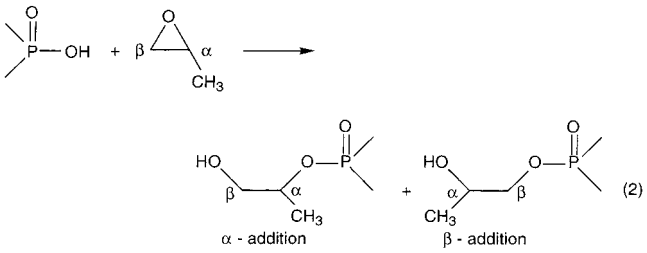
Introduction

The addition of organophosphorated reagents onto oxirane rings by the intermediate of P−OH functions does not necessitate the use of a catalyst. A kinetic study of the addition of dihydroxyethylphosphoric acid onto ethylene oxide showed that, without catalyst, the addition is autocatalyzed by the acid functions P−OH of the reagent.[1] The activation of the oxirane ring is due to the formation of a hydrogen-type bond[2] between the oxirane oxygen and the acid function of the reagent (eq 1), which increases the electrophilicity of the oxirane ring.



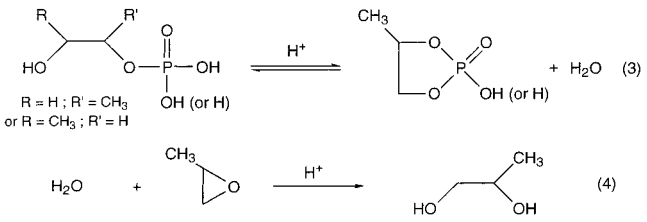
(1)

The previous studies concerning this field of research showed that the addition on terminal epoxides is not regioselective: the opening of the oxirane ring occurs either in the α or in the *β* position. It was noticed in the case of propylene oxide (studies realized with diethylphosphoric acid, phosphorous acid, and phosphoric acid)[3] (eq 2) that the relative proportions in 1:1 adducts, resulting from oxirane ring opening in α or *β*, are independent of the functionnality of the phosphorated reagent (mono-, di-, or triacid), of the temperature and of the nature of solvent. Whatever the organophosphorated reagent, the regioisomer ratio calculated from the intensities of the ^{1}H or ^{31}P NMR respective signals[3] is always about 50/50 (eq 2). On the other hand, the orientation of the addition can be influenced by the steric hindrance and the nature of substituents of the oxirane ring: for instance, in the case of 1,2-epoxy-2-methylpropane, the *β*-addition is favored[3].



(2)

Moreover, it was noticed that the 1:1 addition is disturbed by secondary reactions, which can lead to the formation of dioxaphospholane and diol derivatives[3] (eqs 3 and 4).



As part of the research realized in the field of chemical modification of epoxidized 1,4-polyisoprene by 2-chloroethylphosphonic acid (or ethephon) **1**,[4] it was decided to investigate the reaction of this reagent onto 2,3-epoxy-2-methylbutane **2**. The synthesis of 1,4-polyisoprenes support of **1** was considered in order to prepare systems able to allow a controlled release of **1** during the time (**1** is linked to the polymer backbone by a hydrolyzable bond), with the objective to prolong the stimulating activity of **1** for latex production by *Hevea brasiliensis*.[5] Compound **2** was chosen the first time, as a model molecule of epoxidized 1,4-polyisoprene unit, to facilitate

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(2) Biela, T.; Szymanski, R.; Kubisa, P. *Makromol. Chem.* **1992**, *193*, 285.
(3) Biela, T.; Kubisa, P.; Penczek, S. *Makromol. Chem.* **1992**, *193*, 1147.

(4) Submitted to *Eur. Polym. J.*

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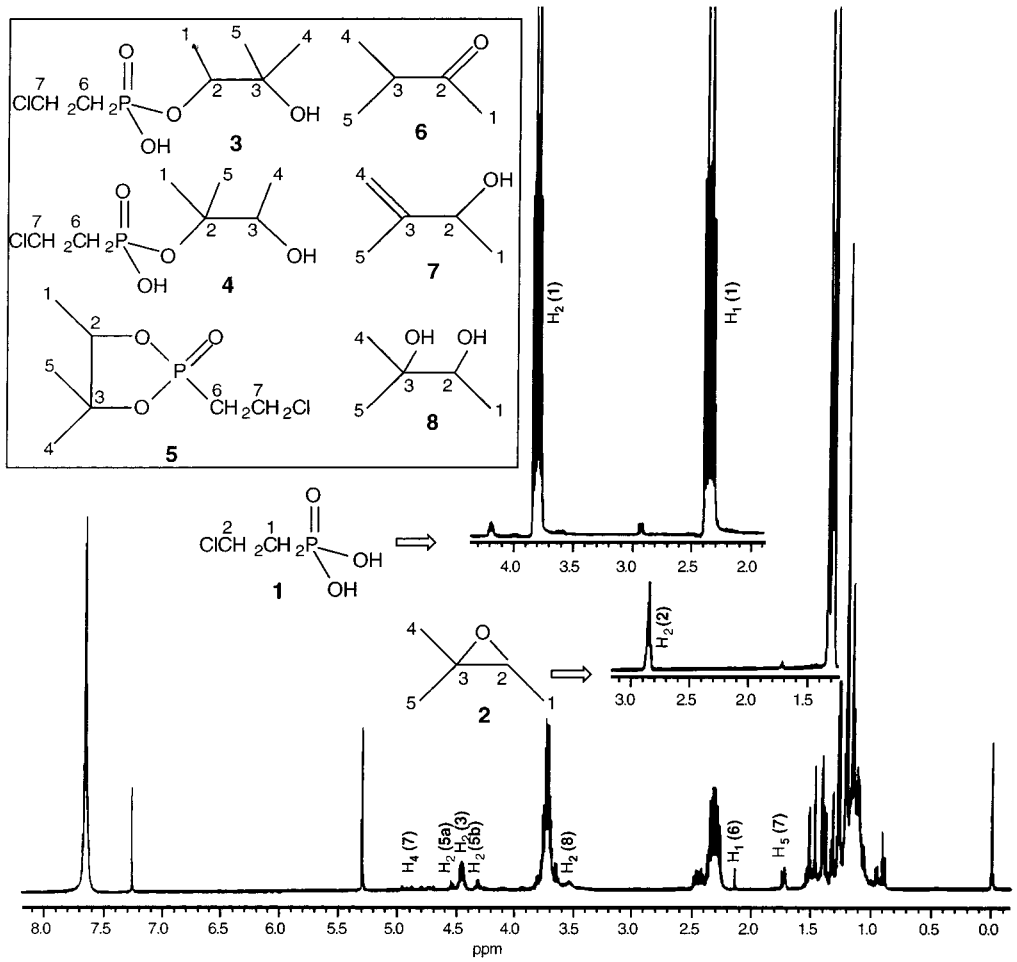


