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Research Article

Environmentally Friendly and Regioselective One-Pot Synthesis of Imines and Oxazolidines Serinol Derivatives and Their Use for Rubber Cross-Linking

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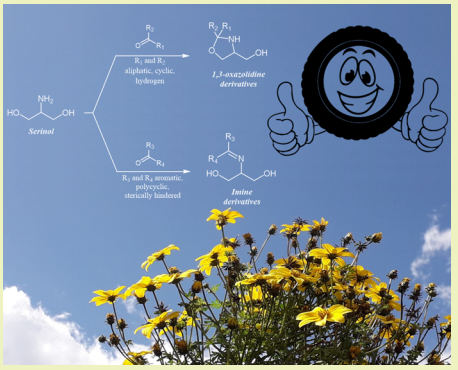
ABSTRACT: High-yield regioselective synthesis of imines and oxazolidines derivatives of 2-amino-1,3-propandiol (serinol) was achieved by performing the reaction with aldehydes and ketones, in the absence of solvents and catalysts. Only imines were obtained when the carbonyl compound was aromatic and/or sterically hindered and when conjugated double bonds were formed. 1,3-Oxazolidines were specifically obtained with either aldehydes or ketones with limited steric hindrance. The "green" reaction conditions here adopted for the synthesis of these classes of derivatives are not due to the structural and functional peculiarity of the serinol as a reactant and can also be extended to lipophilic amines with the same good results in terms of yield and selectivity. A revision of the mechanism typically accepted in the presence of solvent and catalysis is proposed, and the quantum mechanics calculations applied to some derivatives are in good agreement with the proposed rationalizations of the selectivity observed. Serinol itself and the imine and oxazolidine derivatives were used, in place of guanidine, as accelerators in compounds based on diene rubbers and silica, suitable for application in tire treads with low environmental impact. Efficient sulfur-based cross-linking and composites with a low dissipation of energy were obtained. The oxazolidine and imine appear to act as protective groups of the serinol primary amine. This work paves the way for the selective synthesis of biosourced families of chemicals, which could be used for large-scale applications, such as the one in rubber compounds, replacing toxic oil-based chemicals.



KEYWORDS: *Serinol derivatives, Imines, 1,3-oxazolidines, isomers, Replacement of guanidines, rubber compounds, sulfur based cross-linking, accelerators*

INTRODUCTION

2-Amino-1,3-propanediol, known as serinol (S), is one of most interesting derivatives of glycerol not yet fully valorized as a versatile starting material in organic synthesis and as an additive for material applications, such as composite materials. Serinol is a nontoxic, odorless, biodegradable chemical substance, which can be obtained from both natural and petrochemical feedstocks.[1−7] In fact, serinol[8] has been synthesized from oil-based precursors such as 2-nitro-1,3-propanediol,[9−11] nitromethane,[12] dihydroxyacetone (DHA),[13] dihydroxyacetone oxime,[14−16] and 5-amino-1,3-dioxane,[17] but it can also be prepared from the biomolecule glycerol.[8] It was found to occur in renewable sources, such as sugar cane (*Saccharum officinarum*) or as a metabolite from sponge (*Stelletta Inconspicua*).[18] Moreover, since serinol is the structural analogous of serin, its preparation starting from this amino acid has been reported.[19] The chemoselectivity of such a prochiral molecule, due to the presence of hydroxyl and amino functional groups, is a valuable tool for developing selective and innovative synthetic strategies.

It is well known that amino alcohols such as serinol exhibit a multitude of applications in medicine and chemical industries.[8,17] A key aspect in amino alcohol chemistry is the selective ability of amino and hydroxyl groups to give rise either to independent or to cooperative reactions to form heterocyclic products.

In scientific literature, the reaction of ketones and aldehydes with amino alcohols is well documented.[20−28] The condensation reaction of a beta amino alcohol with a carbonyl compound allows one to obtain imine and also 1,3-oxazolidine.

Imines, also known as Schiff bases,[29] are chemical compounds containing a carbon−nitrogen double bond. Imines can be prepared by the self-condensation of amines

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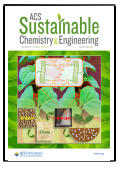
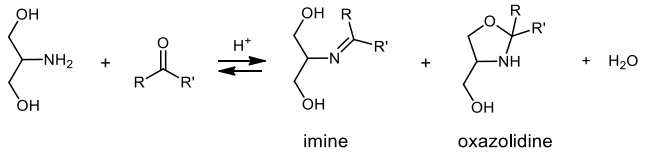


upon oxidation[30,31] but are traditionally synthesized from the reaction of primary amines with aldehydes or ketones,[29] in the presence of an acid catalyst, with elimination of a water molecule. Acid catalysts and water removal play key roles to significantly increase the reaction yields, which can have values as high as 95%.

The synthesis of the oxazolidine ring is an important subject in organic chemistry because they are structural moieties in many biologically active compounds. A general synthetic method for the synthesis of 1,3-oxazolidines is the condensation of 1,2-amino alcohols with carbonyl compounds in the presence of an acid catalyst.[28]

By using *C*-substituted serinol, ring chain tautomerism occurring after the nucleophilic attack of a hydroxyl group was documented. Mixtures of oxazolidines and imines were obtained, as summarized in Scheme 1.

Scheme 1. Preparation of Mixture of Imines and Oxazolidines by Condensation of Serinol and Carbonyl Compounds in Presence of Acidic Catalyst



It would be highly desirable to identify reaction conditions suitable to promote the selective synthesis of either imines or 1,3-oxazolidines, starting from serinol as the amino alcohol compound.

This work had the aim to develop synthetic strategies to reach this goal, by adopting reaction conditions inspired by the basic principles of green chemistry.[32] Indeed, in green chemistry, the best solvent is no solvent. In particular, attention was focused on the possibility to carry out reactions in the absence of a specific catalytic species and without solvent to improve the reaction mass efficiency and to reduce the need of recycling. Aldehydes and ketones, aliphatic and aromatic, were tested as the carbonyl substrate devising some details of the reaction mechanism useful to rationalize the results.

Serinol itself and the imine derivative obtained through the reaction with 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (camphor) (SCam) were tested as accelerators in sulfur-based cross-linking of rubbers: poly(1,4-*cis*-isoprene) from *Hevea brasiliensis*, better known as natural rubber (NR), poly(styrene-*co*-butadiene) (styrene butadiene rubber, SBR), and poly(1,4-*cis*-butadiene) (BR). NR is the most important rubber,[33] with about 60% of the global rubber consumption, about 13 million ton/year. SBR is the most important synthetic rubber, and BR is the most important synthetic diene rubber. The largest application of rubbers is, by far, for tire compounds and, among them, for tire tread. To achieve the required dynamic-mechanical properties, rubbers have to be cross-linked, with sulfur-based systems. Serinol and serinol derivatives could be used as accelerators[34] of the sulfur-based cross-linking (vulcanization) in place of substances such as 1,3-diphenylguanidine (DPG), which presents concerns regarding human health. Composites were prepared based on SBR, NR, and BR as the rubbers and silica as the filler. The behavior of vulcanization of serinol and serinol derivatives such as imine, oxazolidine, bisoxazolidine, and amide is presented, in comparison with composites without accelerator and based on DPG.

