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High value-added application of rosin as a potential renewable source for the synthesis of acrylopimaric acid-based botanical herbicides

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ABSTRACT

Turning natural products into value-added herbicide preparation is an alternative to synthetic compounds for environmentally friendly weed management. In continuation of our research on rosin-based herbicidal agents, 33 acrylopimaric acid (APA) derivatives were synthesized, and were structurally characterized using proton nuclear magnetic resonance, elemental analysis, electrospray ionization mass spectra, melting point, infrared spectroscopy, and X-ray crystallography. In addition, the herbicidal activity of APA derivatives against *Amaranthus retroflexus*, *Echinochloa crus-galli*, and *Brassica campestris* L. were investigated. Among the APA derivatives, the diacylthiourea compounds **3a–f** showed significant post-emergence herbicidal activity against *E. crus-galli*. Moreover, compounds **3b–d** (with EC_{50} values of 13.191, 13.441, and 13.191 g ai/ha, respectively) displayed more promising herbicidal activity against *E. crus-galli* than sulfentrazone (a commercial herbicide with an EC_{50} value of 15.606 g ai/ha). In quantitative structure–activity relationship (QSAR) study, optimal conformers and best multilinear regression analysis were performed using Gaussian and CODESSA software. The four descriptors correlating the molecular structures with their herbicidal activities were as follows: Total Charge, log MS, q^{N}_{max} and q^{C}_{max}. The generated QSAR model had a correlation coefficient of 0.9625, a Fisher significance ratio of 185.96, and a squared standard error of the estimates of 0.0012. Preliminary studies on the structure–activity relationship and QSAR showed that the higher electron density around the substituent groups on the nitrogen atoms of rosin-based backbone structure and smaller volume of spatial structure played a beneficial effect on the herbicidal activity. Thus, rosin is a promising source of a value-added product for crop protection.

1. Introduction

Synthetic herbicides are widely used in modern agriculture to control unwanted plants or weeds (Jiang et al., 2010). FAO statistics showed that sustained herbicide use could potentially increase annual global food production by more than 10% (Varejão et al., 2013). However, extensive use of agrochemicals produces herbicide resistance among weeds and causes other environmental problems (Coda et al., 2015; Hahn et al., 2015; Iwakami et al., 2015; Keshtkar et al., 2015). Therefore, highly active and less toxic herbicides are desirable (Carbone and Velkov, 2013). The natural products resources attracted more and more attention of researchers owing to their irreplaceable advantage compared with petrochemical products. So, as an alternative strategy, slight modification of the chemical composition of natural products is a feasible solution for producing new herbicides for resistant species (Wang et al., 2008a).

Rosin is a widely distributed renewable terpenoid resource (Li et al., 2012a). Recently, rosin has been used as an active starting material owing to its broad range of bioactivities, such as plant growth regulation, anticancer, antibacterial, and anti-inflammation (Naumov et al., 2015; Tretyakova et al., 2014). However, oxidization and crystallization are two constraints for the application of rosin, which thus requires chemical modification prior to its uti-

