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RETRO-DIELS-ALDER REACTION OF ASATONE: SYNTHESIS OF HETEROTROPANONE AND ISOHETEROTROPANONE

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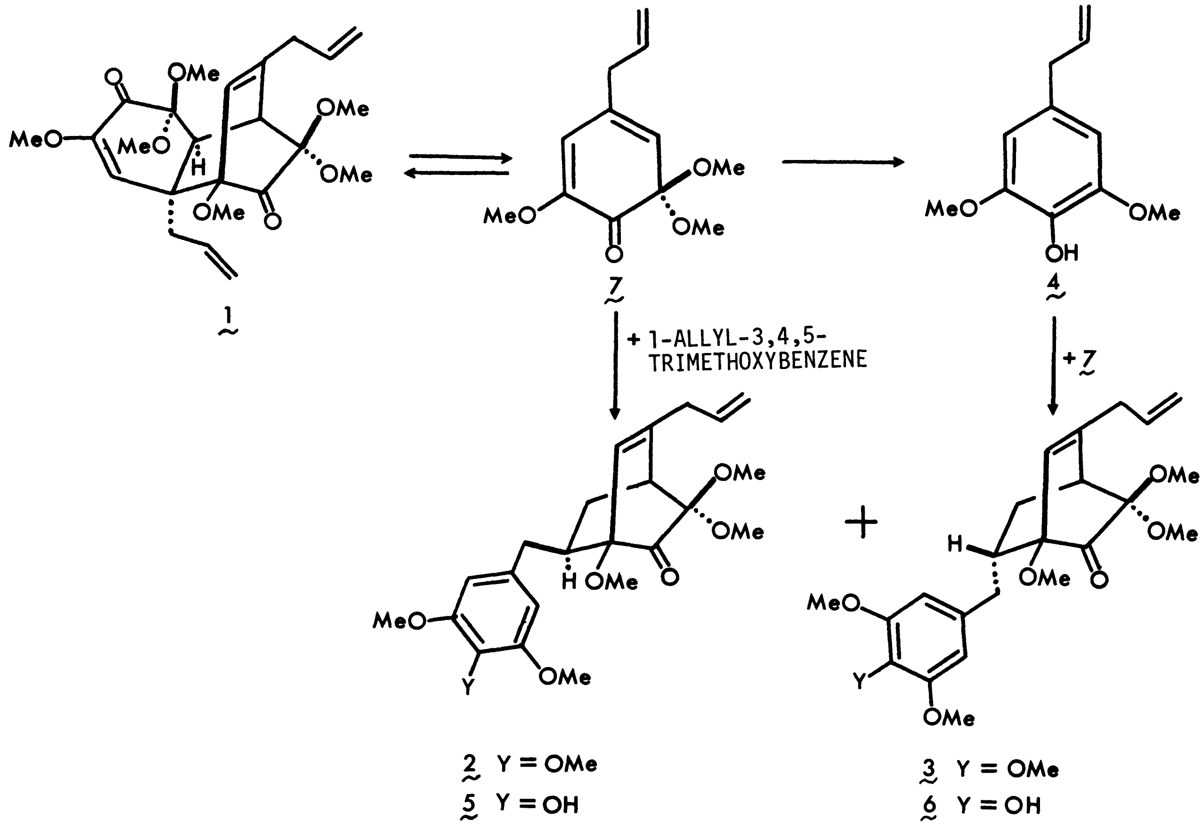
Two novel neolignans, heterotropanone and isoheterotropanone, have been synthesized by retro-Diels-Alder reaction of asatone in 1-allyl-3,4,5-trimethoxybenzene. These two neolignans have also been obtained on thermal reaction of asatone followed by methylation.

From view points of biological and antitumor activities, lignans and neolignans both are attracting increasing attention. In connection with asatone (1),[1] we have made great efforts to search for such a neolignan as 1, resulting in the isolation of several novel neolignans (heterotropanone (2),[2] isoheterotropanone (3),[2] and heterotropatriones[3]) as minor components, in addition to 1 as a main product. Particularly, it seems difficult to isolate both 2 and 3 from the plant Heterotropa takaoi M., in large quantities enough to test their antitumor activity. In the present paper, we wish to report the synthesis of both heterotropanone (2) and isoheterotropanone (3) using retro-Diels-Alder reaction of asatone (1), which has been already synthesized by means of anodic oxidation of 4-allyl-2,6-dimethoxyphenol (4).[4]

When heated at 175 - 180 °C for 1.5 h in a sealed tube, a solution of asatone (1 eq) in 1-allyl-3,4,5-trimethoxybenzene (4 eq) became a pale brown oil, which was separated by preparative TLC [Kieselgel 60 PF_{254}; hexane - EtOAc (1 : 1)] to afford heterotropanone (2) and isoheterotropanone (3) in 14 and 13% yields, respectively.[5] In addition, 4-allyl-2,6-dimethoxyphenol (4), demethylheterotropanone (5),[6] and demethylisoheterotropanone (6)[3] were also obtained in ca. 3, 1 - 2, and 1 - 2% yields, respectively. Under the similar condition as that of 6,[3] 5 was readily converted into heterotropanone (2) in almost quantitative yield, using CH_2N_2 in ether containing MeOH. Clearly, the dienone (7) as an important intermediate was competitively decomposed into 4-allyl-2,6-dimethoxyphenol (4), as shown in Scheme 1. We also carried out thermal reaction of asatone (1), as follows.

Scheme 1. Thermal reaction of asatone in 1-allyl-3,4,5-trimethoxybenzene



A solution of 1 (0.1 mmol) in mesitylene (1 ml) was heated at 160 - 165 °C for 2.5 h to afford demethylheterotropanone (5) and demethylisoheterotropanone (6) in 19 and 18% yields, respectively. In this case, 4-allyl-2,6-dimethoxyphenol (4) was also obtained in 27% yield.

Further synthetic studies are in progress to find the optimum condition leading to the formation of heterotropanone and related compounds.

References and Notes

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5. 1-Allyl-3,4,5-trimethoxybenzene was recovered in ca.70% yield.
6. Physical data of 5: $C_{23}H_{30}O_7$ [m/e 418(M^+), 343, 285, and 167]; ν_{max}(film) 3500br., 1750, 1610, and 1520 cm^{-1}.

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