Figure 1. ^{1}H NMR spectrum of the crude mixture ($CDCl_3$, δ in ppm), compared with ^{1}H NMR spectra of initial products **1** and **2**.

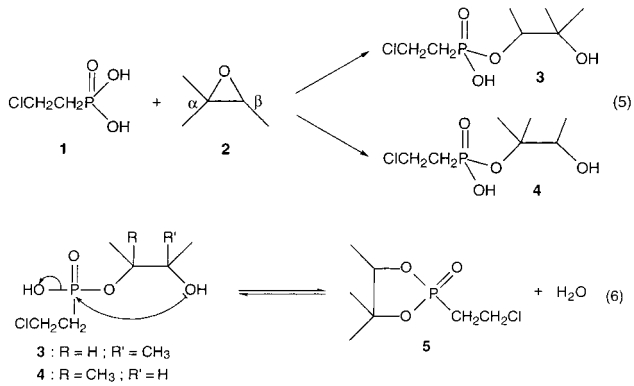
the identification and the characterization of the various phosphorated adducts and secondary products formed during the reaction. The purpose of this paper is to enhance the understandings on the addition mechanisms of reagents of alkylphosphonic acid type onto the epoxides, for instance, in the present case, the trialkyl-substituted epoxides.

Results and Discussion

To better understand the reaction between 2-chloroethylphosphonic acid **1** and 2,3-epoxy-2-methylbutane **2**, convenient reaction conditions were selected to obtain simultaneously a good representation of the different products (1:1 adducts and secondary derivatives) formed during the reaction. For that, the reaction between acid **1** and epoxide **2** in equimolecular quantities was carried out at 20 °C, in the absence of solvent.

The crude mixture obtained after 24 h of stirring was analyzed by ^{1}H NMR and then by ^{31}P NMR. ^{1}H NMR analysis of the crude mixture (Figure 1) shows a total disappearance of the triplet at 2.85 ppm (oxirane ring protons) which indicates a complete transformation of the epoxide, even though ethephon **1** ($CDCl_3$, δ = 27.2 ppm) is not totally consumed as shown also on the ^{31}P NMR spectrum (Figure 2). According to the measures realized from the ^{1}H and ^{31}P NMR spectra, only 43% (^{1}H NMR) [54% (^{31}P NMR)] of **1** is transformed. This result is explained by the existence of secondary reactions that lead to the transformation of part of the initial epoxide in nonphosphorated derivatives, which are also characterized by ^{1}H NMR.

Analysis and Characterization of the Phosphorated Adducts Formed. By reference to the works of Biela et al.,[1−3] it was initially established that the following phosphorated adducts could be formed: the regioisomers **3** and **4** (1:1 adducts) issued from the addition of **1**, respectively, in the α and β positions on the oxirane ring of **2** (eq 5), and the dioxaphospholane **5** issued of **3** or **4** after elimination of water[6] (eq 6).



(5) (a) Audley, B. G.; Archer, B. L. *Chem. Ind. London* **1973**, 634. (b) Audley, B. G. *Phytochemistry* **1979**, *18*, 53. (c) Mayard, J. A.; Swan, J. M. *Aust. J. Chem.* **1963**, *16*, 596. (d) Kays, S. J.; Beaudry, R. M. *Acta Horticulturae* **1987**, 201. (e) Biddle, E.; Kerfoot, D. G. S.; Hwa Kho, Y.; Russell, K. E. *Plant Physiol.* **1976**, *58*, 700.

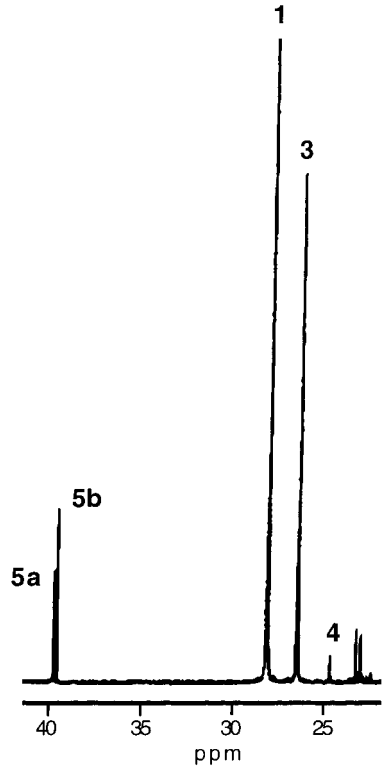
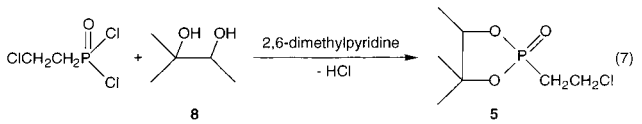


Figure 2. ^{31}P NMR spectrum of the crude mixture ($CDCl_3$, δ in ppm).

The various 1:1 adducts formed during the reaction are identified in ^1H NMR by three signals at, respectively, δ = 4.32, 4.42, and 4.54 ppm (Figure 1), characteristic of C*H*OP protons corresponding to each phosphorated adduct formed.

