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# Reduction of Monoacyl Hydrazobenzenes with Lithium Aluminium Hydride and Direct Alkylation of Hydrazobenzene by Ion Pair Extraction

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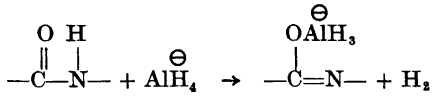
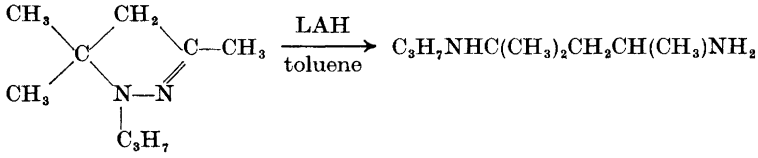
Lithium aluminium hydride reduces monoacyl hydrazobenzenes in refluxing diethyl or dibutyl ether in fair yields to the corresponding monoalkyl hydrazobenzenes. In most cases the monoalkyl anilines are formed as by-products. When using ion pair extraction for the direct alkylation a common ion effect was observed with inorganic halides.

For the preparation of mono- and dialkylhydrazines reduction of acylhydrazines with lithium aluminium hydride is of some interest.[1–3] Acylhydrazines having a hydrogen on the acylsubstituted nitrogen are reported to be reduced very slowly due to complex formation with the hydride:[4]

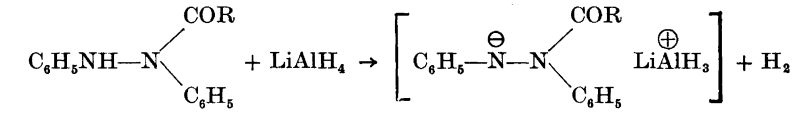


With 2-acyl-1,1-diphenylhydrazines, however, LAH-reduction goes smoothly,[5] *e.g.* by using 2 mol of the reducing agent and refluxing dibutyl ether (b.p. 141°C) as a solvent, the 2-monoalkyl-1,1-diphenylhydrazines are prepared in good yields. At this temperature lithium aluminium hydride causes some cleavage of the N–N bond.[5] By refluxing *N*-propyl-3,5,5-trimethyl-2-pyrazoline in toluene with LAH,[6] the N–N bond breaks, and the double bond is reduced.



Monoacyl hydrazobenzenes are not able to form complexes of the mentioned kind. Benzoyl hydrazobenzene was reduced by lithium aluminium hydride

(30 % excess) in refluxing ether during 5.5 h while the acetyl analogue after 48 h gave a crude product which was a dark viscous liquid and difficult to purify. Changing the solvent to dibutyl ether did not improve this result, nor were propionyl and isobutyroyl hydrazobenzenes reduced under these conditions. When 160 % excess of the reducing agent was used, 13 – 21 % yield of the alkyl hydrazobenzene was isolated after 2.5 h. Monoacyl hydrazobenzene has one moderately active hydrogen, and, assuming that replacement of this is the first reaction which occurs, 1 mol of lithium aluminium hydride will be occupied in forming a complex.



This complex seems not to be inactivated towards LAH, as a reduction rapidly takes place with a second mol of the hydride. The reaction time was from 2 to 3 h and the yield varied greatly with the type of acyl group, as can be seen from Table 1. With pivaloyl and 2,4,6-trimethylbenzoyl hydrazobenzene, only the corresponding alkyl aniline could be found in the reduction mixture.

*Table 1.* Yields, melting points and *m/e* from the mass spectra from lithium aluminium hydride reduction in refluxing dibutyl ether of monoacyl hydrazobenzenes.