EXPERIMENTAL SECTION

Materials and Methods. Reagents and solvents, commercially available, were purchased and used without further purification. 2-Amino-1,3-propanediol was kindly provided by Bracco and 2,5-hexanedione from Merck Schuchardt. For the preparation of imines and oxazolidines, the ingredients were camphor, acetone, cyclohexanone, fluorenone, acetophenone, benzophenone, cinnamaldehyde, 3-methylbenzaldehyde, formaldehyde, 4-methyl-pentan-2-one, *n*-octylamine, propanoyl chloride, trimethylamine, and CH_2Cl_2 (Aldrich). For the preparation of composites with natural rubber, the ingredients were poly(1,4-*cis*-isoprene) from *Hevea brasiliensis* (NR) (EQR−E.Q. Rubber, BR-THAI, Eatern GR. Thailandia, Chonburi) with the trade name STR20; styrene−butadiene rubber (S-SSBR) from solution; commercial grade Styron 4630 (from Styron), 25% as styrene content; polybutadiene, commercial grade Europrene neocis (from Polimeri Europa), ZnO (Zincol Ossidi); stearic acid (Sogis). sulfur (Solfotecnica), bis[3-(triethoxysilyl)-propyl]tetrasulfide (silane) from Evonik; silica is ZEOSIL 1165MP (supplier SOLVAY RHODIA OPERATIONS); aliphatic oil from Eni (MES oil); *N*-(1,3-dimethylbutyl)-*N*′-phenyl-*p*-phenylenediamine from Crompton (6-PPD); *N*-*tert*-butyl-2-benzothiazyl sulfenamide (TBBS) from Flexsys; and 1,3-diphenylguanidine (Rhenogran DPG) from Rhein Chemie.

Instrumental. ^{1}H NMR and ^{13}C NMR spectra were registered on a Bruker 400 MHz (100 MHz ^{13}C) instrument at 298 K. Chemical shifts were reported in ppm with the solvent residual peak as the internal standard (DMSO-d_6: δ_H = 2.50 ppm; $CDCl_3$: δ_H = 7.26 ppm). Mass spectra were recorded by using electrospray ionization (ESI) with a Bruker Esquire 3000 plus ion-trap mass spectrometer instrument equipped with an ESI Ion Trap LC/MSn System. The instrument for GC-MS analysis was an Agilent 5973 network mass selective detector with a 6890 Series GC system mass spectrometer. The column used for all analyses was a J&W GC Column HP-5MS [(5%-phenyl)-methylpolysiloxane] 30 m, 0.25 mm internal diameter, and 0.25 μm film thickness.

General Procedure for Synthesis of 1,3-Oxazolidine Derivatives. Aldehyde or ketones **1a−1d** in excess (**1b**, 10 mL (136 mmol); **1c**, 2 mL (16 mmol); **1d**, 20 mL (192 mmol)), Serinol (1 g, 10.98 mmol), and Na_2SO_4 (1 g, as drying agent) were placed in a round-bottomed flask. The reaction mixture was stirred at room temperature overnight. Then, the mixture was first filtered and the excess of aldehyde or ketone was removed at reduced pressure. Products **2a−2d** were in yields from 56% to 95%.

*1,3-Oxazolidin-4-ylmethanol (**2a**).* Pale yellow oil (0.63 g, 56% yield). ^{1}H NMR ($CDCl_3$) δ (ppm): 4.45−4.37 (m, 2H, C$\underline{H}_{2cycl.}$), 4.09−3.99 (m, 1H, C$\underline{H}_{2cycl.}$), 3.85−3.75 (m, 1H, C$\underline{H}_{2cycl.}$), 3.70−3.61 (m, 1H, C$\underline{H}_{cycl.}$), 3.53−3.41 (m, 1H, C$\underline{H}_2$OH), 3.39−3.31 (m, 1H, C$\underline{H}_2$OH). ^{13}C NMR ($CDCl_3$) δ (ppm): 84.78, 71.45, 67.19, 61.87.

*(2,2-Dimethyl-1,3-oxazolidin-4-yl)methanol (**2b**).* Yellow oil (1.30 g, 90% yield). ^{1}H NMR (DMSO-d_6,) δ (ppm): 4.63 (br s, 1H, OH), 4.28 (br s, 1H, NH), 3.73−3.69 (t, 1H), 3.48−3.45 (dd, 1H), 3.39−3.35 (q, 1H), 3.36−3.32 (dd, 1H), 3.23−3.19 (m, 1H), 1.27(s, 3H), 1.16 (s, 3H). ^{13}C NMR ($CDCl_3$) δ (ppm): 94.93, 66.61, 61.53, 59.12, 27.41, 26.28.

*(2-Isobutyl-2-methyl-1,3-oxazolidin-4-yl)methanol (**2c**).* Colorless oil (1.81 g, 95% yield). ^{1}H NMR ($CDCl_3$) δ (ppm): 3.90−3.81 (m, 1H), 3.71−3.51 (m, 4H, C$\underline{H}_{2cycl.}$, C$\underline{H}_{cycl}$, C$\underline{H}_2$−OH), 2.84 (br s, 1H, OH), 1.83−1.65 (m, 1H), 1.58−1.41 (m, 2H), 1.23 (s, 3H), 0.94 (d, 6H). ^{13}C NMR ($CDCl_3$); δ (ppm): 97.2, 66.7, 64.43, 61.8, 49.2, 27.6, 24, 23.

*1-Oxa-4-azaspiro[4.5]decan-3-ylmethanol (**2d**).* Yellow pale oil (1.69 g, 90% yield). ^{1}H NMR ($CDCl_3$) δ (ppm): 3.85−3.82 (t, 1H, CH−C$\underline{H}_2$−O), 3.63−3.59 (q, 1H, CH−C$\underline{H}_2$−OH J= 4.03 Hz), 3.51−3.49 (dd, 2H, C$\underline{H}_2$−OH, *J* = 3.30 and 5.50 Hz), 3.47−3.45 (dd, 1H, C$\underline{H}_2$−OH, *J* = 3.30 and 5.50 Hz), 1.62−1.42 (m, 9H,

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$-CH_2-_{cyclohexyl}$), 1.33−1.23 (m, 1H, $-CH_2-_{cyclohexyl}$). ^{1}H NMR (DMSO-d_6) δ (ppm): 3.72−3.68 (t, 1H, −OH), 3.48−3.34 (m, 4H, CH_2−O), 3.33−3.26 (m, 1H, CH−CH_2−), 1.57−1.27 (m, 10H, $-CH_2-_{cyclohexyl}$). ^{13}C NMR (DMSO-d_6) δ (ppm): 95.26, 66.25, 61.41, 58.58, 37.00, 35.41, 25.05, 23.58, 23.32.

GC-MS (solvent acetone): 171 (M+), 154, 142, 128(100), 123, 115, 110, 98, 84, 74, 72, 69, 55, 41. ESI mass spectra, m/z (MeOH): 194.0 ([M + Na]$^+$), 172.0 ([M + H]$^+$). Mass−mass spectra of 172.0, m/z: 154.0, 142.0, 110.1, 98.1, 84, 74.2 (100).

Synthesis of Imine Derivatives. *Synthesis of 2-((E)-((E)-3-Phenylallylidene)amino)propane-1,3-diol (**3e**).* **1e** (6.61g, 50 mmol) and serinol (4.55 g, 50 mmol) were poured in a 100 mL round-bottomed flask equipped with a magnetic stirrer. The mixture was left to stir at 100 °C for 2 h. After this time, the reaction mixture was cooled to room temperature. Pure product was obtained by washing yellow crystals using water. White crystals were recrystallized from diethyl ether (9.42 g, 92% yield).

^{1}H NMR ($CDCl_3$) δ (ppm): 8.14 (d, 1H, CHN, J = 8.5 Hz), 7.45 (dd, 2H, CH, J = 8.1 Hz; J = 1.7 Hz), 7.38−7.33 (m, 3H, CH), 6.99 (d, 1H, CH, J = 16.0), 6.89 (dd, 1H, CH, J_1 = 16.0 Hz; J_2 = 8.5 Hz), 3.84−3.86 (m, 4H, CH_2), 3.43−3.38 (m, 1H, CH); ^{13}C NMR ($CDCl_3$) δ (ppm): 165.3, 143.3, 135.4, 129.4, 128.8, 127.3, 73.3, 63.7.

*Synthesis of (E)-2-((3-Methylbenzylidene)amino)propane-1,3-diol (**3f**).* 1f (1 g, 8.33 mmol), serinol (0.758 g, 8.33 mmol) and Na_2SO_4 (1g) were poured in a 50 mL round-bottom flask equipped with magnetic stirrer. The mixture was left to stir at 25 °C for 12 h. After this time the reaction mixture was first filtered. An orange oil was obtained (1.56 g, 98% yield).