The analysis by ^{31}P NMR (Figure 2) shows four peaks at δ = 39.2, 39.1, 26.5, and 24.3 ppm characteristic of four phosphorated adducts. The proportion of these adducts determined by ^{31}P NMR represents about 48% of the organophosphorated compounds contained in the crude mixture obtained after 24 h of reaction. Residual ethephon is also noticed at δ = 27.2 ppm (~46% of the phosphorated compounds), which demonstrates that the addition is accompanied by secondary reactions because the starting epoxide is totally transformed. The small peaks identified betwen δ = 22 and 23 ppm indicate the presence of a low proportion of secondary phosphorated derivatives (≈ 6%).

The formation of dioxaphospholane **5** was confirmed after comparison of the ^1H, ^{31}P, and ^{13}C NMR spectra of the crude mixture with those of the dioxaphospholane prepared at low temperature by reaction between 2-chloroethylphosphonyldichloride and 3-hydroxy-2-methylbutan-2-ol **8** (eq 7), in a nonpolar solvent (benzene) and in the presence of 2,6-dimethylpyridine to neutralize the HCl formed.[7]



8 **5**

The dioxaphospholane is characterized in ^{31}P NMR by two peaks at δ_a = 39.27 ppm and δ_b = 39.1 ppm due to the formation of two diastereomers *R*,*R* (or *S*,*S*) and *R*,*S* (or *S*,*R*) (Figure 3) explained by the existence of two asymmetric centers in the molecule (a carbon and the phosphorus).[8]

The existence of the two dioxaphospholane diastereomers is also confirmed by the analyses realized in ^{13}C and ^1H NMR. In ^{13}C NMR, the carbons Cl*C*H_2, *C*HOP, and *C*OP are all characterized by two singlets, and the carbon *C*H_2P by two doublets explained by the coupling with the phosphorus atom. Moreover, six peaks (singlets) characteristic of the methyl groups are noticed between δ = 15 ppm and δ = 26 ppm. In ^1H NMR ($CDCl_3$) (Figure 4), two doublets of quadruplets are noticed for the C*H*OP protons respectively at δ = 4.54 and 4.32 ppm (coupling constants: $^3J_{HP}$ = 2.1 Hz and $^3J_{HH}$ = 6.4 Hz; $^3J_{HP}$ = 1.9 Hz and $^3J_{HH}$ = 6.4 Hz). The methyl protons are characterized by four singlets (δ = 1.31, 1.55, 1.42, and 1.48 ppm) and two doublets at δ = 1.39 ppm ($^3J_{HH}$ = 6.4 Hz) and δ = 1.33 ppm ($^3J_{HH}$ = 6.4 Hz).

The relative proportions in **5a** and **5b** in the crude mixture were calculated from the ^{31}P NMR spectrum by comparing the intensities of the respective signals: [**5a**]/[**5b**] = 0.56.

To complete the characterization of **5a** and **5b** (see the Experimental Section), the 2D H−H (and H−C) NMR and proton selective irradiation were used. By these means, it was demonstrated that the doublets of quadruplets characteristic of the C*H*OP protons at δ = 4.54 ppm and δ = 4.32 ppm were coupled with the doublets characteristic of the methyl protons respectively at δ = 1.33 and 1.39 ppm. Moreover, the analysis by 2D C−H NMR allowed to identify the chemical shifts of the methyls *Me*CHOP and (*Me*)$_2$COP knowing their attribution in ^1H NMR.

Knowing that electronegative atoms, such as oxygen, cause deshielding of hydrogen atoms and taking into account the fact that very low values of the $^3J_{PHOCH}$ indicate a low dihedral angle P−O−C−H, which is the case in the present diastereomers (see above), it was possible to give a complete ^1H NMR characterization for the diastereomers **5a** and **5b**. Thus, the signal of the C*H*OP proton in the diastereomer *S*,*R* (or *R*,*S*), which is sterically closer to the oxygen atom of the P=O bond than in the case of the diastereomer *S*,*S* (or *R*,*R*), corresponds to the chemical shift at the lowest field (δ = 4.54 ppm). According to a similar approach, the chemical shifts of the various methyls could be identified leading to the conclusion that for the methyls **a** and **b**, the higher chemical shift corresponds to the methyls of the diastereomer *R*,*R* (or *S*,*S*) and for the methyls **c**, to the methyl of the diastereomer *R*,*S* (or *S*,*R*).

According to the literature,[3] the addition on epoxides is nonregioselective: the two other phosphorated adducts characterized on the ^{31}P NMR spectrum of the crude mixture (Figure 2), respectively, at 26.5 ppm (high peak) and 24.3 ppm (very small peak) can be attributed to the two regioisomers **3** and **4**. The difference of peaks intensities seems to indicate that the addition on trialkyl-substituted epoxides would be quasi regioselective.

The regioisomer mainly formed was characterized in ^1H NMR as being **3**. After subtraction of the signals

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(7) Fontaine, L.; Derouet, D.; Brosse, J. C. *Eur. Polym. J.* **1990**, *26*, 857.

(8) Biela, T.; Klosinski, P.; Penczek, S. *J. Polym. Sci, Part A: Polym. Chem.* **1989**, *27*, 763.

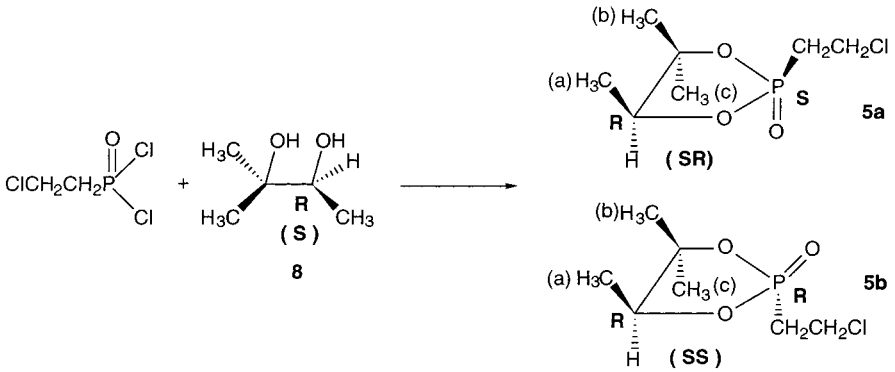


Figure 3. Diastereomer **5a** and **5b** of the dioxaphospholane **5**.

