Synthesis and Characterization of Polychlorinated Naphthalenes.
IV. C-13 Labelled Compounds.

Vladimir A. Nikiforov, Vladimir S. Karavan*, Sergei A. Miltsov, Vyacheslav G. Tribulovich*

St.Petersburg University, Institute of Chemistry, 198904, Universitetskii pr., 2, St.Petersburg, Stary Peterhof, Russia
* St.Petersburg University, Department of Chemistry, 198904, Universitetskii pr., 2, St.Petersburg, Stary Peterhof, Russia

Introduction

It was found recently, that several isomers of PolyChloroNaphthalenes (PCNs) are persistent in the environment and show the tendency to bioaccumulation[1)]. Some samples may contain certain PCNs in concentrations well exceeding those of PCBs and PCDDs/PCDFs, therefore PCNs should be taken into consideration for correct environmental risk assessment.

In the past several years many isomerically pure native PCN congeners have been synthesized, characterized and made available as analytical standard solutions[2-5)]. In this article we report preparation of $^{13}C_{10}$-labelled naphthalene and several tetra- to octachloronaphthalenes.

General synthetic and QA/QC considerations

Two reports on this subject have been found in the literature. The first work by Wightman et al gives details of synthesis of the $^{13}C_8$-naphthalene and its octa- and hexachloroderivatives[6)]. The emphasis of the second one is QA/QC considerations for the synthesis of a series of partially C-13 labelled PAHs[7)]. We have followed the directions from these two articles in our work.

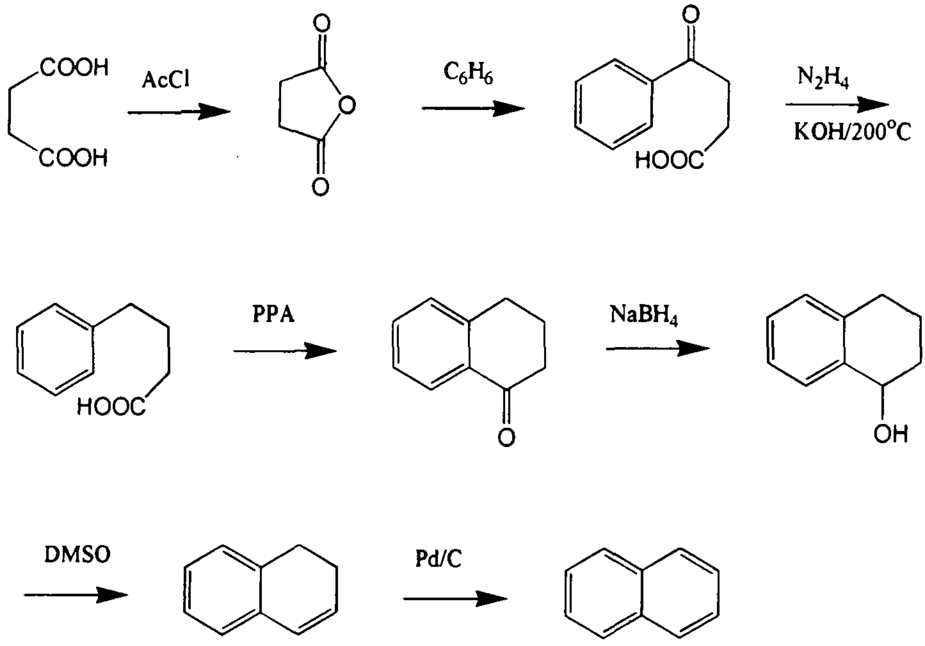
The first task was to determine the required number of labels in a molecule and structures of most wanted PCN isomers. After discussions with several analytical groups and literature investigation, it was determined that complete labeling is highly appreciated and the best looking set of compounds consists of 1,3,5,7-substituted tetra- to octa- chlorinated congeners, namely 1,3,5,7-TeCN, 1,2,3,5,7-PeCN, 1,2,3,5,6,7-HxCN, 1,2,3,4,5,6,7-HpCN and OctaCN.

After careful analysis of available synthetic methods in chloronaphthalene chemistry, the project was divided into five stages :

1) Complete synthesis of native naphthalene from benzene and succinic acid on a gram scale
2) Syntheses of all target native polychloronaphthalene congeners from naphthalene on a multi-mg scale
3) Synthesis of labelled naphthalene from labelled benzene and labelled succinic acid on a gram scale
4) Pilot syntheses of labelled target polychloronaphthalenes on a mg-scale
5) Syntheses of labelled target polychloronaphthalenes on a multi-mg scale

Synthesis of native and $^{13}C_{10}$-labelled naphthalene (stages 1 and 3)

2g of $^{13}C_{10}$-labelled naphthalene were prepared according to procedure of Wightman from 3g of $^{13}C_4$-succinic acid and 2g of $^{13}C_6$-benzene (yield 60%). Preliminary experiments on stage 1 included test runs of every synthetic step with commercially available compounds, followed by complete step-by-step synthesis of native naphthalene from benzene and succinic acid.