^{1}H NMR ($CDCl_3$) δ (ppm): 8.14 (s, 1H, N=CH), 7.40−7.38 (d, 2H, CH_{Ar}), 7.29−7.12 (m, 3H, CH_{Ar}), 4.01 (br s, 1H, OH), 3.79−3.61 (m, 4H, CH_2−OH), 3.42−3.30 (m, 1H, CH), 2.30 (s, 3H, CH_3; ^{13}C NMR ($CDCl_3$) δ (ppm): 163.8, 137.8, 135.1, 131.5, 128.6, 128.1, 125.4, 73.6, 62.8, 20.9.

*Synthesis of 2-((1-Phenylethylidene)amino)propane-1,3-diol (**3g**).* Serinol (1 g, 10.98 mmol) and **1g** (1.31 g, 10.98 mmol) were placed in a 20 mL glass vial. The reaction mixture was heated to 130 °C and maintained at this temperature under vigorous stirring for 2 h. Then, the mixture was cooled to room temperature. The white crystals obtained were recrystallized from diethyl ether (1.76g, 83% yield).

^{1}H NMR (DMSO-d_6) δ (ppm): 7.64 (m, 2H), 7.52 (m, 3H), 4.5 (t, 2H, −OH), 3.68 (m, 1H), 3.45 (m, 4H), 1.9 (s, 3H). ^{13}C NMR (DMSO-d_6) δ (ppm): 166.2, 140, 132.9, 128.2, 128, 66.3, 62.9, 19.1.

*Synthesis of 2-((9H-Fluoren-9-ylidene)amino)propane-1,3-diol (**3h**).* **1h** (1.8 g, 9.98 mmol) and serinol (0.910 g, 9.98 mmol) were poured in a 50 mL round-bottomed flask equipped with a magnetic stirrer. The mixture was left to stir at 130 °C for 6 h. After this time, the reaction mixture was cooled to room temperature. Then, toluene was first added to the mixture, and the obtained solution was refluxed for 5 min. White crystals were recrystallized from toluene (2.02 g, 80% yield).

^{1}H NMR (DMSO-d_6) δ (ppm): 8.13−8.10(d, 1H, Ar−CH), 7.87−7.86 (d, 1H, Ar−CH), 7.79−7.77(d, 1H, Ar−CH), 7.71−7.70(d, 1H, Ar−CH), 7.53−7.44 (2t, 2H, Ar−CH), 7.38−7.30 (2t, 2H, Ar−CH), 4.70- 4.64 (m, 3H), 3.63−3.58 to 3.82−3.78 (two dd, 4H). ^{13}C NMR (DMSO-d_6) δ (ppm) = 162.4. 143.3, 140.7, 138.5, 131.8, 131.4, 128.7, 128.2, 122.8, 121.0, 120.1, 66.0, 63.5.

ESI mass m/z (MeOH): 277 ([M + Na]$^+$) 254([M + H]$^+$). mp = 146 °C.

*Synthesis of 2-((Z)-((1S,4R)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-ylidene)amino)propane-1,3-diol (**3i**).* Serinol (0.910 g, 9.98 mmol) and **1i** (2.0 g, 13.14 mmol) were placed in a 20 mL glass vial. The reaction mixture was heated to 170 °C and maintained at this temperature under vigorous stirring for 4 h. Then, the mixture was first cooled to room temperature and subsequently dissolved in hot hexane (3× 5 mL) to remove the excess camphor. The so-obtained white crystals were recrystallized from hexane (1.57 g, 70% yield).

^{1}H NMR (DMSO-d_6) δ (ppm): 4.28−4.24 (m, 2H, OH), 3.54−3.44 (m, 2H, CH_2), 3.30−3.26 (m, 2H, CH), 3.26−3.19 (m, 2H, CH_2), 2.41−2.36 (dt, 1H, CH, J_1 = 16.7 Hz; J_2 = 7.5 Hz), 1.92 (d, 1H, CH, J = 16.7 Hz), 1.86 (t, 1H, CH, J = 8.6 Hz), 1.82−1.70 (m, 1H), 1.62−1.52 (m, 1H, CH), 1.31−1.24 (m, 1H, CH), 1.19−1.12 (m, 1H, CH), 0.84 (s, 3H, CH_3) 0.73 (s, 3H, CH_3).

^{13}C NMR (DMSO-d_6) δ (ppm): 180.5, 65.3, 63.0, 62.7, 53.0, 46.0,, 43.2, 35.4 31.9, 27.0, 19.3, 18.7, 11.5.

ESI mass spectra, m/z (rel. int.%) (MeOH): 248 ([M + Na]$^+$), 226 ([M + 1]$^+$). Mass−mass spectra of 226: m/z (rel. int.%): 226 (28), 208 (90), 196 (16), 190 (11), 183 (34), 178 (20), 170 (25), 164 (72), 152 (100), 143 (74), 135 (48), 122 (18), 107 (82), 102 (17), 96 (28), 93 (60), 81 (22), 74 (28). mp = 100−103 °C

*Synthesis of 2-((Diphenylmethylene)amino)propane-1,3-diol (**3j**).* In a 25 mL flask equipped with a magnetic stirrer and Claisen, 2.1 g of serinol (0.023 mol) and 3.78 g of **1j** (0.027 mol) were loaded. The mixture was heated at 180 °C. After 15 min, the water formed is removed by distillation. After 3 h, the mixture is cooled at room temperature. The viscous pale yellow oil obtained is dispersed in 10 mL of a mixture of water/cyclohexane = 1/1 for 1 h under vigorous stirring. The white solid formed was filtered and purified by crystallization from a mixture cyclohexane/toluene = 1/1. Yield: 85%.

^{1}H NMR (DMSO-d_6) δ (ppm): 7.52−7.24 (**3m**, 10H aromatic rings of benzophenone residue), 4.42 (t, 2H, −OH), 3.62−3.54 (m, H, CH_2−CHNR−CH_2), 3.51−3.40 (m, 3H, CH_2−CHNR-CH_2),

^{13}C NMR (DMSO-d_6) δ (ppm): 167.18, 139.73, 136.48, 129.52, 127.99, 127.95, 127.87, 127.70, 66.34, 62.63.

GC-MS, m/z (rel. int.%): 255 (M.$^+$ 0.1%), 224 (100%), 206 (10%), 194 (23%), 178 (43%) 167 (31%), 165 (33%), 105 (17%), 77 (15%). ESI mass spectra, m/z (MeOH): 533.1 [2M+Na]$^+$, 278.3 [M + Na]$^+$, 256.3 [M + H]$^+$. Mass mass spectra 256.3 m/z: 238.3, 220.2, 208.3, 194.2, 182.2 (100), 167.2, 130.2, 117.2, 104.3, 91.3, 74.5. mp = 176 °C

*Synthesis of (2Z,4E)-4-((1,3-Dihydroxypropan-2-yl)iminio)pent-2-en-2-olate (**3k**).* Serinol (0.91 g, 10 mmol) was dissolved in 10 mL of water. **1k** was added to this solution (1.1 g, 11 mmol), and the mixture was left to stir at room temperature for 18 h. Then, the water was removed by a rotary evaporator, and the yellow solid residue was crystallized from THF. Yield: 95%.

^{1}H NMR (DMSO-d_6) δ (ppm): 10.70−10.67 (d, 1H, R=NH-R J = 8.8 Hz.), 4.89 (s, 1H, RCH=COH−CH_3), 4.75 (dd, $-CH_2OH$, J = 4.8, 5.3 Hz), 3.54−3.40 (m, 1H, $HOCH_2CHCH_2OH$, J = 4.8, 5.3 Hz), 3.47−3.43(dd, 4H, $(HOCH_2)_2CH$, J = 4.8, 5.3 Hz), 1.93 (s, 3H, CH_3), 1.84 (s, 3H, CH_3). ^{1}H NMR (D_2O) δ (ppm): 4.39 (s, 1H, RCH=COH−CH_3), 4.05 (m, 1H, $HOCH_2CHCH_2OH$), 3.94−3.33 (m, 4H, $(HOCH_2)_2CH$), 2.26 (s, 3H, CH_3), 2.20 (s, 3H, CH_3). ^{13}C (DMSO-d_6) δ (ppm): 192.37, 162.35, 94.62, 60.94, 55.97, 28.48, 18.77.