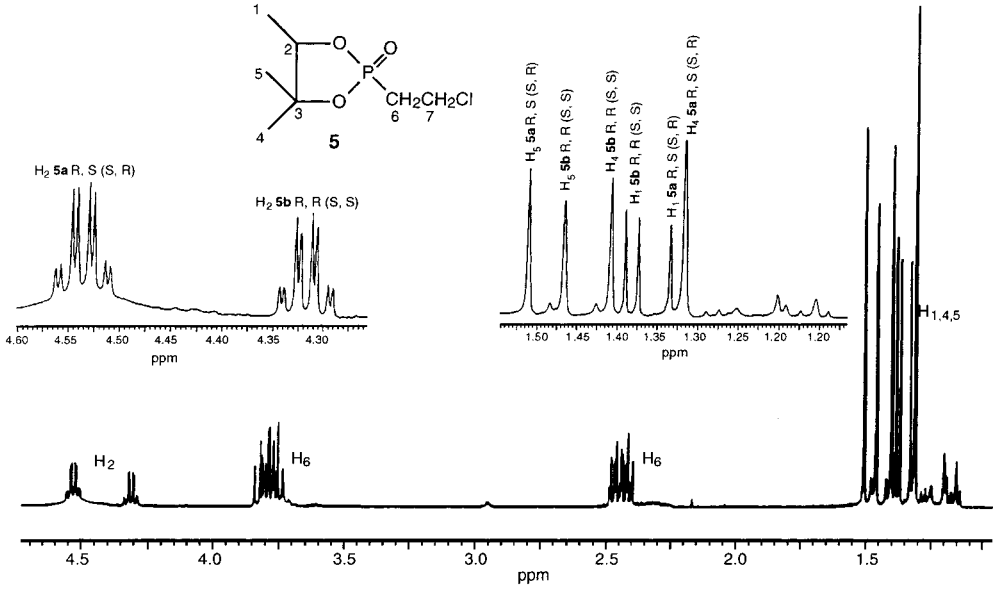


Figure 4. ^{1}H NMR spectrum of the dioxaphospholane diastereomers obtained from the reaction between 2-chloroethylphosphonyldichloride and **8**.

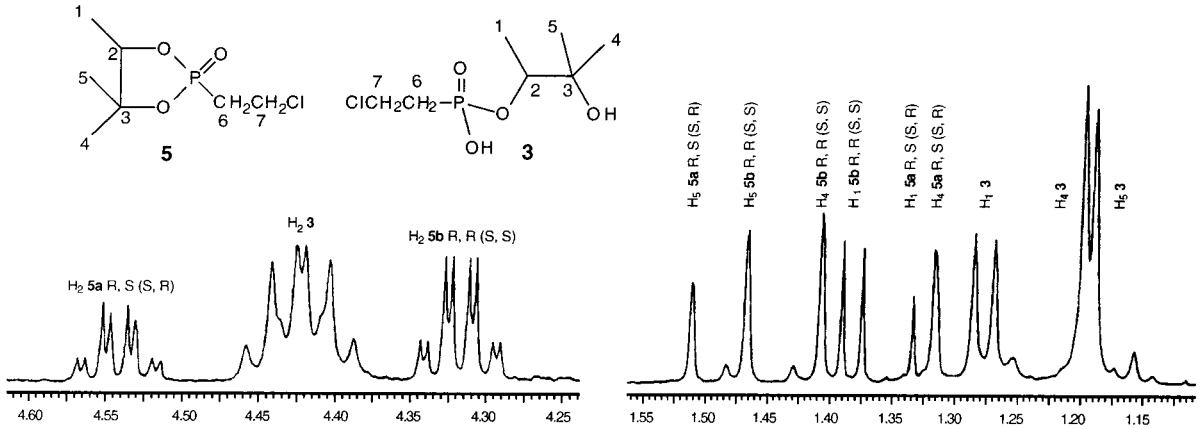


Figure 5. Characterization of **3** by ^{1}H NMR ($CDCl_3$, δ in ppm).

characteristic of dioxaphospholane protons of **5**, it was possible to notice on the ^{1}H NMR spectrum of the crude mixture (Figure 5) at $\delta = 4.42$ ppm, a doublet of quadruplets characteristic of the P−O−C*H*(Me)-C proton of **3** ($^3J_{HH} = 6.45$ Hz, $^3J_{HP} = 8.8$ Hz), and also a doublet at $\delta = 1.27$ ppm ($^3J_{HH} = 6.45$ Hz) for the protons of the methyl POCH(*Me*)C and two singlets at $\delta = 1.19$ and 1.17 ppm for that of the methyls (*Me*)$_2$COHC−. The ^{1}H, ^{31}P, and ^{13}C NMR characteristics of **3** are summarized in Figure 6. The other regioisomer **4** was not identified on the ^{1}H NMR spectrum of the crude mixture analyzed after 24 h of reaction: normally, a signal characteristic of the C*H*OH proton should be noticed around $\delta = 3.5$ ppm.

Characterization of Secondary Derivatives. Three secondary products derived from **2** were identified: a ketone, an allylic alcohol, and an α,*β*-diol (Figure 7). They were characterized on the ^{1}H NMR spectrum of the crude

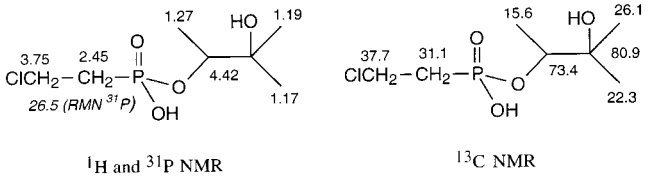
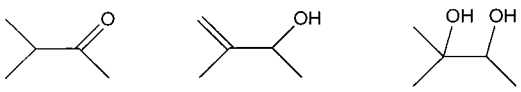


Figure 6. ^{1}H, ^{31}P, and ^{13}C NMR characteristics of **3** ($CDCl_3$, δ in ppm).



