

Chem. Ber. **116**, 751–760 (1983)The Metallation-Elimination Reaction, II<sup>1)</sup>**Monocyclic Anions and Polyanions***Dieter Wilhelm, Timothy Clark, Thomas Friedl, and Paul von Ragué Schleyer\**Institut für Organische Chemie der Universität Erlangen-Nürnberg,  
Henkestr. 42, D-8520 Erlangen

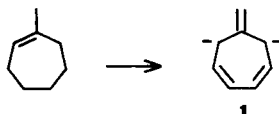
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Equimolar mixtures of *n*-butyllithium and potassium *tert*-amyloxide effect metallation and metal hydride elimination of cyclic olefins directly to give conjugated anions and polyanions in a single operation. 1-Methyl-1-cycloalkenes or methylenecycloalkanes are particularly well suited and give highly unsaturated products. Odd-membered rings eliminate better than their even-membered counterparts, and eight-membered rings eliminate particularly slowly. Reactions with methyl iodide and trimethylsilyl chloride proceed smoothly in high yield.

**Die Metallierungs-Eliminierungs-Reaktion, II<sup>1)</sup>****Monocyclische Anionen und Polyanionen**

Äquimolare Mischungen von *n*-Butyllithium und Kalium-*tert*-amyloxid bewirken Metallierung und Metallhydrid-Eliminierung an cyclischen Olefinen und führen direkt in einer Eintopf-Reaktion zu konjugierten Anionen und Polyanionen. 1-Methyl-1-cycloalkene oder Methylenecycloalkane sind besonders gut geeignet und geben stark ungesättigte Produkte. Ringe mit ungerader Kohlenstoffzahl eliminieren besser als die geradzahligen. Achtgliedrige Ringe eliminieren extrem langsam. Reaktionen mit Methyljodid und Trimethylsilylchlorid verlaufen glatt und in guter Ausbeute.

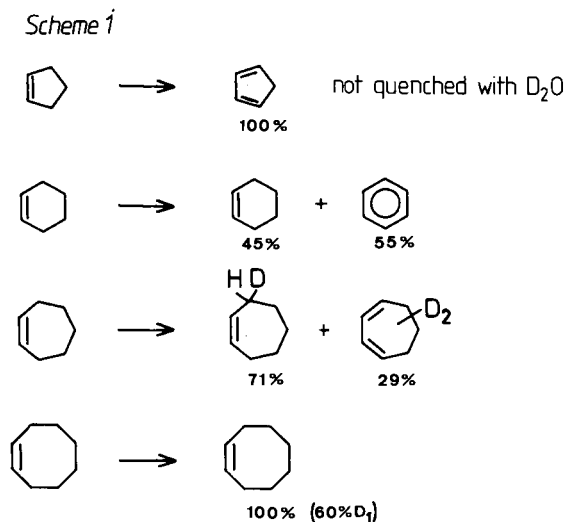
Mixtures of *n*-butyllithium (BuLi) with potassium tertiary alkoxides are highly active metallation reagents. *Lochmann's* base (BuLi/KOtBu)<sup>1a)</sup> has been used extensively to generate anions and dianions<sup>2–9)</sup>, but other potassium tertiary alkoxides such as potassium menthoxide<sup>4)</sup> or potassium *tert*-amyloxide<sup>10)</sup> have the advantage of solubility in hydrocarbon solvents. In the first paper of this series<sup>11)</sup> a BuLi/potassium *tert*-amyloxide (BuLi/KOtAm) mixture was shown to be effective for the catalysis of metal hydride eliminations, which normally require higher temperatures<sup>12–17)</sup> or are carried out using hydride acceptors<sup>18–25)</sup>. By combining the metallation and elimination reactions we were able to prepare the heptafulvene dianion<sup>11)</sup> (**1**), which is inaccessible by direct metallation (BuLi adds to cycloheptatrienes). *Bates'* calculations<sup>26)</sup> indicate **1** to be one of the least stable dianions which have been prepared.



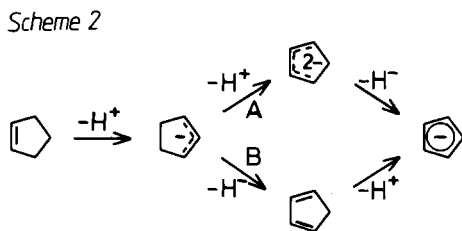
We have now investigated the applicability and synthetic utility of the metallation-elimination reaction for a variety of monocyclic olefins, dienes, and aromatic molecules. The conjugated anions and polyanions which result can be converted to useful derivatives.