ESI mass spectra, m/z (MeOH): 369 ([2M + Na]$^+$), 196 ([M + Na]$^+$), 174 (M + H]$^+$). Mass mass spectra 174 m/z (rel. int.%): 174 (100%), 156 (13%), 116.1 (45%). mp= 148 °C

Synthesis of N-(Diphenylmethylene)octan-1-amine. N-Octylamine (350 mg, 2.69 mmol) and **1j** (491 mg, 2.69 mmol) were placed into a 10 mL round-bottomed flask equipped with a magnetic stirrer. The reaction mixture was heated to 140 °C and maintained at this temperature under stirring for 20 h. Then, the mixture was cooled to room temperature. The so-obtained compound was a brown oil (793 mg, 94% analytical yield).

Synthesis of Bis-oxazolidines. *Synthesis of 4a,6a-Dimethylhexahydro-1,4-dioxa-6b azacyclopenta[cd]pentalene.* A mixture of 2,5-hexanedione (41.4 g, 0.36 mol) and serinol (30.0 g, 0.33 mol) was poured into a 100 mL round-bottomed flask equipped with magnetic stirrer. The mixture was then stirred at room temperature for 6 h. The so-obtained compound was a pale yellow oil (55.2 g, 99% yield).

^{1}H NMR (DMSO-d_6) δ (ppm): 3.94 (q, 1H, CH), 3.60 (m, 4H, CH_2), 1.93 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.28 (s, 6H, CH_3).

^{1}H NMR ($CDCl_3$, T = 305 K, δ ppm): 4.05 (dd, 2H, $-CH_2$ serinol), 3.74−3.67 (m, 3H, $-CH_2$ serinol + −CH serinol), 2.17−2.07 (m, 2H, $-CH_2$ pirrolydine), 1.88−1.78 (m, 2H, $-CH_2$ pirrolydine), 1.34 (s, 6H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 104.79, 69.49, 62.75, 35.26, 25.32.

ESI mass spectra, m/z (rel. int.%) (MeOH): 169.

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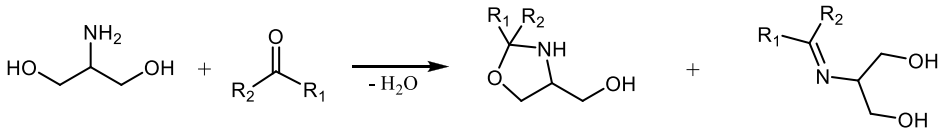
Table 1. Formulations of NR-Based Composites[a]

		Composite					
Ingredient	1	2	3	4	5	6	7
NR[b]	15.0	15.0	15.0	15.0	15.0	15.0	15.0
S-SSBR[c]	96.25	96.25	96.25	96.25	96.25	96.25	96.25
BR[d]	15.0	15.0	15.0	15.0	15.0	15.0	15.0
Silane[e]	5.2	5.2	5.2	5.2	5.2	5.2	5.2
Silica	65	65	65	65	65	65	65
Mes oil[f]	10	10	10	10	10	10	10
Stearic acid	2	2	2	2	2	2	2
ZnO	2.5	2.5	2.5	2.5	2.5	2.5	2.5
6-PPD[h]	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Sulfur	1.1	1.1	1.1	1.1	1.1	1.1	1.1
TBBS[g]	1.9	1.9	1.9	1.9	1.9	1.9	1.9
DPG[i]	0.0	2.4	0.0	0.0	0.0	0.0	0.0
S[j]	0.0	0.0	0.83	0.0	0.0	0.0	0.0
SCin[k]	0.0	0.0	0.0	2.04	0.0	0.0	0.0
SOxa[l]	0.0	0.0	0.0	0.0	1.2	0.0	0.0
DMHHP[m]	0.0	0.0	0.0	0.0	0.0	1.5	0.0
SAmide[n]	0.0	0.0	0.0	0.0	0.0	0.0	1.3

[a]Amounts are in parts per hundred rubber (phr). [b]Natural poly(1,4-*cis*-isoprene) (NR). [c]Styrene−butadiene rubber from solution. [d]Polybutadiene. [e]Bis[3-(triethoxysilyl)propyl]tetrasulfide. [f]Aliphatic oil. [g]*N*-*tert*-Butyl-2-benzothiazyl sulfenamide. [h]*N*-(1,3-Dimethylbutyl)-*N*′-phenyl-p-phenylenediamine. [i]1,3-Diphenylguanidine. [j]S: serinol. [k]SCin: imine of serinol with cinnamaldehyde. [l]SOxa: 1,3-oxazolidine of serinol with acetone. [m]DMHHP: tricyclic bis-oxazolidine of serinol with 2,6-hexanedione. [n]SAmide: serinol propanamide of serinol with propanoil chloride.

Scheme 2. Carbonyl Compounds 1 Used in This Work for the Synthesis of Serinol-Based Oxazolidines 2 and Imines 3



1

a $R_1 = R_2 = H$
b $R_1 = R_2 = CH_3$
c $R_1 = CH_3$, $R_2 = CH_2CH(CH_3)_2$
d $R_1 R_2 = (CH_2)_5$
e $R_1 = H$, $R_2 = CH{=}CH\text{-}C_6H_5$
f $R_1 = H$, $R_2 = CH_3\text{-}C_6H_5$
g $R_1 = CH_3$, $R_2 = C_6H_5$
h $R_1 R_2$ = 3,3'-biphenyl
i R_1COR_2 = camphor
j $R_1 = R_2 = Ph$
k $R_1 = CH_3$, $R_2 = CH_2(CO)CH_3$

2

a $R_1 = R_2 = H$
b $R_1 = R_2 = CH_3$
c $R_1 = CH_3$, $R_2 = CH_2CH(CH_3)_2$
d $R_1 R_2 = (CH_2)_5$

3

e $R_1 = H$, $R_2 = CH{=}CH\text{-}C_6H_5$
f $R_1 = H$, $R_2 = CH_3\text{-}C_6H_5$
g $R_1 = CH_3$, $R_2 = C_6H_5$
h $R_1 R_2$ = 3,3'-biphenyl
i R_1COR_2 = camphor
j $R_1 = R_2 = Ph$
k $R_1 = CH_3$, $R_2 = CH_2(CO)CH_3$

Synthesis of Hexahydro-2H-1,4-dioxa-2a[1]*-azacyclopenta[cd]-pentalene.* 2,5-Dimethoxytetrahydrofuran (1.32 g, 0.01 mol) was mixed with 0.1 N HCl (50 mL). The mixture was warmed to 55 °C for 30 min and then cooled at 20 °C and neutralized with $NaHCO_3$. Then, 0.82 g (0.009 mol) of serinol was added to the solution, and the mixture was left under stirring at room temperature overnight. The water was removed by a rotary evaporator, and the residue was treated with ethanol (5 mL). The mixture was filtered, and the solvent was removed by a rotary evaporator obtaining a pale yellow oil. The mixture was then distilled under vacuum at 40 °C collecting a colorless oil (1.0 g, 86% yield).

^{1}H NMR (DMSO-d_6) δ (ppm): 4.72 (br t, 2H, CH−O), 3.79−3.73 (m, 4H, $-CH_2-CH_2-$), 3.58−3.54 (m, 1H, $CH_2-CH-CH_2$), 2.00−1.87 (m, 4H, $CH_2-CH-CH_2$). ^{13}C NMR (DMSO-d_6) δ (ppm): 98.8. 71.58, 62.46, 28.66. ESI mass spectra, m/z (rel. int.%) (MeOH): 141.