The reaction time was 2 – 3 h. $C_6H_5NHN(C_6H_5)CH_2R$

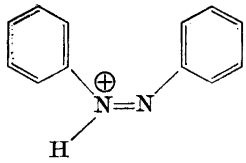
| R | Molar ratio LAH/ acyl comp. | Crude product of $C_6H_5NHN(C_6H_5)CH_2R$ Yield % | Purified product Yield % | Melting point °C | *m/e* | Crude product of $C_6H_5NHCH_2R$ Yield % | *m/e* |
|---|---|---|---|---|---|---|---|
| $CH_3$ | 2.4 | 28 | 18[a] | 38 – 40 | 212 | 16 | 121 |
| $C_2H_5$ | 1.6 | 35 | 8[a] | 32 – 34 | 226 | 6 | 135 |
| $CH(CH_3)_2$ | 2.7 | 10 | [b] | [b] | 240 | 13 | 149 |
| $C(CH_3)_3$ | 2.6 | 0 | | | | 20 | 163 |
| $C_6H_5$ | 1.3 | 60[c] | 42[d] | 72 – 74[e] | 274 | 0 | |
| $CH_2C_6H_5$ | 2.0 | 17 | 9[d] | 111.5 – 113 | 288 | 3 | 197 |
| $CH{=}CHC_6H_5$ | 3.5 | 20 | 10[d] | 83.5 – 85.5 | 300 | 4 | 211[g] |
| $CH{=}CHCH_3$ | 2.2 | 11[f] | [b] | [f] | 240 | | |
| 2,4,6-$C_6H_2(CH_3)_3$ | 2.0 | 0 | | | | | |

[a] From petrol ether (40 – 60°C) at – 10°C. [b] Liquid at 0°C, contaminated with azobenzene, boiling point and yield of purified product not found. [c] Reduced in diethyl ether. [d] From methanol. [e] Lit. m.p. 60 – 61°C.[14] [f] Contained a mixture of R = $CH_2CH_2CH_3$ and R = $CH{=}CHCH_3$ in the ratio 3:2, found by integration of the NMR-spectrum. [g] R = $CH_2CH_2CH_3$.

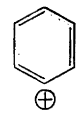
After removal of the solvent the reaction mixture was a dark viscous liquid and contained some unreacted starting material, the reduction product, the corresponding alkyl aniline, azobenzene and other by-products. The

mixture was separated by column chromatography. Azobenzene emerged first from the column together with the product and was very difficult to separate from the alkyl hydrazobenzenes. It can be seen from Table 1 that the attempts to separate the products from isobutyroyl and crotonoyl hydrazobenzene were not successful. The NMR-spectra were not disturbed by azobenzene since its absorptions occurred between $\tau$ 1.97 and $\tau$ 2.67 which is at a lower field than the aromatic protons of the alkyl hydrazobenzenes. Having a molecular weight of 182, azobenzene did not interfere with the *m/e* of the mass spectra.

The infra-red spectra showed marked differences in the N – H stretching vibrations for the three types of compounds. For the acyl hydrazobenzenes the N – H absorptions were in the range 3250 – 3285 $cm^{-1}$, for the alkyl hydrazobenzenes 3300 – 3330 $cm^{-1}$ and for the alkyl anilines 3380 – 3410 $cm^{-1}$. The mass spectra all show the molecular ion and have *m/e* 183 due to

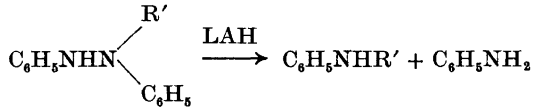


as well as *m/e* 77 due to



The data from the NMR-spectra are collected in Table 5.

The formation of alkyl anilines indicates an attack on the N – N hydrazine bond by the reducing agent, *e.g.*




Attempts at direct alkylation of hydrazobenzene with some reactive halides as allyl bromide, benzyl bromide, *p*-nitrobenzyl bromide, *p*-bromophenacyl bromide, 1-chloro-2,4-dinitrobenzene and 1-fluoro-2,4-dinitrobenzene in ethanol or in dimethylformamide with potassium carbonate as a base did not give any results even after 30 days at room temperature.

Good results were obtained by using the ion pair extraction method of Brändström,[7] even if hydrazobenzene is a very weak acid which only to a negligible extent can be extracted as an ion pair with tetrabutylammonium hydroxide. The solid residue from the organic phase was mainly unchanged hydrazobenzene contaminated by some azobenzene even after refluxing for 1.5 h in methylene chloride, 1,1-dichloroethane or in chlorobenzene. When these solutions were treated with certain alkyl halides until the aqueous layer became neutral or acidic (during 1 to 30 h), alkylated products were obtained. Methylene chloride was generally superior to chlorobenzene or 1,1-dichloroethane as a solvent even if the reaction time were somewhat longer as shown in Table 2. The yields are calculated from the NMR-spectra of the crude products which also contained azobenzene and hydrazobenzene.