### Cycloalkenes

The  $C_5$  to  $C_8$  cycloalkenes were subjected to the standard metallation-elimination conditions (see exp. section) with the results shown in Scheme 1.



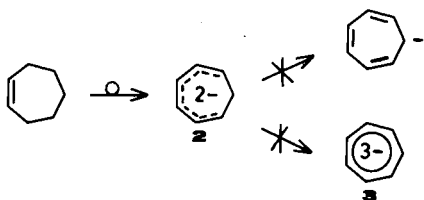
Interestingly, the  $6\pi$  electron cyclopentadienyl anion is formed quantitatively, whereas the yield of benzene, a neutral aromatic, is only 55%. In the latter case, neither cyclohexadienes nor dideuterated cyclohexenes were found. BuLi addition products were not detected in any of these reactions; this rules out extensively conjugated polyenes as intermediates. There are two likely pathways to the cyclopentadienyl anion (Scheme 2).



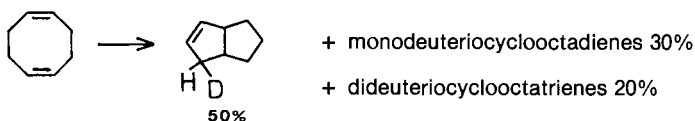
Path A involves a dianion intermediate formed directly by deprotonation of a preformed allyl anion. Path B is more conventional and involves a neutral diene inter-

mediate. A decision between paths A and B is not possible on the basis of our results. The final step to give the aromatic product is obviously fast, as shown by the behavior of cyclohexene. It is also not obvious that either A or B should be so much slower as the rate determining step for cyclohexene than for cyclopentene. We were also unable to observe any intermediate polyenes from the reaction of 1-methyl-1-cycloheptene<sup>11</sup>.

The difference in behaviour between cycloheptene and cyclooctene is also striking. Cycloheptene gives an almost 30% yield of products derived from the cycloheptadienyl dianion **2** which neither eliminates to the antiaromatic cycloheptatrienyl anion nor metallates to give the  $10\pi$  trianion **3**<sup>27</sup>:



The isolation of quench products from **2** is indirect evidence for mechanism A. Cyclooctene, on the other hand, gives no polyolefinic products and no evidence of dianion formation. Although ring strain (preventing coplanarity) may be responsible in this instance, there appears to be an alternation in the elimination behavior of cycloalkenes: the odd-membered rings eliminate better than their even-membered counterparts, even when the even-membered product is aromatic. In an attempt to obtain the aromatic cyclooctatetraenyl dianion<sup>28-33</sup>, 1,5-cyclooctadiene was treated with BuLi/KOtAm under the usual conditions. The products showed only 20% elimination to the desired product; the main reaction was the known ring closure to *cis*-bicyclo[3.3.0]oct-2-ene<sup>34</sup>:

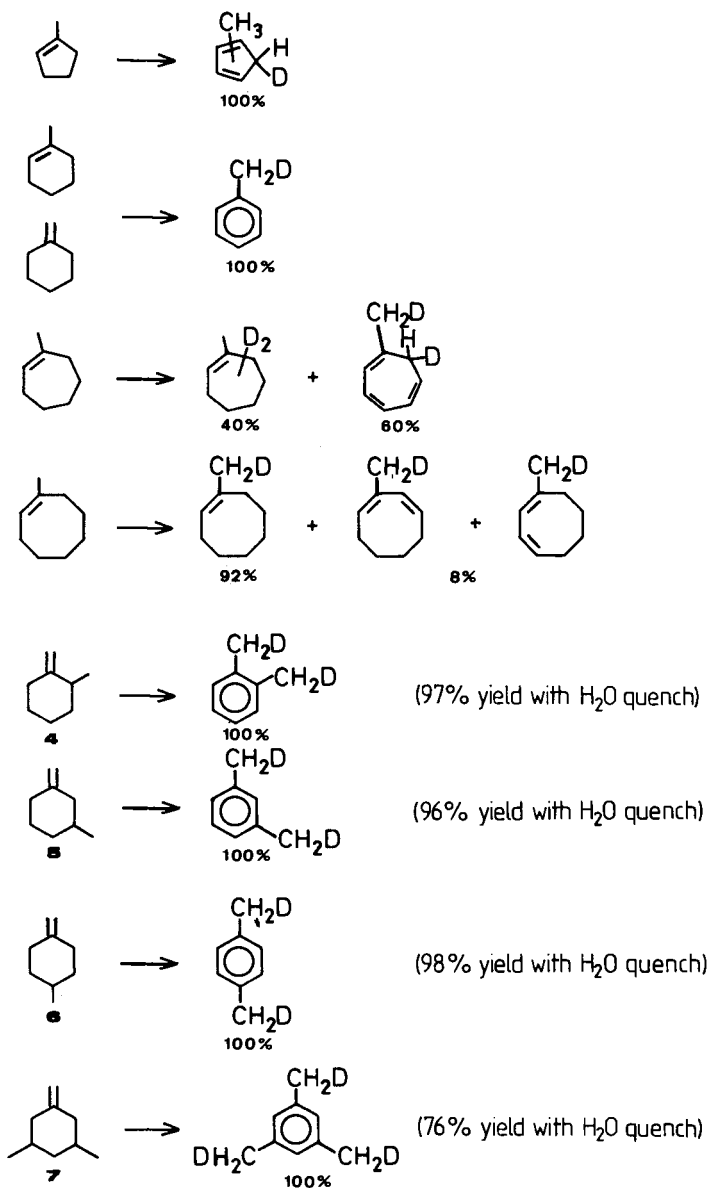


### 1-Methyl-1-cycloalkenes and Methylenecycloalkanes

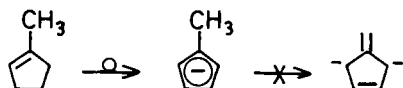
In our earlier work<sup>11</sup> we postulated that the trimethylenemethane dianion derivative was a key intermediate in the formation of dianion **1**. A direct comparison between cycloalkenes and compounds containing an isobutene unit is therefore of interest. A series of 1-methyl-1-cycloalkenes and methylenecycloalkanes illustrate the effect of this structural unit on the metallation-elimination reaction. The results are summarised in Scheme 3.

The inclusion of an isobutene unit in the substrate clearly strongly favours the elimination reaction, as suggested previously<sup>11</sup>. The methylcyclopentadienyl anion (not the fulvene dianion) is formed in quantitative yield.

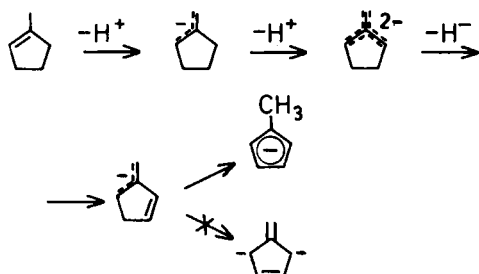
Scheme 3



This result probably indicates that a rearrangement takes place during the metallation-elimination as the methyl protons are almost certainly the most acidic (Scheme 4).



Scheme 4

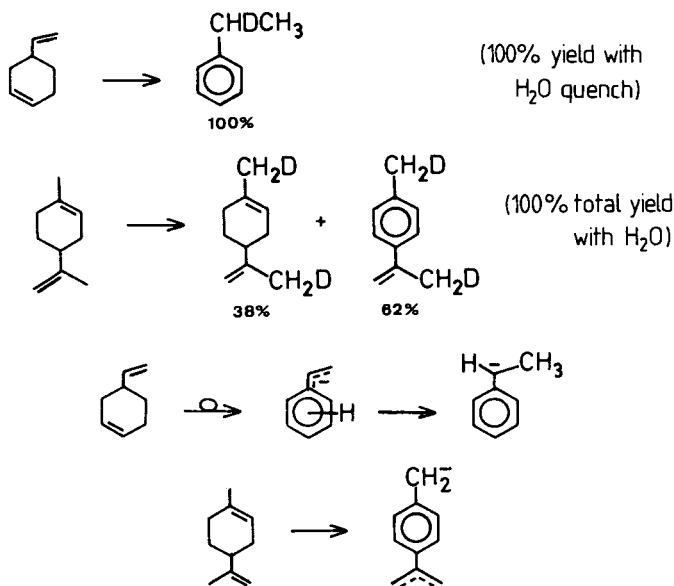


The six-membered rings, either with one, two, or three methyl groups, all undergo a smooth elimination reaction in high yield to give the mono-, di-, or tri-benzyl anions<sup>26,35</sup>. Surprisingly, the yields obtained by this procedure are better than those obtained by direct metallation of xylenes or of mesitylene<sup>26,35</sup>. The formation of the heptafulvene dianion<sup>11</sup>) also emphasises the usefulness of metallation-elimination in synthesising unusual conjugated anions.