Synthesis of *N*-(1,3-Dihydroxypropyl)-propionamide (SAmide). A 100-mL one-necked flask equipped with a magnetic stirrer was charged with 0.1 g (1.1 mmol) of serinol and 0.1 g (1.1 mmol) of acryloyl chloride at 0 °C. The mixture is stirred at this temperature for 30 min. After this time, 10 mL of CH_2Cl_2, 10 mL of water, and triethylamine (0.5 mL) were added. The organic phase was dried over Na_2SO_4, filtered, and solvent was removed at reduced pressure. Then, 0.11 g of product was obtained (67% yield).

Composites Based on Diene Rubbers and Silica as the Filler. Composites' recipes are shown in Table 1.

Preparation of the Composites. NR, S-SBR, and BR were put in an internal mixer of the Brabender type having a mixing chamber with a volume equal to 50 cc, and mastication was carried out at 145 °C for 1 min. Then silica, silane, stearic acid, and MES oil were added, mixing for a further 5 min and discharging the composite obtained at 150 °C. The composite prepared in this way was then put in the internal mixer at 50 °C, adding ZnO and 6-PPD, and mixing for 2 min. Then, sulfur and TBBS were added, mixing for a further 2 min. The composite was discharged at 65 °C. Further mixing was performed for 5 min, without adding any ingredient or adding either DPG or one of the alternative secondary accelerators (S, SCin, SOxal, DMHHP, SAmide). All the composites were finally homogenized by

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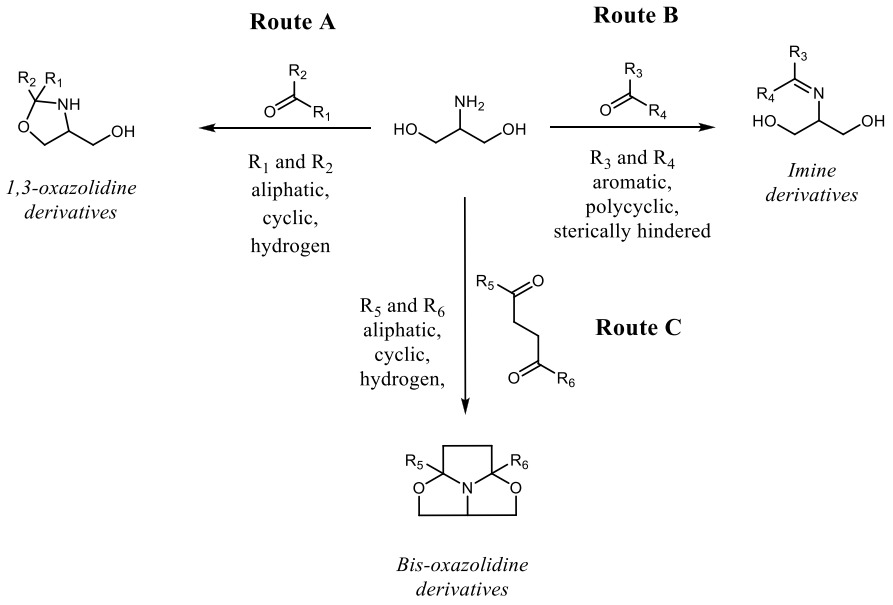
Scheme 3. Synthetic Routes to 1,3-Oxazolidines (Route A), Imines (Route B), and Bis-oxazolidine (Route C) from Reaction of Serinol with Carbonyl Compounds



passing them five times on a two roll mill operating at room temperature.

Characterization of the Composites. Vulcanization and Strain Sweep Test. The test was carried out with a Monsanto RPA 2000 rheometer. The samples of elastomeric composite material were held in the rheometer at 50 °C for 90 s; stress was then applied at 50 °C in the range of strain amplitude between 0.1% and 25%, with a frequency of 1 Hz, increasing the amplitude of the strain in the interval stated above. This treatment is carried out to cancel the "thermo-mechanical prior history". Vulcanization was then carried out at 170 °C for 20 min, at a frequency of 1.667 Hz and an angle of 6.98% (0.5 rad). The vulcanized sample was left in the instrument for 10 min at 50 °C. The sinusoidal stress was then applied in the same conditions already stated, at 50 °C. The sinusoidal stress is then applied again, still with the same experimental conditions. Curves are then obtained that give the value of the moduli as a function of the amplitude of the strain. These moduli are illustrated hereunder. Modulus G' is the elastic modulus, and modulus G'' is the loss modulus. The ratio G''/G' is given as tan delta. The strain sweep test gives the values of the following parameters: $G'y$ = 0.28% which is the value of G' at minimum strain, $\Delta G'$, which is the difference between the value of G' at minimum strain and the value of G' measured at the maximum strain reached, G''max, which is the maximum value of G'' observed on the curve of G'', Tan delta max, which is the maximum value of tan delta observed on the curve.

RESULTS AND DISCUSSION

Synthesis of Imines and Oxazolidines. A variety of carbonyl compounds were selected for the reaction with serinol: aldehydes and ketones, aliphatic and aromatic, with and without sterically hindered substituents. Carbonyl compounds with low steric hindrance were formaldehyde, (2*E*)-3-phenylprop-2-enal (cinnamaldehyde), propan-2-one (acetone), and 4-methyl-pentan-2-one, whereas sterically hindered ketone was 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (camphor). Aromatic compounds were 3-methylbenzaldehyde, 1-phenylethan-1-one, and fluoren-9-one. A chemical containing two carbonyl groups, 2,5-hexane-dione, was also used. Carbonyl compounds used in this work are summarized in Scheme 2.

Reaction between serinol and carbonyl compounds can be considered to occur through three main routes (Scheme 3).

The reaction of serinol with either aldehydes or ketones without sterically hindered substituents leads to the formation of 1,3-oxazolidines (Route A in Scheme 3). Also the reaction with 2,5-hexanedione, which leads to the bis-oxazolidine derivative DMHHP (Route C), can be considered to belong to this family of reactions. Aromatic or sterically hindered aliphatic carbonyl molecules lead to the formation of imines (Route B). An exception to this recollection appears to be the reaction of serinol with cinnamaldehyde. The stability of the conjugated double bond can explain the opening of oxazolidine intermediate with formation of imine.

As mentioned in the Introduction, the fundamental objective of this work was to investigate reactions in line with the basic principles of green chemistry, like minimizing the use of solvents and catalysts, without renouncing to reach higher yield and selectivity. Just as a significant example, the tricyclic compound 4a,6a-dimethyl-hexahydro-1,4-dioxa-6bazacyclopenta[cd]pentalene (DMHHP) (see Table 4) can be prepared without solvent and catalyst to quantitative yield, while following the typical reaction conditions reported in the scientific literature[35] only 19% of compound is formed. Absence of catalyst and a solvent-free approach was thus selected for revisiting the reactivity of amines with ketones and aldehydes. Details are in the Experimental Section. In brief, a reaction temperature has been set in order to have at least one reagent in the liquid state: either room temperature or at a temperature just above the reagent's melting point. The reaction temperature was thus in the range from 25 to 170 °C. Each reaction was stopped when conversion achieved a constant value. Products were isolated at room temperature by removing the excess of reactants, washing the crystals, or collecting oils.

All the reactions led to the selective preparation of either imine or oxazolidine. Serinol reactions with carbonyl compounds (**1a−1d**) which led to 1,3-oxazolidines are reported in Table 2.

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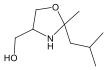
Table 2. Reaction of Serinol with Carbonyl Compounds (1a−1d) to Oxazolidines

Entry	Reagent[a]	time (h)	Temperature (°C)	Yield (%)	Product
1	Formaldehyde **1a**	12	25	56	 **2a**
2	Acetone **1b**	12	25	90	 **2b**
3	Acetone **1b**	2	70	90	 **2b**
4	4-methyl-pentan-2-one **1c**	12	25	95	 **2c**
5	Cyclohexanone **1d**	12	25	90	 **2d**

[a]Molar ratio with serinol: **1a** = 4, **1b** = 12.4, **1c** = 1.4, **1d** = 17.5.