3-methylbutane-2-one **6** 3-methyl-3-buten-2-ol **7** 3-hydroxy-2-methylbutan-2-ol **8**

Figure 7. Secondary products derived from **2** obtained during the reaction of **1** with **2**.

mixture (Figure 1) from their specific chemical shifts beforehand obtained from the bibliography (in the case of **6** and **7**[9]) or after synthesis of the compound (in the case of **8** prepared by addition of water onto **2** catalyzed by cerium ammonium nitrate[10]).

The secondary derivatives that represent about 51% of the compounds obtained from **2** are distributed as follows: 43.6% of **8**, 5.5% of **7**, and 1.8% of **6** (determined from the intensities of the respective characteristic signals noticed on the ^{1}H NMR spectrum). Consequently, only 49% of **2** was really transformed in phosphorated adducts.

Kinetic Study of the Addition of 1 onto 2. The evolution of the reactional mixture composition versus time was followed by ^{31}P NMR, by comparing the intensities of the various peaks characteristic of the phosphorated products present in the mixture. To stop the reaction, each sample was plunged into a bath maintained at −40 °C until NMR analyses that were also carried out at low temperature (−20 °C).

The kinetic studies were realized without solvent (Figure 8, graph A) and then in $CDCl_3$ (Figure 8, graph B). ^{1}H and ^{31}P NMR spectra were obtained in $CDCl_3$.

The analysis of the ^{31}P NMR spectra of samples taken at different times showed the presence of four main phosphorated adducts, that is one more than in the final mixture after 24 h of reaction. The secondary phosphorated derivatives also formed during the addition of **1** onto **2** are minority (∼10% of the totality of the organophosphorated compounds for the reaction carried out in the absence of solvent and ∼5% for that carried out in chloroform).

The ^{31}P NMR analysis of the sample taken immediatly after the start of the reaction was surprising because it revealed the instantaneous formation of high proportions of the regioisomer corresponding to the fixation of the phosphorated group on the more substituted carbon of the oxirane, that is **4** (Figure 9). Until now, the adduct **4** was not identified in the crude mixtures characterized after 24 h of reaction, because it is immediately transformed into dioxaphospholane.

The kinetic curves (Figure 8) show the evolution of the contents in ethephon **1**, dioxaphospholanes **5**, 1:1 phosphorated 1:1 adducts **3** and **4**, versus time (the secondary phosphorated derivatives were taken into account in the calculation of the proportions, but they are not represented on the graphs).

These graphs show, as well without solvent as in chloroform, that the reaction is excessively fast since a significant ethephon consumption, about 50%, is observed immediatly after the start of the reaction. Thereafter, the ethephon consumption does not progress any more, which is explained by the rearrangement reactions of part of the oxirane rings (the increase of ethephon content of about 10%, which is noticed during the first 30 min of the reaction carried out in chloroform is probably due to the hydrolysis of part of the phosphorated 1:1 adducts according to eq 9). It is especially significant to note that it is the regioisomer **4**, that is the 1:1 adduct with the phosphorated group fixed on the most substituted carbon of the oxirane, which really results from the addition of **1** onto **2**, whereas this same regioisomer is not present after 24 h of reaction. It is also important to specify that the totality of **1** is consumed during the first minutes of the reaction, which explains why the proportion of residual ethephon remains almost constant thereafter, this proportion corresponding to that of **1** transformed in nonphosphorated secondary derivatives.

Thereafter, an evolution of the mixture composition in 1:1 phosphorated adducts formed is noticed since the initially formed regioisomer **4** disappears gradually to reach a final proportion of 5%. At the same time, the dioxaphospholanes **5** and the regioisomer **3** appear within the first seconds of the reaction. As the global proportion in dioxaphospholanes increases during the first 2 h and then decreases, that of the regioisomer **3** follows a constant increase during the time to reach respectively 30% after 8 h of reaction in $CDCl_3$ and 25% without solvent.

Consequently, the formation of the dioxaphospholanes **5** and afterward, that of the 1:1 adduct **3** in which the phosphorated entity is on the less substituted carbon of the oxirane ring, would be the result of several successive conversions from the regiosiomer **4** initially formed. Because the proportions of dioxaphospholane adducts **5** decrease after 2 h of reaction, it was deduced that the formation of the regiosiomer **3** observed after long durations of reaction occurred from the dioxaphospholane intermediate.

From these results, a mechanism was suggested (Figure 10). The addition of ethephon on the epoxides would occur according to the following way. Initially, after acid activation of the oxirane ring, a regioselective binding of the phosphorated group on the most hindred carbon of the oxirane ring, that is the most stable carbocation, leads to the 1:1 adduct **4**. Thereafter, **4** gives the dioxaphospholane **5** by elimination of a molecule of water.[6] The dioxaphospholane adduct **5**, very sensitive to acid hydrolysis, can then generate the regioisomer **3** which is more stable than **4** (Figure 10).

The secondary reactions can be easily explained according to the acidity of the reaction medium and the presence of water formed in situ during the cyclization step which leads to the dioxaphospholane structure (Figure 10). The ketone **6** and the allylic alcohol **7** result from a rearrangement of the epoxide, a well-known reaction that can occur in acid medium[11−13] (eq 8). The

(9) Pouchet, C. J.; Behnke, J. *The Aldrich Library of ^{13}C and ^{1}H NMR*, 1993.
(10) Iranpoor, N.; Baltork, I. M.; Zardaloo, F. S. *Tetrahedron* **1991**, *47(47)*, 9861.