1-Methyl-1-cyclooctene undergoes only a small amount of elimination to methylcyclooctadiene (the mixture of isomers is probably due to rearrangement during the work up procedure). The deuterium distribution in the products, however, suggests that only monoanions were present in the reaction mixture and that any dianions formed eliminated. No ring-closed products were detected.

As the six-membered rings gave practically quantitative elimination we investigated two other possible precursors for benzyl-type anions (Scheme 5).

Scheme 5

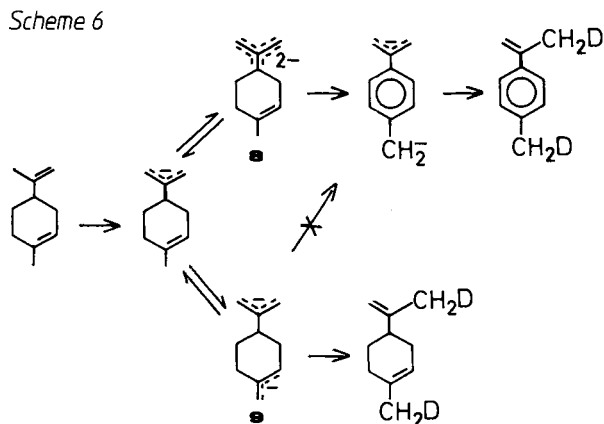


4-Vinyl-1-cyclohexene eliminates quantitatively to give the 1-phenylethyl anion. As in the case of the methylcyclopentadienyl anion, the aromatisation must occur by rearrangement, rather than elimination.

Limonene, on the other hand, retains the trimethylenemethane dianion unit in the aromatic anion.

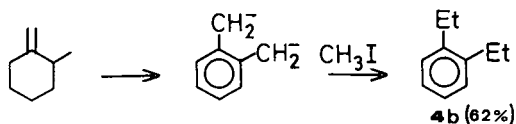
The mechanism of the limonene reaction is particularly interesting as it is possible that the trimethylenemethane dianion derivative **8** is the precursor for elimination, whereas the dianion **9** does not eliminate (Scheme 6).

The deuterium distribution in the recovered limonene supports this mechanism.



## Quench Reactions

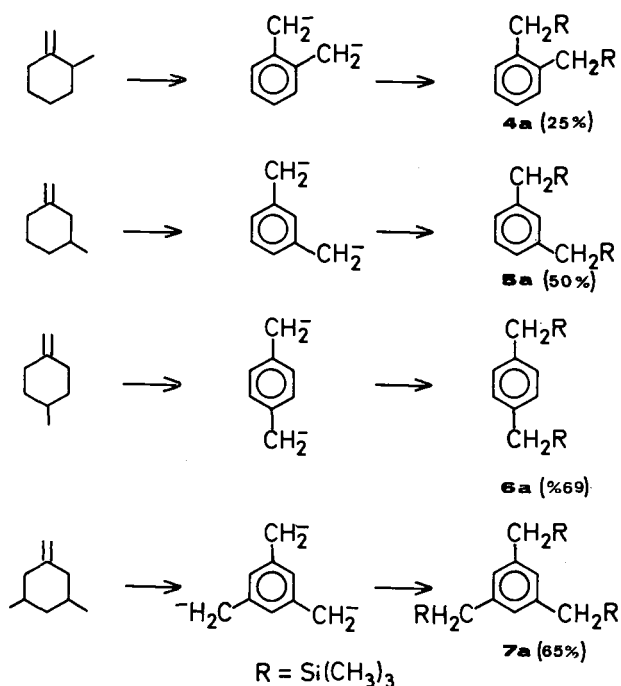
The xylyl dianions and the mesityl trianion were allowed to react with methyl iodide and with trimethylsilyl chloride. The reaction mixture obtained from the metallation-elimination of 1-methyl-2-methylenecyclohexane was cooled to  $-78^{\circ}\text{C}$  and methyl iodide was added. After the reaction mixture had warmed to room temperature, a further 20 hours were required until the anion colour disappeared. Work up gave a 62% yield of 1,2-diethylbenzene (**4b**) based on the starting material.