In most cases, a yield of at least 90% was obtained. Only the reaction with formaldehyde led to a moderate oxazolidine yield (56%). The main coproduct was tetrahydro-1*H*-1,3-oxazolo-[3,4-*c*]-1,3-oxazole, the bis-oxazolidine compound, which was obtained with a yield of 20% (Table 4). The total yield to oxazolidines was thus about 75% for this reaction. It is worth noting that most reactions were performed at room temperature. To investigate the effect of a different reaction temperature, a reaction with acetone was also carried out at 70 °C; again, a selective synthesis to oxazolidine, with the same high yield (90%), was obtained.

Reactions of serinol with carbonyl compounds (**1e−1i**) which led to imines are reported in Table 3.

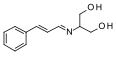
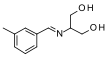
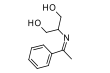
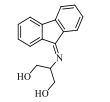
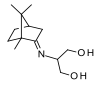
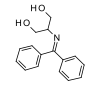
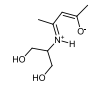
Yields were high in most cases, at least 80%, and quantitative in the case of 3-methylbenzaldehyde. Only with the most sterically hindered carbonyl compound, camphor, lower yield was obtained, (70%) without the formation of significant amount of side products (comparable conversion of the starting material).

Reactions which led to bis-oxazolidines are shown in Table 4. As mentioned above, the reaction with formaldehyde as reagent gave the bis-oxazolidine coproduct dihydro-1H,3H,5H-oxazolo[3,4-*c*]oxazole (HOO). The reaction of serinol with a dicarbonyl compound led to bis-oxazolidines with very high yields. The following dicarbonyl compounds were used, 2,5-hexanedione and 1,4-butandial, this last formed *in situ* from 2,5-dimethoxy-tetrahydrofuran.

The reaction scheme for the preparation of the tricyclic compound 4a,6a-dimethyl-hexahydro-1,4-dioxa-6bazacyclopenta[cd]pentalene (DMHHP), from serinol (S) and 2,5-hexanedione (HD), is shown in Scheme 4.

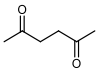
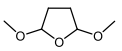
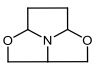
Such a reaction has been already reported.[35−37] DMHHP was prepared at room temperature, whereas by heating either the reaction mixture or DMHHP at 140 °C, 2-(2,5-dimethyl-1*H*-pyrrol-1-yl)-1,3-propanediol (SP) was obtained (Scheme 4). It appears that DMHHP could be a stable intermediate of the Paal Knorr reaction.[38,39] This compound required significant thermal energy to isomerize to the corresponding pyrrole.

Table 3. Reaction of Serinol with Carbonyl Compounds (1e−1i) to Imines

Entry	Reagent	time (h)	Temperature (°C)	Yield (%)	Product	
1	Cinnamaldehyde[a] **1e**	2	100	92		**3e**
3e2	3-methylbenzaldehyde[a] **1f**	12	25	98		**3f**
3	Acetophenone[a] **1g**	2	130	83		**3g**
4	Fluorenone[a] **1h**	6	130	80		**3h**
5	Camphor[b] **1i**	4	170	70		**3i**
6	Benzophenone[a] **1j**	3	170	75		**3j**
7	2,4-pentandione[c] **1k**	18	25	95		**3k**

[a]Molar ratio serinol:carbonyl compound = 1:1. [b]Molar ratio serinol:camphor = 1:1.31. [c]Molar ratio serinol:2,4-pentandione = 1:1.1.

Table 4. Bis-oxazolidines Obtained from Reaction of Serinol with Dicarbonyl Compounds or with Formaldehyde[a,b]

Entry	Reagent	time (h)	Yield (%)	Product	
1	 Formaldehyde	12	20		HOO
2	 2,5-hexanedione	12	95		DMHHP
3	 2,5-dimethoxy-tetrahydrofuran	12	99		HHP

[a]Molar ratio serinol carbonyl compound = 1:1. [b]Reactions were performed at room temperature.

Inspection of the reaction products shown in Tables 2 and 3 allows us to attempt an overall rationalization of the results. Our results show that working in the absence of catalyst and solvents, either oxazolidines or imines can be selectively prepared from serinol by properly selecting the carbonyl compound. This selectivity is lost when the synthesis is carried out in the presence of specific acidic catalysts as reported in the scientific literature.[40]

On the basis of the chemistry knowledge, mechanistic elaborations to account for these results are proposed in the text below.

Mechanistic Considerations. As mentioned above, reactions between carbonyl compounds and amines to give

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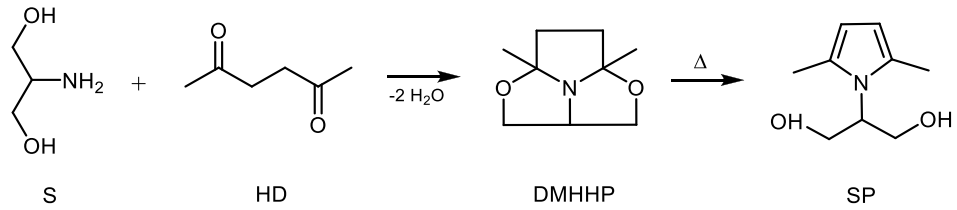
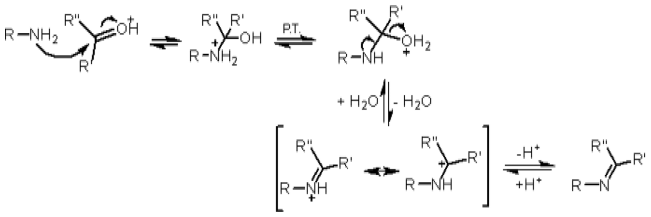
Scheme 4. Reaction Scheme for Selective Preparation of DMHHP and Its Heterocyclic Isomer 2-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-1,3-propanediol (SP) Starting from S and HD



Schiff bases have been largely studied in the past. In the literature, it is reported that the process is kinetically favored by the presence of a weak acidity (the best value is pH 6 in water or protic solvents), useful to activate the carbonyl group to nucleophilic attack and to help the evolution of the hemiaminal intermediate to the final product. Obviously, acidity must be moderate to disadvantage the protonation equilibrium of the amine. Scheme 5 shows the accepted mechanism for the synthesis of imines under acidic conditions.

Scheme 5. Reaction Mechanism for Synthesis of Schiff Bases under Acidic Conditions



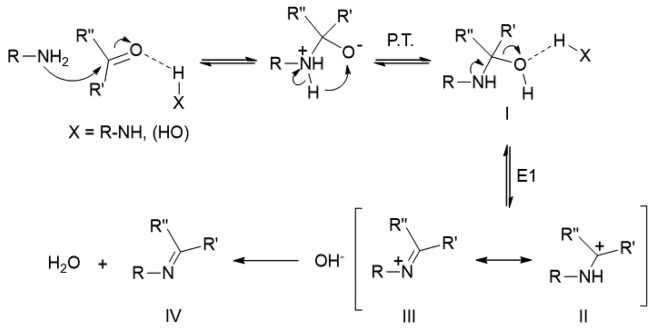
Considering the reactions of carbonyl compounds with β-amino alcohols under acidic conditions, a mixture of imines and oxazolidines is generally obtained; in accordance with the literature,[40] the ring–chain tautomerism of Schiff bases is involved. The reaction between carbonyl compounds and serinol, in the absence or presence of a specific acidic catalyst, as far as we know, has not been reported in literature.

Now, as remarked, the reactions here investigated were performed in the absence of solvent and acidic catalyst and under dehydrating conditions (dehydrating agent or high temperature); therefore, the general mechanism of the reaction shown in Scheme 5 has to be partially revised.

Serinol is an interesting polyfunctional molecule endowed with hydrogen donor groups and with the structural characteristics suitable, in principle, to promote dehydrative reactions based on template catalysis processes.[41,42]

Considering the role of this possible component in the mechanism, we verified the reactivity of a couple of low polar, hydrophobic, monofunctional reactants like the *n*-octylamine and benzophenone. The reaction between these two molecules at 140 °C was fast and clean to give the corresponding imine (see Experimental Section). Now, although the reaction proceeds in the absence of properly so-called acids, and template structures are not favored; it has to be considered that the carbonyl group and the hemiaminal intermediate can be activated by the presence of the hydrogen bonds network generated by the intimate contact of the polar functional groups reacting, enhanced, in the absence of solvent, by the strong lipophilicity of the medium. So, the mechanism can be redrawn as reported in Scheme 6, where for simplicity the hydrogen bond draw is limited to one molecule interacting.

