

A New Efficient Synthesis of *p*-Nitrocalix[4]arene

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Abstract: A new efficient synthesis of *p*-nitrocalix[4]arene from calix[4]arene by using nitrogen dioxide is described. The compound is an useful intermediates for the introduction of other functional groups to obtain N containing substituted calix[4]arene. The reaction mechanism is briefly discussed.

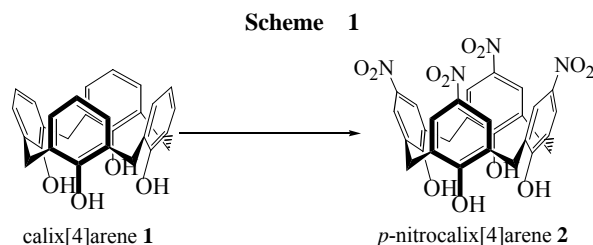
Keywords: Nitration, calix[4]arene, nitrogen dioxide.

Calix[n]arenes and their derivatives have attracted considerable interests during the past decade because of their prominent behavior in host-guest chemistry¹. Easy substitution both at the phenolic groups (lower rim) and the para positions of the phenyl rings (upper rim) provides convenient approaches to a variety of functionalized calixarene derivatives.

p-Nitrocalixarenes are a class of useful intermediates for the introduction of other functional groups to obtain N containing substituted calixarenes². A number of researchers have carried out the nitration of calixarenes, and some direct (the parent *p*-tert-butylcalixarenes as the starting materials) or indirect methods have been developed³⁻⁸. For example, Shinkai *et al.* have first reported the synthesis of *p*-nitrocalix[6]arene via *p*-sulfonatocalix[6]arene by nitric acid, while the overall yield was low.³ Ipso nitration of *p*-tert-butylcalix[4]arene methyl ether has been reported by Reinhoudt *et al.* using fuming nitric acid, but failed when applied to the parent *p*-tert-butylcalix[4]arene^{5a}. Recently Huang *et al.* have completed a series of the nitration of calix[4]arene and its derivatives⁷. However, nearly all of the procedures reported to date for *p*-nitrocalix[4]arenes involve the application of nitric acid and suffer with either long reaction time or low yields as well as inconvenient treatment of reagents. On the other hand, nitrogen dioxide is also a favorable nitration agent, which has been widely investigated and used in nitration of aromatic compounds such as phenols⁹⁻¹¹, whereas no research employing it in nitrating calixarenes has been reported.

We have been interested in the inclusion interaction of nitric oxide (NO and NO₂) with calixarenes and accidentally found a facile synthetic route to *p*-nitrocalix[4]arenes by blowing gaseous nitrogen dioxide into a solution of calix[4]arene **1**. The gas resource is easily generated and removed, the procedure can be carried out much more conveniently than previous methods and especially with a surprising high yield. Herein the preliminary

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results are described and the reaction mechanism is briefly discussed.

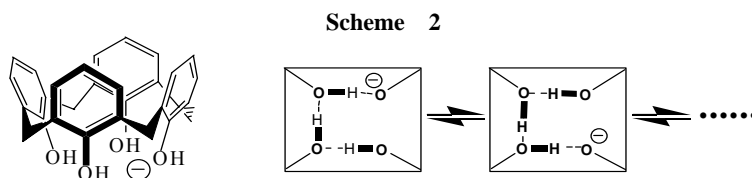
Experimental

The synthesis was accomplished at ambient temperature (as shown in **Scheme 1**). Nitrogen dioxide or a mixture of nitric oxide and oxygen (two separate inlets)^{12,13} was bubbled through a solution of **1** (0.1 g) in chloroform (about 30 mL)¹⁴⁻¹⁶. Soon the solution turned to yellow and the precipitate appeared rapidly within a few minutes. After 20 min the solids were filtrated and washed with acetone and methanol to give pure **2** (0.15 g) as a pale yellow powder. It was found that this reaction proceeded almost quantitatively (yield > 90 %). Other conventional solvents such as toluene have also been tried and the same results were obtained. The compound **2** was identified by ¹H-NMR, MS, IR and elemental analysis¹⁷. The ¹H-NMR spectrum of compound **2** shows that the peaks of the benzene protons changed to singlet and shifted apparently to low field, which indicates that nitro groups were introduced in the *para* positions.