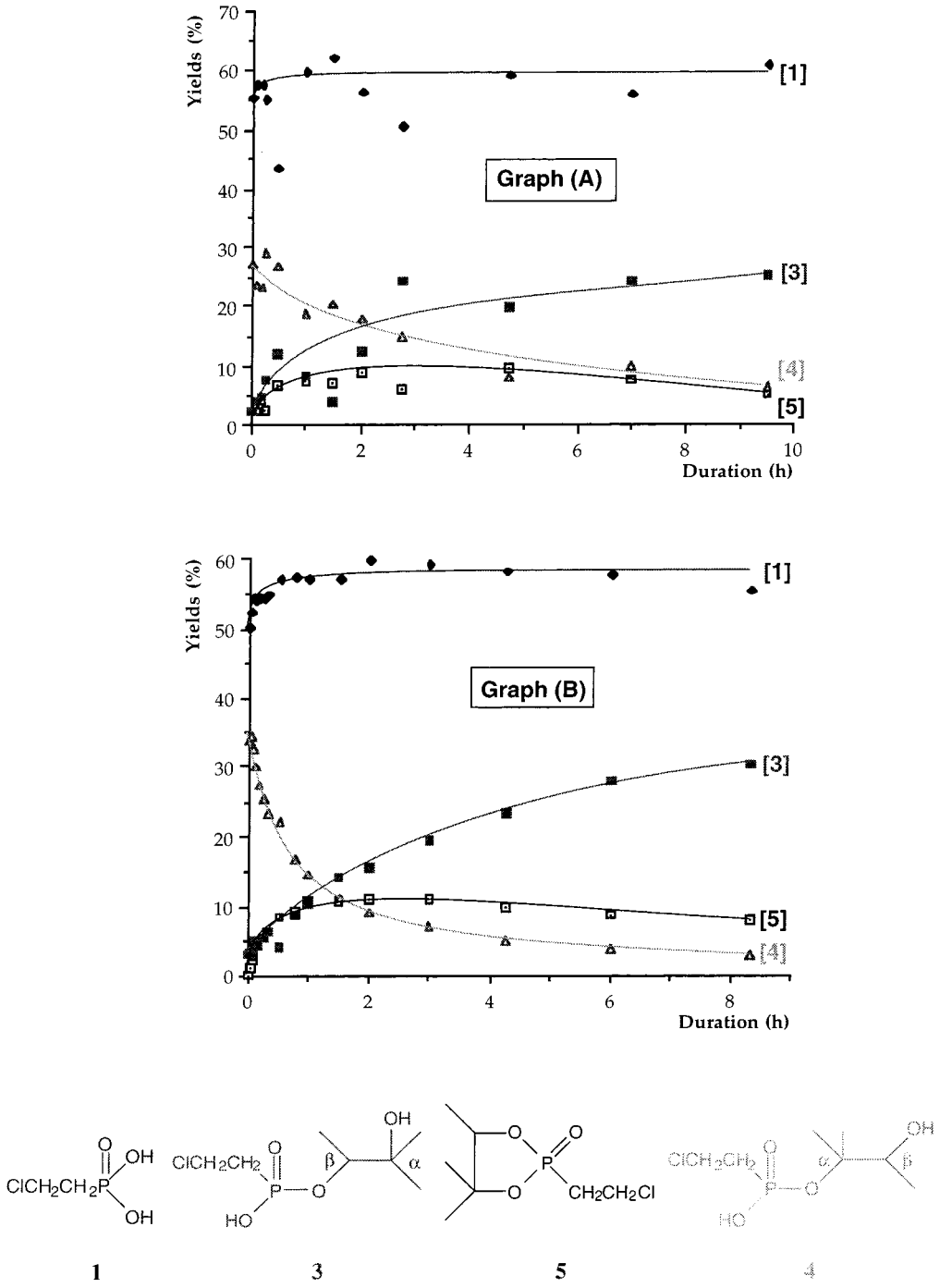


Figure 8. Kinetic study of the addition of **1** onto **2**, respectively, without solvent (graph A) and in $CDCl_3$ (graph B).

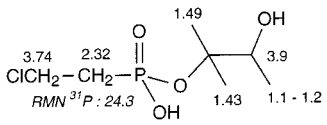


Figure 9. ^1H and ^{31}P NMR characteristics of **4** ($CDCl_3$, δ in ppm).

origin of the α,β-diol **8** is more uncertain. However, thanks to the information obtained from the kinetic study, it is probable that it results from the hydrolysis of the C−O−P bond of **4** (eq 9).

In summary, we have found that the addition of 2-chloroethylphosphonic acid **1** onto trialkyl-substituted oxirane rings occurs with formation of two categories of products: (1) organophosphorated adducts of type 1:1 adduct and dioxaphospholane (formation of diastereomers), issued from the addition of **1** on the oxirane of **2**; (2) nonphosphorated derivatives including allylic alcohol and ketone (formed by rearrangement of **2**) and α,β-diol (probably issued from the acid hydrolysis of the phosphorated 1:1 adduct formed in first).

From the kinetic study of the addition of **1** onto **2**, it was possible to understand the various mechanisms that

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(12) Maruoka, K.; Bureau, R.; Ooi, T.; Yamamoto, H. *Synlett.* **1991**, 491.
(13) Smith, J. G. *Synthesis* **1984**, 629.