Despite the relatively slow reaction the overall yield of the metallation-elimination and methylation procedure is acceptable for synthetic purposes.

The reaction with trimethylsilyl chloride also is slow, but the yields are somewhat better. After the normal metallation-elimination procedure and the addition of an excess of trimethylsilyl chloride, 18 hours at room temperature and 30 hours reflux are needed to quench the anion. The yields are, however, comparable with, or better than, those obtained by direct metallation of xylenes or mesitylene and subsequent reaction

with trimethylsilyl chloride. Only the *o*-xylyl dianion gives a yield lower than 50% and the mesityl trianion smoothly incorporates three trimethylsilyl groups in an overall yield of 65% based on olefin starting material.



Despite the complexity and heterogeneity of the metallation-elimination reaction mixtures, synthetically useful yields of anion or polyanion products can be obtained.

## Conclusions

Odd-membered cycloalkenes are better suited for elimination than their even-membered counterparts. The presence of an isobutene unit facilitates the metallation-elimination reaction.

The reaction probably occurs *via* the formation of a dianion, which then eliminates.

Aromatisation may occur *via* an anionic rearrangement, rather than a metallation or elimination.

Benzyl anions do not eliminate.

Quench reactions with methyl iodide or trimethylsilyl chloride proceed in good yield.

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## Experimental Part

$^1\text{H}$  NMR spectra: JEOL PMX-60 (TMS as internal standard). – Mass spectra: Varian MAT CH 4 and Varian MAT 311-A. – GLC analyses and preparative separations: Perkin Elmer F 21 preparative gas chromatograph (flame ionization detector). – HPLC: Du Pont 830. – The methylenecycloalkenes **4**, **5**, **6**, and **7** were obtained in 30–35% yield by Wittig reaction of the corresponding ketones<sup>36–38</sup>. The other starting materials were commercially available.

The number of deuterium atoms and positions of substitution were confirmed by mass spectrometry and by NMR. Dry nitrogen atmosphere was used for all reactions. The butyllithium and potassium *tert*-alkoxide solutions used were approximately 1.6 M. Yields quoted in the tables are based on GLC analysis of the recovered olefins which in all cases were obtained in at least 80% total yield, based on starting material.

*Preparation of potassium tert-amyloxide (potassium 1,1-dimethylpropoxide) solution (KOtAm)*: Freshly cut pieces of potassium metal (50 g, 1.28 mol) were added to a stirred solution of 88.2 g (1.0 mol) *tert*-amyl alcohol in 500 ml dry hexane. The reaction was allowed to proceed overnight, during which time the mixture became almost solid, and then cautiously heated to 70°C and refluxed for 72 h. The hot solution was allowed to cool enough to allow the residual potassium to solidify, and was then filtered under nitrogen. The solution was standardized by hydrolysis with excess water and titration with standard acid.

*Preparation of 1:1 BuLi/KOtAm*: 1.6 M *n*-butyllithium in hexane was standardized by the Gilman double titration procedure<sup>39</sup>. BuLi/KOtAm was prepared in the reaction flask by adding one equivalent of KOtAm solution slowly to vigorously stirred BuLi in hexane. The rate of addition is not critical as long as excessive heating of the mixture is avoided.

*Metallation-elimination reactions*: An appropriate amount of olefin (Table 1) was added slowly by syringe to stirred BuLi/KOtAm. The mixture was stirred at room temperature for *x* hours (see Table 1), during which time the intense colour of the metallated olefins developed. The reaction mixture was then slowly heated to reflux and maintained at that temperature for *y* hours. For all but the most volatile olefins (see below) the reaction mixture was allowed to cool to room

Table 1. Olefins reacted *x* hours at room temperature and *y* hours at reflux in an *n*-fold excess of BuLi/KOtAm