Scheme 6. Reaction Mechanism Proposed for Synthesis of Schiff Bases in Absence of Acidic Catalyst and Solvent



Regarding the serinol reactions here investigated, the distribution of imines and oxazolidines observed can be mainly justified on the basis of two parameters: the steric hindrance around the carbonyl group and the stabilization of the C═N bond by π conjugation with the appropriated substituents R′ and R″. Scheme 7 summarizes the mechanism suggested in this work.

Thanks to the assistance of intramolecular and/or intermolecular hydrogen bonds, the hemiaminal intermediate I evolves to the protonated forms represented by the mesomeric structures II and III in equilibrium with species IV. Depending on the nature of the R and R′ groups, the reaction can lead preferentially to imine V or to oxazolidine VI. The discriminant factors are the presence or the absence of relevant steric hindrance of the substituents R and R′ and the possible π stabilizations offered by them if they are able to conjugate the C═N double bond of species III. In the case of α-amino alcohols, as indeed is serinol, we cannot exclude the formation of intermediate IV by intramolecular nucleophilic substitution in I′, which evolves to the products following the same criteria described above.

Molecular Modeling. In order to support the rationalization of the experimental results, quantum mechanical calculations have been accomplished. In particular, density functional theory (DFT) methods have been employed to investigate the energy of the molecular systems under study. The B3LYP functional[43,44] has been used including empirical dispersion correction (DFT-D)[45] together with the standard double-ζ (with polarization functions on all atoms) 6-31G** basis set. The Gaussian 09 suite of programs[46] has been employed in all the calculations. Relative electronic energies, enthalpies (at 298 K), and free energies (at 298 K) have been estimated. The calculated values are reported in Table 5.

The analysis of the results clearly shows that, as anticipated in the Experimental Section, thermodynamically more stable structures are formed. The only exception is compound **3i′**. This outcome can be ascribed to the hindrance of the bulky

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Scheme 7. Proposed Mechanism for Synthesis of Imines and Oxazolidines from β-Hydroxy Amines and Carbonyl Compounds (This Work)

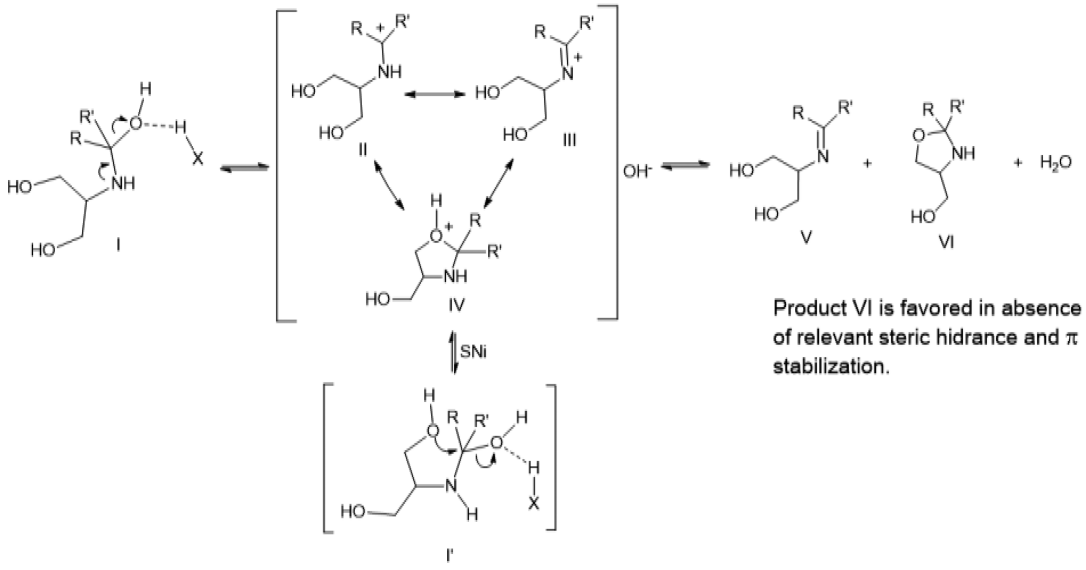
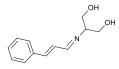


Table 5. Relative Electronic Energies (E_{rel}), hentalpies (H_{rel}, at 298 K), and free energies (G_{rel}, at 298 K) of Selected Molecular Systems as Obtained at the DFT-D (B3LYP/6-31G) Level**

Compound		E_{rel} kcal/mol	H_{rel} kcal/mol	G_{rel} kcal/mol
2b		0.00	0	0
2b'		8.61	7.67	4.12
3i		8.72	7.86	5.43
3i'		0.00	0	0
2d		0.00	0	0
2d'		13.04	12.14	9.37
3e		0.00	0.00	0.00
3e'		1.29	2.19	2.89

norbornane moiety. In order to assess this hypothesis, the path of the oxygen of one hydroxyl group of serinol approaching the hemiaminal carbon (Figure 1) has been studied at the same level of the DFT-D theory. Compound **2d** has been chosen as a reference compound with a thermodynamic reaction control.

The maximum energy structures found in the two cases are shown in Figure 1.

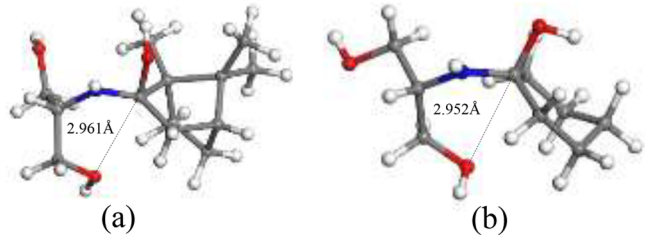


Figure 1. Maximum energy structures (miming sketch I′ in the framework of Scheme 7) obtained at the B3LYP/6-31G** level (including Grimme dispersion corrections) for compounds **3** (a) and **2** (b).

The intermediate I′ coming from the reactions between camphor (Figure 1(a)) and cycloexanone (Figure 1(b)), respectively, with serinol shows two maxima at very similar O···C distances (2.96 and 2.95 Å) but very different relative energies (about 90 and about 30 kcal/mol). These results support the hypothesis according to which steric hindrance plays the main role in the formation of intermediate IV (Scheme 7) and so to the selectivity of the reactions observed.

Rubber Cross-Linking. Serinol and serinol derivatives can be used as accelerators in sulfur-based cross-linking of diene rubbers. Some of the authors reported some results arising from these studies in the patent[47] and scientific[48] literature. In the present article, a comparison is presented for the first time among serinol and subtances representative of all the families of serinol derivatives prepared so far: imine, oxazolidine, bisoxazolidine, and amide.

As anticipated in the Introduction, the most important application of rubber is for tire compounds and, among them, for tire tread. A tire tread guarantees road traction and plays a major role for the reduction of the tire environmental impact. Silica is the filler of election for the reduction of the carbon footprint.[49] The study of serinol and serinol derivatives as accelerators was performed in a composite with a typical formulation for a tire tread with a low environmental impact: SBR, NR, and BR were the rubbers and silica the filler, with a sulfur-based silane, bis(triethoxysilylpropyl)tetrasulfide

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Table 6. Parameters from Sulfur-Based Cross-Linking of Composites of Table 1[a]

		Composite[b]						
Parameter	Measure unit	1	2	3	4	5	6	7
M_L	dNm	3.08	2.55	3.38	2.92	3.15	2.94	3.12
M_H	dNm	14.08	15.1	15.48	14.06	14.91	13.04	14.32
ts_1	min	1.16	1.13	0.84	0.85	0.76	1.1	1.12
t_{90}	min	10.11	5.6	7.3	7.2	7.8	9.3	9.01

[a]For the explanation of the parameters, see the text above. [b]Secondary accelerator in the composite: **1**, =; **2**, DPG; **3**, S; **4**, SCin; **5**, SOxa; **6**, DMHHP; **7**, Samide

Table 7. Average Values of Storage Modulus G' at Minimum Shear Strain Amplitude and of Maximum Value of Loss Modulus (G''max), $\Delta G'$, and Tan Delta Max for Composites of Table 1

		Composite[a]						
Parameter	Measure unit	1	2	3	4	5	6	7
$G'_{\gamma min}$	MPa	1.47	1.54	1.58	1.61	1.59	1.63	1.595
$\Delta G'$	MPa	0.77	0.84	0.86	0.89	0.87	0.94	0.88
G'' max	MPa	0.21	0.21	0.22	0.23	0.22	0.25	0.24
Tan delta max		0.18	0.17	0.17	0.18	0.18	0.20	0.20

[a]Secondary accelerator in the composite: **1**, =; **2**, DPG; **3**, S; **4**, SCin; **5**, SOxa; **6**, DMHHP; **7**, Samide.