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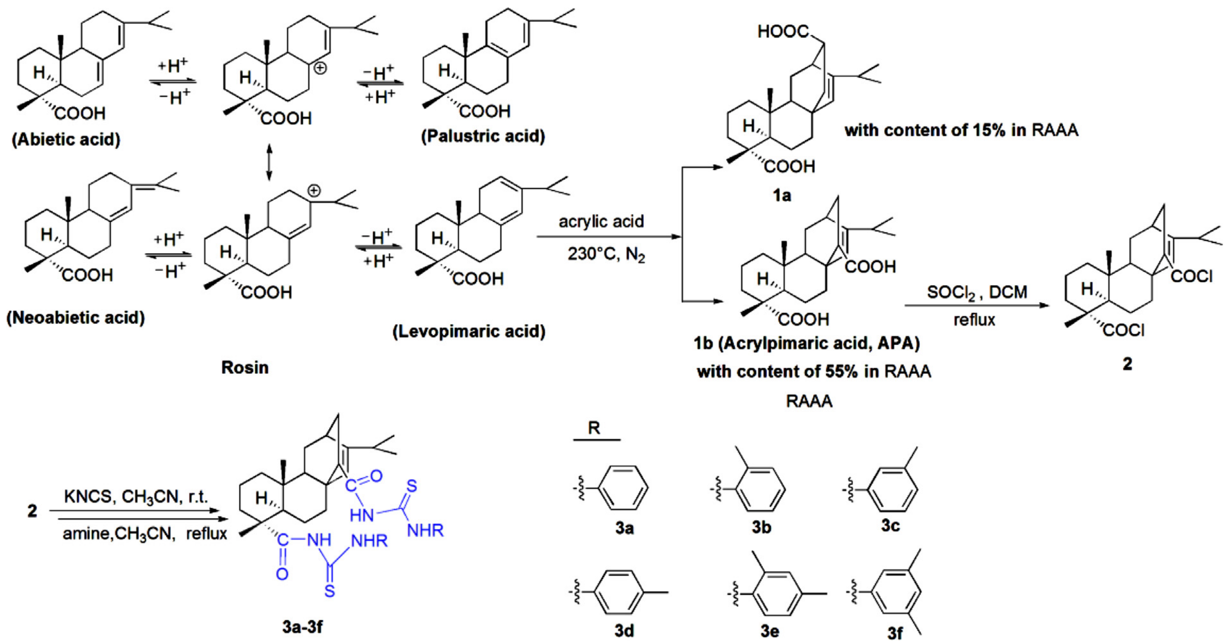
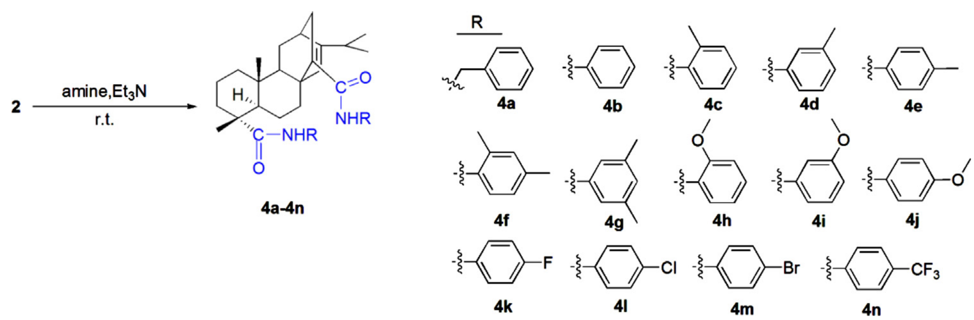


Scheme 1. Synthetic route for APA-based diacylthiourea compounds **3a**–**f**.



Scheme 2. Synthetic route for APA-based dicarboxamides compounds **4a**–**n**.

lization. Acrylopimaric acid, referred to APA, is prepared through Diels–Alder reaction between rosin and acrylic acid (Wang et al., 2009). However, only a few studies have investigated the biological activities of APA and its derivatives, even though this rosin-derived substance is an important starting material for identification of biologically active compounds (González, 2014; Wang et al., 2015; Xing et al., 2013).

Developing and screening candidates with insecticidal activity from numerous compounds is virtually and economically impossible (Mai and Koo, 2014), and employing quantitative structure–activity relationship (QSAR) study is a means to reduce problems on cost and time requirements for screening (Hansch and Verma, 2009; Naik et al., 2009; Speck-Planche et al., 2011). QSAR reveals numerous important physiochemical properties that are correlated with insecticidal activity; thus, QSAR is useful in designing and developing potential rosin-based pesticides (Shibi et al., 2015). However, few QSAR studies rosin-derived herbicidal agents exist.

In the present study, 33 APA analogues were prepared and their herbicidal activity was evaluated against *Amaranthus retroflexus*, *Echinochloa crus-galli*, and *Brassica campestris* L. The QSAR model of the APA derivatives correlating their structure with their herbicidal activity against *E. crus-galli* was built using Gaussian and CODESSA. We investigated the most important structural factors influencing the herbicidal activity of these APA derivatives by describing their physicochemical descriptors. Results of this study may improve the applicability of a renewable resource i.e., rosin, as an herbicidal material.

2. Materials and methods

2.1. Synthesis and characterizations

The dried compounds were prepared to obtain fourier transform infrared (FT-IR) spectra by the KBr pellets technique in a Nicolet IS10 fourier transform infrared spectrophotometer (Thermo Nicolet Co., Madison, USA). Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured on a Bruker AV-300/500 (300/500 MHz) spectrometer using tetramethylsilane as an internal reference and $CDCl_3$ or DMSO-d_6 as the solvent and electrospray ionization (ESI) mass spectra were obtained on a Bruker Q-TOF mass spectrometer (Bruker Co., Karlsruhe, Germany). The thin-layer chromatography analysis was used to monitor the reaction. Elemental analysis was performed using Vario EL-III (Elementar Co., Hanau, Germany). X-ray data (XRD) were recorded on a CAD-4 diffractometer (Bruker/Enraf-Nonius) at 22 °C. All reagents were chemically pure, except for the crude rosin, which was purchased from Wuzhou Pine Chemicals Ltd., and was used directly without treatment.