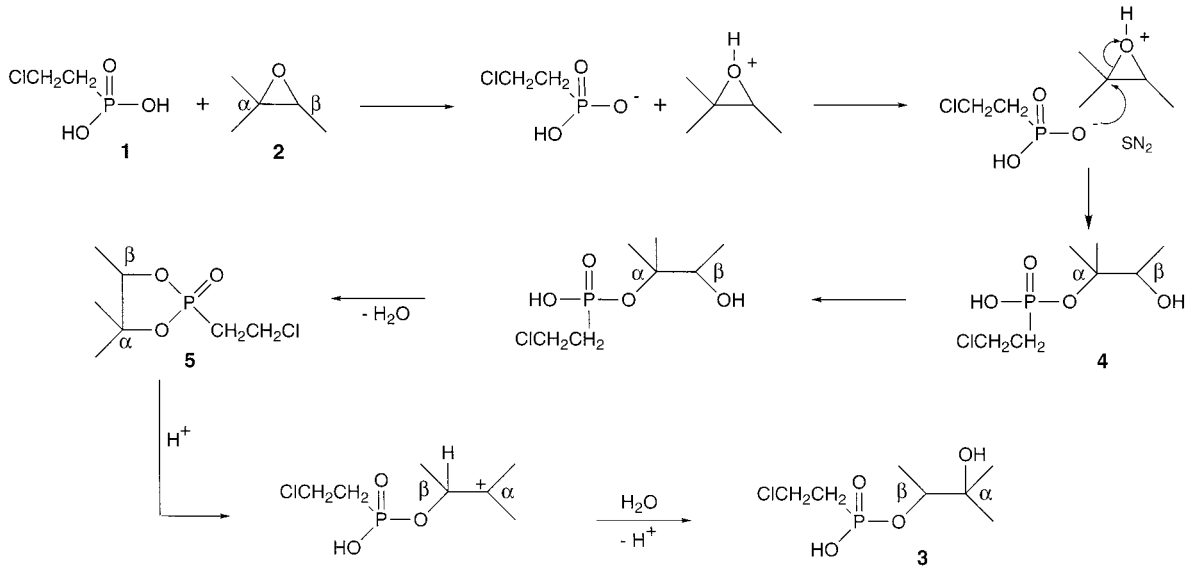
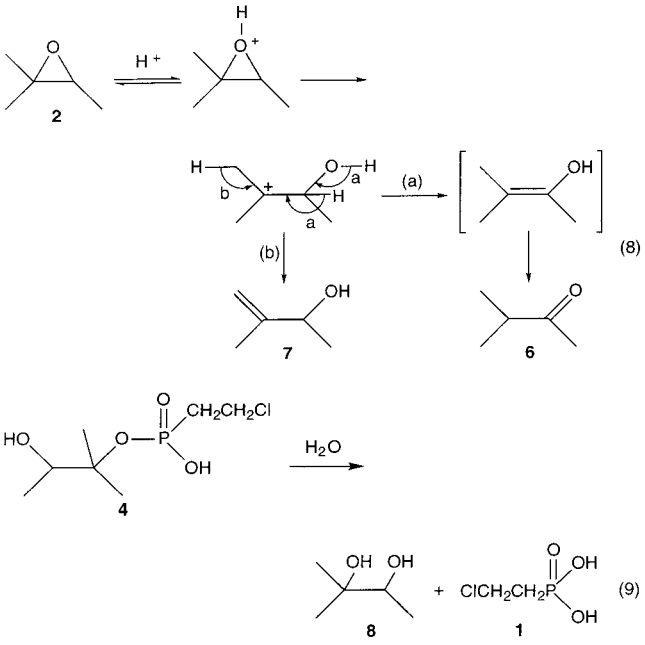


Figure 10. Mechanism of the addition of **1** onto **2**.



are involved during the reaction and, especially, to highlight that the formation of the 1:1 adduct **3** with the phosphorated group on the less substituted carbon of the initial oxirane is the result of several chemical conversions starting from the regiosisomer **4** formed instantaneously after the start of the reaction.

Experimental Section

General Materials and Methods. 2-Methyl-2-butene **2** (98% purity) was purchased from Aldrich Chemical Co and used without further purification, as well as deuterated chloroform-*d* (99.8% purity; Spectrométrie Spin et Techniques). 2-Chloroethylphosphonic acid **1** was prepared according to the method previously described.[14,15] All other reagents were obtained from commercial sources and were used without further purification. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AC 400 (400.13, 100.62, and 161.98 MHz, respectively) in $CDCl_3$. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane (TMS) as internal standard [H_3PO_4 in ^{31}P NMR], and coupling constants are reported in hertz. 2D ^{1}H/^{13}C correlated spectroscopy was performed on a Bruker DPX 200 Fourier transform spectrometer operating at 200.13 MHz for ^{1}H and at 50.32 MHz for ^{13}C, by using the XH-CORR Bruker program. Fractionations by semipreparative HPLC were realized with a Waters Delta Prep 3000 apparatus equipped with a μBondapack C18 column (19 mm i.d. and 15 cm in length; particle size: 10 μm) and a Waters R 401 differential refractometer detector. IR spectra were recorded on a Fourier transform Perkin-Elmer 1750 spectrometer in the 4000−500 cm^{-1} range (liquid films samples between two KBr or NaCl cells).

Epoxidation of 2-Methyl-2-butene. A 39.7 mmol portion of 2-methyl-2-butene in 100 mL of dichloromethane was introduced in a round-bottomed flask equipped with a magnetic stirrer and a dropping funnel. The reactor was placed in a bath thermostated at 0 °C. Then, a solution of 52.9 mmol (9.12 g) of *m*-chloroperbenzoic acid (75% purity) in 100 mL of dichloromethane was slowly added. After 6 h of stirring, the *m*-chlorobenzoic acid formed was removed by filtration. The filtrate was washed with an aqueous solution of 10% $Na_2S_2O_3$ to eliminate the peracid excess, a solution of $NaHCO_3$ (5%), then with distilled water until neutral pH. Afterward, the organic layer was dried on anhydrous magnesium sulfate. After filtration and evaporation of dichloromethane in a vacuum, the epoxidized product **2** was isolated by distillation [$Eb_{(760\ mmHg)}$ = 70 °C], yield = 40%. Characterization of **2**: ^{1}H NMR ($CDCl_3$) δ 1.27 (d; CH_3 on the CH of the oxirane ring), 1.28 and 1.31 (2 s; CH_3 on the C of the oxirane ring), 2.85 (q; CH of the oxirane ring); ^{13}C NMR ($CDCl_3$) δ 13.93 (s; CH_3 on the CH of the oxirane ring), 18.18 and 24.45 (2 s; CH_3 on the C of the oxirane ring), 53.13 (s; CH of the oxirane ring), 57.84 (s; C of the oxirane ring); IR (KBr; cm^{-1})[16] 2964 (ν_{CH}), 1461 (asym), 1378 (sym) (δ_{CH}), 1255 ($\nu_{P=O}$), 860 (δ_{CO}).

Addition of 1 onto 2. Equimolecular quantities of **1** and **2** (1.38 mmol of each reagent) were placed in a 10 mL Pyrex glass tube equipped with a magnetic stirrer and closed by a screwed stopper with a joint of sealing covered with Teflon. The reaction was carried out without solvent and then in $CDCl_3$. The reaction mixture was stirred at 20 °C for 24 h and then analyzed by NMR.