It is necessary to acknowledge here the excellent job done by Wightman et al., the reactions used for the preparation of naphthalene are nicely stable to incidental changes in synthetic conditions (ambient and reaction temperature variations, changes in substrate/reagent ratio, different reaction times, effect of moisture, use of different glassware). For instance, the most suspicious step, reaction of succinic anhydride with benzene, which requires "stirring at room temperature under exclusion of moisture for 5 days", was repeated by us 3 times with unlabelled material and once with C-13 labelled succinic acid and benzene. In all four cases the yields varied from 82% to 86%, despite some differences in carrying the synthesis.

The only significant difference between our procedure and that of Wightman was on the last step - conversion of dihydronaphthalene to naphthalene. We failed to achieve conversion better than 60% with available batch of Pd/C (while it was the same product number, as used by Wightman). Almost quantitative conversion was achieved with help of sulfur, added to reaction mixture in equimolar amount.

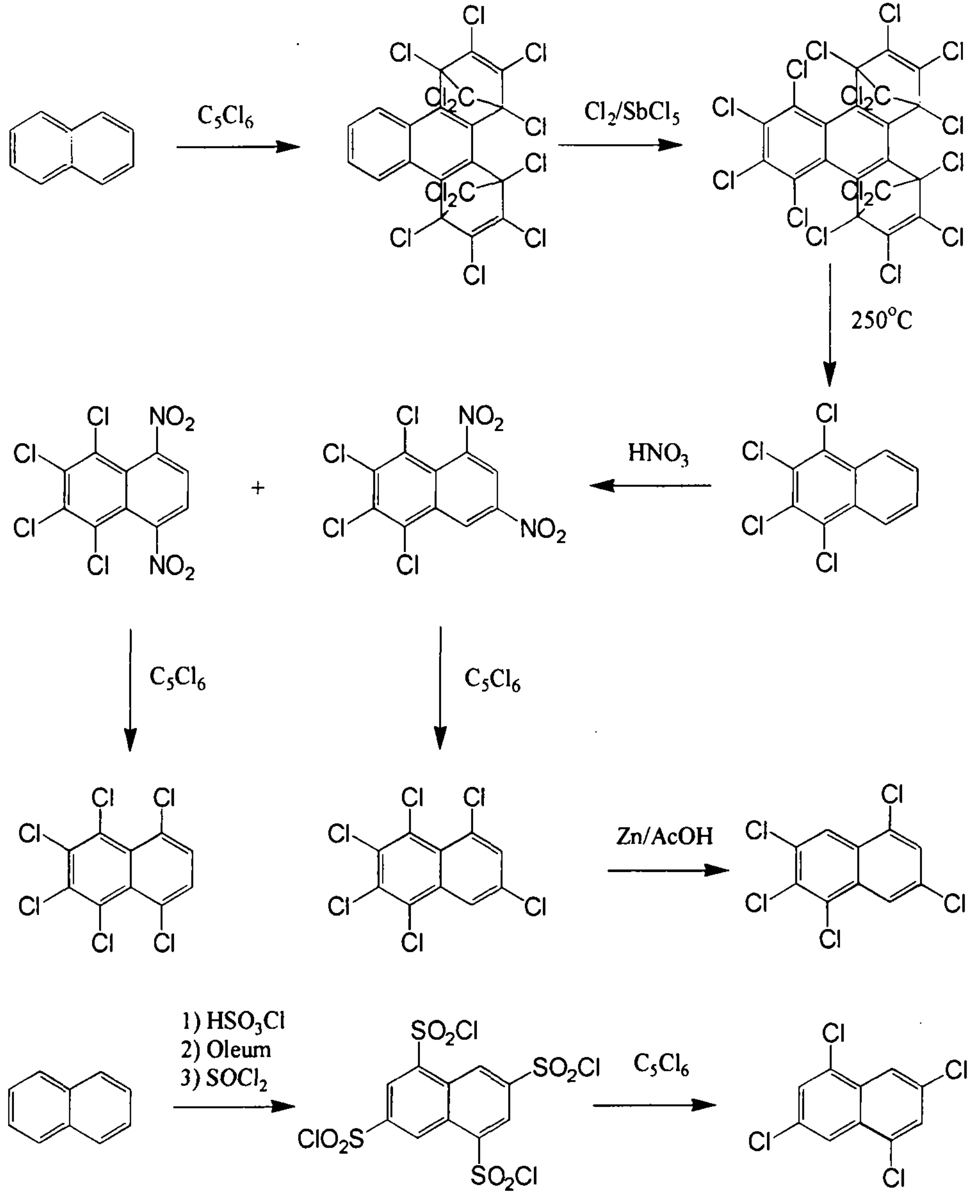
Small amount of naphthalene, >98% pure according to GC/FID, was further purified by sublimation for archive purposes.