(TESPT), as the coupling agent. Cross-linking of the composite was done with a sulfur-based system. Since Goodyear's times, it is known that sulfur alone leads to a slow cross-linking reaction. It is acknowledged that efficient vulcanization of diene rubbers is obtained with an active sulfurating species, formed *in situ* through the reaction of sulfur, ZnO, and a sulfenamide, which acts as accelerator.[34] In the composites studied in this work, whose formulations are in Table 1, *N-tert*-butyl-2-benzothiazyl sulfenamide (TBBS) was used as the sulfenamide. It is also known that to have vulcanization kinetics suitable for industrial applications for silica-based composites, another accelerator, named secondary accelerator, is required. Substances such as DPG is traditionally used in spite of its critical impact on human health. In particular, it is acknowledged that DPG is a reprotoxic substance.[50] In this work, the secondary accelerators that were used are serinol and the following serinol derivatives: S, SCin, SOxal, DMHHP, SAmide. The behavior of the composites in vulcanization and the dynamic-mechanical properties upon applying a sinusoidal shear stress were investigated, in comparison with compounds with DPG as the secondary accelerator and without any accelerator other than TBBS. The secondary accelerators were used in the same molar amount. In the case of serinol, only 0.8 parts per hundred of rubber was needed. Vulcanization was performed at 170 °C: data arising from the rheometric tests are in Table 6, which shows the values of the following parameters: M_L, minimum value of torque; M_H, maximum value of torque; ts_1, time required to have torque increase of 1 dNm, with respect to M_L; t_{90}, time required to achieve 90% the maximum torque value, taken as M_H.

The minimum modulus M_L is usually taken as an index of the composite viscosity. With respect to the reference composite, guanidine leads to the lowest viscosity value, serinol to slightly higher, and the serinol derivatives to similar values. M_H is affected both by the structure of the cross-linking network and by the extent of the filler network, which is not completely disrupted at the strain amplitude used for the vulcanization. DPG and serinol lead to similar M_H values (slightly higher for serinol). Taking into consideration the results from the strain sweep experiments (discussed below in the text), it can be commented that both these chemicals promote an efficient cross-linking network. This appears to be the case also of the oxazolidine derivative, whereas lower M_H values were obtained with the other derivatives, in line with the reference compound.

Serinol, the imine, and the oxazolidine derivatives act indeed as efficient secondary accelerators: the values of t_{s1} and t_{90} are appreciably lower than those of the reference compound. These chemicals promote a faster vulcanization with respect to DPG (lower t_{s1}) and a lower vulcanization rate, as is shown by the higher t_{90} values. The bis-oxazolidine and the amide derivative clearly have a minor effect on the vulcanization kinetics: both t_{s1} and t_{90} are similar to those of the reference compound.

The similar t_{s1} and t_{90} and ($M_H - M_L$) data of the composites with serinol and the oxazolidine and imine derivatives could lead to hypothesize that the serinol primary amine is released from the derivatives, at least under the experimental conditions experienced during cross-linking, whereas there are no indications in this direction in the case of the tricyclic and amide derivatives. It is worth commenting that, in a previous study,[48] with NR as the only rubber, in the absence of any filler and by cross-linking at 151 °C, serinol was observed to be a more efficient accelerator with respect to the imine derivative with camphor. These findings could be explained, in particular, with the absence of silica and different curing temperatures.

Results from shear strain sweep tests are shown in Table 7, which shows values of shear storage modulus G' at minimum strain (0.28%) ($G'_{\gamma min}$) and the difference ($G'_{\gamma min} - G'_{25\%}$) ($\Delta G'$), as well as the maximum value of the shear loss modulus G'' (G'' max) and the G''/G'ratio (Tan delta max).

The strain sweep test is traditionally used to investigate the extent of the filler network and its dynamic evolution, which is known as filler networking phenomenon.[51] The values of G' at minimum strain and of $\Delta G'$ are representative of these phenomena. $\Delta G'$ is traditionally taken as the index of the so-called Payne Effect,[52,53] that means the nonlinearity of the storage modulus. Higher values of $\Delta G'$, G'' max, and Tan delta max are indications of larger dissipation of energy. The composites with DPG, serinol, and the imine and oxazolidine

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derivatives show similar if not very similar values. Hence, these composites promote similar dissipation of energy. The compounds with the bisoxazolidine and the amide as the secondary accelerators reveal appreciably different values for all the parameters and, more in particular, larger dissipation of energy.

The experimental findings documented in Tables 6 and 7 reveal the similar behavior in vulcanization and the similar dynamic-mechanical properties for the composites based on serinol and on the imine and oxazolidine derivatives. As commented above, the serinol primary amine seems to be released from the derivatives, at least at the step of vulcanization. It can thus be commented that the imine and oxazolidine act as protective groups of the serinol primary amine. This has to be considered as an important technological advantage. Indeed, the protective groups could prevent a premature vulcanization of the compounds during the processing, particularly when a high amount of mechanical energy has to be applied.

CONCLUSION

Synthesis of either imines or oxazolidines, highly regioselective and with high yield, was achieved by reacting serinol with carbonyl compounds. Imines were obtained when sterically hindered and aromatic carbonyl compounds were used and when conjugated double bonds were formed. 1,3-Oxazolidines came from the reaction of the other carbonyl compounds, without steric hindrance or delocalized electrons. Reactions were performed in the absence of any solvent or catalyst. DFT-D calculations supported the rationalization of the experimental results. The neat synthesis of either imines or oxazolidines allowed the easy preparation of substances which were used as secondary accelerators in silica-based compounds suitable for a tire tread. Results from rheometric and strain sweep tests reveal that serinol and the imine and oxazolidine derivatives behave as efficient accelerators and lead to composites characterized by a low dissipation of energy. The imine and oxazolidine seem to act as protective groups of the serinol primary amine, and this has to be considered an important technological advantage, as it allows one to explore more severe processing conditions, avoiding premature vulcanization. The present research was also inspired by the replacement of the substances such as the guanidines, which as critical for the impact on health and safety. Indeed, serinol has almost an ideal safety data sheet.[54] The derivatives have still to be investigated, but they are hypothesized to release the starting reagents in the final compound: serinol, acetone, cinnamaldehyde. Moreover, the chance of performing a neat synthesis allows one to hypothesize a synthesis *in situ* in a rubber matrix, preparing a masterbatch. Finally, all these results appear to make using the substances suitable on a large commercial scale.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acssuschemeng.0c01603.

NMR spectra of compound **2a** (Figure S1), NMR spectra of compound **2b** (Figure S2), NMR spectra of compound **2d** (Figure S3), NMR spectra of compound **3e** (Figure S4), NMR spectra of compound **3f** (Figure S5), NMR spectra of compound **3g** (Figure S6), NMR spectra of compound **3h** (Figure S7, NMR spectrum of compound **3i** (Figure S8), NMR spectra of compound **3j** (Figure S9), and NMR spectra of compound **3k** (Figure S10) (PDF)

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Notes

The authors declare no competing financial interest.

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