Synthesis of the Dioxaphospholane (5). A 1.08 mmol portion of **8** and 2.16 mmol of 2,6-dimethylpyridine in 5 mL of

(14) Cauret, L.; Brosse, J. C.; Derouet, D.; de Livonnière, H. *Synth. Commun.* **1997**, *27*, 647.

(15) Cauret, L.; Brosse, J. C.; Derouet, D.; de Livonnière, H. *Bull. Soc. Chim. Fr.* **1997**, 463.

(16) Socrates, G. *Infrared Characteristic Group Frequencies*; John Wiley & Sons Ltd.: New York, 1980.

benzene were placed, under nitrogen atmospohere, in a round-bottomed flask equipped with a magnetic stirrer and a dropping funnel. The reaction mixture was cooled at −5 °C by using an ice bath, and 1.08 mmol of 2-chloroethylphosphonyl-dichloride in 5 mL of benzene was added dropwise under stirring for about 3 h. At the end of the addition, the stirring was maintained for 2 h, and then the amine chlorohydrate was separated from the solution by centrifugation. The liquid layer was isolated, and then the benzene was evaporated in a vacuum with a rotating evaporator, yield 95%.

Characterization of 2-(2-Chloroethyl)-4,4,5-trimethyl-2-oxo-1,3,2-dioxaphospholane (5) (Figure 3). Diastereomer **5a** (*R*,*S* or *S*,*R*): ^{1}H NMR ($CDCl_3$) δ 1.33 [dt; CH_3(a); $^3J_{HH}$ = 6.9 Hz], 1.31 [s; CH_3(b)], 1.55 [s; CH_3(c)], 2.45 (dt; CH_2P; $^3J_{HH}$ = 7.9 Hz; $^2J_{HP}$ = 18.2 Hz), 3.75 (dt; $ClCH_2$; $^3J_{HH}$ = 7.9 Hz; $^2J_{HP}$ = 12.2 Hz), 4.54 (dq; CH−O−P; $^3J_{HH}$ = 6.4 Hz; $^3J_{HP}$ = 2.1 Hz); ^{13}C NMR ($CDCl_3$) δ 15.47 [s; CH_3(a)], 22.05 [s; CH_3(b)], 26.31 [d; CH_3(c); $^3J_{HP}$ = 5.7 Hz], 32.01 (d; CH_2P; $^1J_{PC}$ = 128.7 Hz), 37.62 (s; $ClCH_2$), 82.01 (s; CH−O−P), 85.10 (s, COP); ^{31}P NMR ($CDCl_3$) δ 39.3. Diastereomer **5b** (*R*,*R* or *S*,*S*): ^{1}H NMR ($CDCl_3$) δ 1.39 [d; CH_3(a); $^3J_{HH}$ = 6.4 Hz], 1.42 [s; CH_3(b)], 1.48 [s; CH_3(c)], 2.45 (dt; CH_2P; $^3J_{HH}$ = 7.9 Hz; $^2J_{HP}$ = 18.2 Hz), 3.80 (dt; $ClCH_2$; $^3J_{HH}$ = 7.9 Hz; $^2J_{HP}$ = 11.3 Hz), 4.32 (dq; CH−O−P; $^3J_{HH}$ = 6.4 Hz; $^3J_{HP}$ = 1.9 Hz); ^{13}C NMR ($CDCl_3$) δ 15.62 [s; CH_3(a); $^3J_{HP}$ = 8.5 Hz], 25.95 [d; CH_3(b); $^3J_{HH}$ = 8.4 Hz], 22.00 [s; CH_3(c)], 30.90 (d; CH_2P; $^1J_{PC}$ = 135.04 Hz), 37.49 (s; $ClCH_2$), 83.82 (s; CH−O−P), 86.70 (s, COP); ^{31}P NMR ($CDCl_3$) δ 39.1.

Synthesis of 2,3-Hydroxy-2-methylbutane (8). Water (5 mL) and cerium ammonium nitrate (10% in weight compared to the epoxide) were placed in a 10 mL Pyrex glass tube equipped with a magnetic stirrer, and then 7 mmol of **2** was added under rapid stirring. The glass tube was closed by a screwed stopper with a joint of sealing covered with Teflon, and stirring was maintained for about 2 h. The aqueous layer was saturated with NaCl, and the diol was extracted with ether. The organic layer was dried (anhydrous Na_2SO_4) and concentrated under vacuum to give the corresponding crude diol, which was purified by using semipreparative HPLC (column C18, eluent 60:40 methanol/water). Characterization of **8**: ^{1}H NMR ($CDCl_3$) δ 1.08 [d; CH_3 in α of CH(OH); $^3J_{HH}$ = 6.3 Hz], 1.10 and 1.30 [2 s; CH_3 in α of C(OH)], 3.55 [q; tertiary H of CH(OH)]; ^{13}C NMR ($CDCl_3$) δ 17.7 [s; CH_3 in α of CH(OH)], 22.75 and 26.61 [s; CH_3 in α of C(OH)], 73.42 [s; C(OH)], 74.36 [s, CH(OH)].

NMR Characterizatics of the Derivatives 6 and 7.[9] 3-Methylbutan-2-one**(6)**: ^{1}H NMR ($CDCl_3$) δ 1.10 (d; CH_3 in α of CH), 2.15 (s; CH_3 in α of C═O), 2.60 (m; CH); ^{13}C NMR ($CDCl_3$) δ 17.5 (s; CH_3 in α of CH), 26.8 (s; CH_3 in α of C═O), 40.9 (s; CH), 211.5 (s; C═O). 3-Methyl-3-buten-2-ol **(7)**: ^{1}H NMR ($CDCl_3$) δ 1.20 [d; CH_3 in α of CH(OH)], 1.75 (s; CH_3 on C═C), 4.20 [m; tertiary H of CH(OH)], 4.80−4.95 (d; C═CH_2); ^{13}C NMR ($CDCl_3$) δ 18 (s; CH_3 on C═C), 22 [s; CH_3 in α of CH(OH)], 65 [s; CH(OH)], 115 (s; −$C(CH_3)$═), 145 (s; ═CH_2).

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