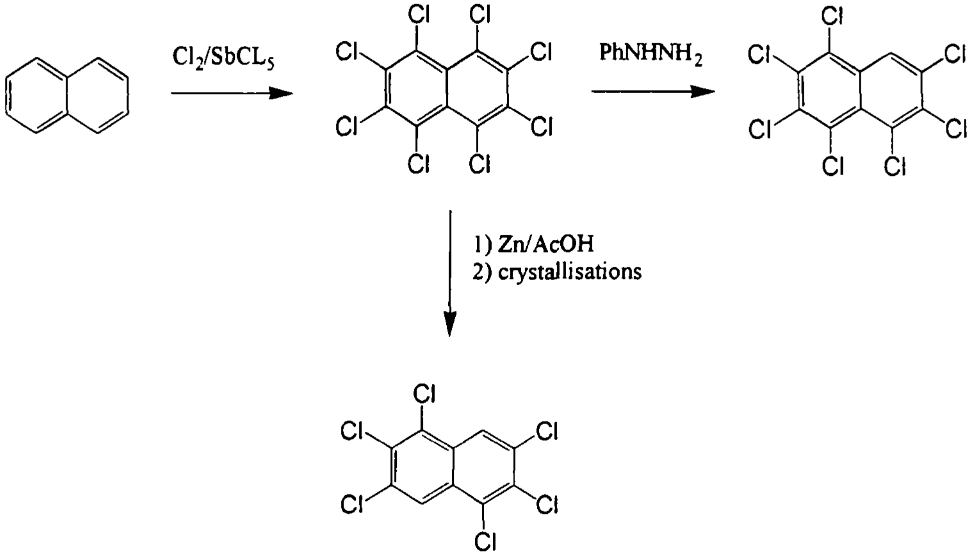
There was found no difference in smell of $^{13}C_{10}$-labelled and unlabelled naphthalene.

Synthesis of $^{13}C_{10}$-labelled chlorinated naphthalenes (stages 2,4 and 5)

A series of $^{13}C_{10}$-labelled PCNs was prepared on a mg-scale via the following reactions. Each procedure was preliminary tested on a multi-mg scale with unlabelled compounds.

Two recently developed synthetic methods have been used to perform the transformations, described above – chlorosubstitution of nitro and chlorosulfonyl groups with hexachlorocyclopentadiene[8] and selective hydrodechlorination of PCNs with Zn/AcOH[9].





Results and Discussion

8 isomerically pure $^{13}C_{10}$-labelled PCNs, namely 1,2,3,4-TeCN, 1,3,5,7-TeCN, 1,2,3,5,7-PeCN, 1,2,3,4,5,7-HxCN, 1,2,3,4,5,8-HxCN, 1,2,3,5,6,7-HxCN, 1,2,3,4,5,6,7-HpCN and OctaCN were prepared in mg amounts, sufficient for use in environmental analysis. These and other isomers can be prepared in larger quantities, if there is significant demand.

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References

1. Schlabach M, Biseth A, Gundersen H, Knutzen J;*Organohalogen Compounds*,**1995**,24,489.
2. Auger P, Malaiyandi M, Wightman R.H., Bensimon C., Williams D.T.; *Environ. Sci. Tech.* **1993**, 27, 1673.
3. Nikiforov V.A., Auger P., Wightman R.H., Malaiyandi M., Williams D.T.; *Organohalogen Compounds*, **1992**, 8, 123.
4. Nikiforov V.A., Karavan V.S., Miltsov S.A., Tribulovich V.G.; *Organohalogen Compounds*, **1993**, 14, 229.
5. Nikiforov V.A., Miltsov S.A., Karavan V.S., Tribulovich V.G., Vlasov S.V., Wightman R.H.; *Organohalogen Compounds*, **1994**, 19, 137.
6. Auger P, Malaiyandi M, Wightman R.H., Williams D.T.; *J. Labelled Compds. Radiopharm.* **1993**, 33, 263.
7. Bolt D.L., Bradley J.C., Re M.A.; *Organohalogen Compounds*, **1995**, 23, 255.
8. Nikiforov V.A., Wightman R.H.; *Chimia*, **1997**, 452.
9. Miltsov S.A., Karavan V.S., Nikiforov V.A., Tribulovich V.G., Varentsov V.V.; *Zh. Org. Khimii(Rus)*, **1998**, in press.