The same nitration method was also used for calix[*n*]arene (*n* = 6, 8). Although the reactions occurred, the products were much more complicated than that for calix[4]arene. In addition, we investigated the nitration of the parent *p-tert*-butylcalix[*n*]arenes (*n* = 4, 6, 8) and tetramethoxycalix[4]arene by nitrogen dioxide, but did not get the expected results.

Results and Discussion

Tetramethoxycalix[4]arene can not be nitrated by means of the present method. That shows that the hydroxyl groups play an important role in the nitration. It has been reported that the reaction of phenols with nitrogen dioxide generally involve the abstraction of phenolic hydrogens in the first step and subsequent radical coupling of NO₂ molecules leads to nitrocyclohexadienones, which rearrange to nitrophenols¹⁰. In the present work, sometimes a small amount of corresponding quinones have been detected in IR spectra (~ 1646 cm⁻¹)^{7b}, which are readily accompanied with nitration of other aromatic compounds by nitrogen dioxide^{11,18}. The fact indicates that the general mechanism on nitration by nitrogen dioxide provided above is available in the present reaction. As well known, calix[4]arenes carrying phenolic OH groups usually are more acidic than other larger calixarenes because the first dissociation of phenolic hydrogens easily occurs due to the stabilization of the calix[4]arene anion by resonance structures of strong intramolecular hydrogen bonds (as shown in **Scheme 2**)¹⁹. As the abstraction of one phenolic hydrogen of calix[4]arene, the negative electrical charge can be freely moved



among the OH groups. As a result, the nitration of calix[4]arene occurs most effectively over the whole molecule. Furthermore, the yield obtained is much higher than those for general phenols and other aromatic compounds because of the peculiar acidity of calix[4]arene.

Calix[*n*]arene (*n* = 6, 8) can also react with nitrogen dioxide. However, MS measurements revealed that the products were complicated and the results were not satisfied as calix[4]arene. This is probably due to that the calix[*n*]arene (*n* = 6, 8) is difficult to take a cone conformation and to form the cyclic resonance structure of hydrogen bonds like calix[4]arene as shown in **Scheme 2**.

The reaction of the parent *p*-*tert*-butylcalix[*n*]arenes (*n* = 4, 6, 8) with nitrogen dioxide underwent much slower than that of calix[4]arene. This fact indicates that the substitution in the *para* position of calixarene is unfavorable in the present nitration method.

Conclusion

A new efficient synthesis of *p*-nitrocalix[4]arene from calix[4]arene by using nitrogen dioxide is described. In the present nitration method, the intramolecular hydrogen bonds play an important role and the substitution in the *para* position of calixarene disturbs the nitration. The reasonable reaction mechanism is suggested.

Finally, it should be noted that the present research work not only provides an easy method to synthesize *p*-nitrocalix[4]arene with high yield, but also forerun potential applications of calix[4]arene in detecting or/and clearing pollutant NO_x gases.

References and Notes

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17. The characteristics of **2**. IR (KBr, cm⁻¹): 3268 (OH), 1594, 1452 and 1340cm⁻¹ (NO₂); ¹H-NMR δ(DMSO-d₆, ppm): 8.14 (s, 8H, ArH), 3.68 and 4.27 (br., 8H, ArCH₂Ar); MS-ESI: *m/z* 603 ([M-H]⁻); Anal. Calcd. For C₂₈H₂₀N₄O₁₂·CH₃OH (%): C 54.70, H 3.80, N 8.80; Found: C 54.55, H 3.28, N 8.10. IR, ¹H-NMR and MS data were as the same as literatures^{3b, 5b, 7a}.
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