Olefin	<i>n</i>	<i>x</i>	<i>y</i>
cyclopentene	2	14	5
cyclohexene	2	24	18
cycloheptene	4	17	7
cyclooctene	4	17	7
1,5-cyclooctadiene	4	17	7
1-methyl-1-cyclopentene	4	17	7
1-methyl-1-cyclohexene	4	17	7
methylenecyclohexane	4	17	7
1-methyl-1-cycloheptene	6	17	7
1-methyl-2-methylenecyclohexane ( <b>4</b> )	6	16	6
1-methyl-3-methylenecyclohexane ( <b>5</b> )	6	16	6
1-methyl-4-methylenecyclohexane ( <b>6</b> )	6	16	6
1,3-dimethyl-5-methylenecyclohexane ( <b>7</b> )	7	16	6
4-vinyl-1-cyclohexene	2.5	17	7
limonene	9	17	6



temperature and then quenched by pouring under nitrogen into a large excess of cooled D<sub>2</sub>O, being careful not to allow any colour to develop in the D<sub>2</sub>O mixture. In this way it is nearly possible to avoid remetallation of quenched species. The organic layer was separated, washed with water, twice with methanol/water (1:1), once more with water, and dried over calcium chloride. Wherever possible the hexane was distilled at atmospheric pressure using a 20 cm Vigreux column. For the more volatile olefins separation was achieved by direct preparative GLC on the hexane solution. Residual *tert*-amyl alcohol and hexane were removed by preparative GLC and the olefins analysed by NMR and mass spectrometry (Table 2). Duplicate experiments were carried out using H<sub>2</sub>O and D<sub>2</sub>O quench. The H<sub>2</sub>O quenched reactions were used to identify products and the D<sub>2</sub>O labelled products to ascertain the degree of metallation. In all cases the total deuterium content determined by mass spectrometry and NMR agreed within experimental reproducibility. Products were identified by GLC and NMR comparison with commercially available samples.

Table 2. GLC conditions for separation of the quenched products

Starting Olefin	Column	Column Temperature in °C
cycloheptene	a	90
cyclooctene	a	100
1,5-cyclooctadiene	a	100
1-methyl-1-cyclohexene	a	100
methylenecyclohexane	a	100
1-methyl-1-cycloheptene	a	120
methylmethylenecyclohexene mixture	b	100
1,3-dimethyl-5-methylenecyclohexane	b	105
5-vinyl-1-cyclohexene	a	110
limonene	b	100

a: 3/8'' 20' × 30% SE-30 on Chromosorb-W.

b: Ucon LB-500 × 5 m 3/8''.

*The quench of cyclopentadiene, benzene, and methylcyclopentadienes:* After the reaction had been carried out in the usual fashion, the hexane solvent was removed under vacuum at room temperature. The reaction flask was then returned to a nitrogen atmosphere and arranged for distillation. H<sub>2</sub>O or D<sub>2</sub>O was then injected into the dry BuLi/KOtAm mixture and the quenching products allowed to flash distill into a cold receiver.

*Quench reaction of the xylyl dianions and the mesityl trianion with trimethylsilyl chloride:* After the normal metallation-elimination reaction, the mixture was cooled to room temperature. A four-fold excess of trimethylsilyl chloride (based on BuLi/KOtAm) was added to the reaction mixture. After stirring for 18 h at room temperature the mixture was refluxed for 30 h. Unreacted trimethylsilyl chloride was removed under vacuum at room temperature, 30 ml of hexane and 20 ml of water were added, the organic layer was separated, washed twice with water and dried over calcium chloride. **6a** and **7a** were recrystallized in 69 and 65% yields from methanol. **4a** and **5a** were obtained by HPLC (Zorbax ODS/MeOH) in 25 and 50% yields. Compounds **4a**–**7a** were characterised by mass spectrometry and <sup>1</sup>H NMR<sup>35</sup>.

*Methylation of o-xylyl dianion:* After the elimination the reaction mixture was cooled to –78°C. A four-fold excess of methyl iodide (based on BuLi/KOtAm) was added by syringe. After warming to room temperature, the mixture was stirred for 20 h, until the colour of the anion had disappeared. Unreacted CH<sub>3</sub>I was removed under vacuum at room temperature and

the mixture was hydrolysed with 20 ml of cooled water. The organic layer was separated, washed twice with water, and dried over calcium chloride. The resulting 1,2-diethylbenzene (**4b**) was separated by GLC (column b/110°C; see Table 2) in 62% yield and was identical with a commercial sample.

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