In his experiments Brändström [7–12] used tetrabutylammonium hydrogen sulphate and sodium hydroxide. He reported [7] that alkylation with a reactive chloride, *e.g.* benzyl chloride, in some cases needed only catalytic amounts

*Table 2.* Yields and reaction times for the alkylation of hydrazobenzene in different solvents with one equivalent each of tetrabutylammonium hydroxide and sodium sulphate.

| Solvent | $CH_2Cl_2$ | | $CH_3CHCl_2$ | | $C_6H_5Cl$ | |
|---|---|---|---|---|---|---|
| Reagent | Yield % | Time | Yield % | Time | Yield % | Time |
| $CH_2=CHCH_2Br$ | 59 | 70 min | 42 | 42 min | 49 | 9 min |
| $CH_3I$ | 39 | 2 h | 34 | 70 min | 40 | 34 min |
| $C_2H_5I$ | 40 | 24 h | 20 | 4 h | 28 | 40 min |

of the quaternary compound. In this work tetrabutylammonium hydroxide (40 % in water) was used. The influence of inorganic salts as potassium bromide, sodium iodide, and sodium sulphate was investigated in alkylations with methyl iodide and allyl bromide. It was also tested whether the use of various equivalents of the tetrabutylammonium cation altered the yield in the alkylations. The amount of hydroxide was always kept at least equivalent to hydrazobenzene.

The yields and reaction times are collected in Table 3. The reactions with small amounts of tetrabutylammonium cation required the longer reaction time and gave the higher yield whether sodium sulphate was present or if this or other inorganic salts were absent.

*Table 3.* Yields and reaction times for the alkylation of hydrazobenzene with methyl iodide and allyl bromide with various amounts of tetrabutylammonium hydroxide and of inorganic salts in methylene chloride.

| Equivalents of | | | | | | Alkyl halide | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $CH_3I$ | | $CH_2=CHCH_2Br$ | |
| $(C_4H_9)_4NI$ | $(C_4H_9)_4NOH$ | $Na_2SO_4$ | KBr | NaI | NaOH | Yield % | Time h | Yield % | Time h |
| | 2 | | | | | 20 | 3 | 63 | 22 |
| | 1 | | | | | 35 | 3 | 60 | 18 |
| | 0.5 | | | | 0.5 | 55 | 22 | 65 | 18 |
| | 2 | 2 | | | | 29 | 2 | | |
| | 1 | 2 | | | | 32 | 2.5 | 57 | 1 |
| | 1 | 1 | | | | 39 | 2 | 59 | 1 |
| | 0.5 | 0.5 | | | 0.5 | 48 | 24 | 67 | 22 |
| | 2 | | 2 | | | 49 | 3.5 | 73 | 3.5 |
| | 1 | | 1 | | | 67 | 19 | 79 | 22 |
| | 0.5 | | 0.5 | | 0.5 | 69 | 41 | 70 | 17 |
| 2 | | | | | 1 | 77 | 23 | | |
| | 1 | | | 1 | | 79 | 21 | 65 | 2.5 |
| | 0.5 | | | 0.5 | 0.5 | 68 | 23 | 49 | 23 |

With methyl iodide the highest yield occurred when one equivalent each of sodium iodide and the quaternary cation was added to the reaction mixtures.

The same result was also found for allyl bromide when one equivalent of potassium bromide was added. This indicates a common ion effect which improves the reaction conditions for the alkylation.

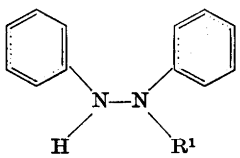
An exploitation of this method is demonstrated in Table 4.

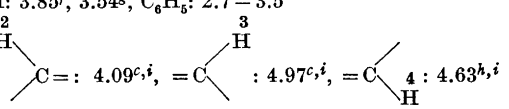
*Table 4.* Yields *etc.* from the alkylation of hydrazobenzene with different alkyl halides RX with one equivalent each of tetrabutylammonium hydroxide and inorganic halide.

| RX | Yield % | Reaction time h | Inorganic salt added | M.p. °C | Lit. m.p. °C |
|---|---|---|---|---|---|
| $CH_3I$ | 79 | 21 | NaI | 70 – 72 | 75 [13] |
| $C_2H_5I$ | 42 | 24 | NaI | 38 – 40 | |
| $(CH_3)_2CHI$ | 13 | 24 | NaI | | 88.0 – 88.4 [14] |
| $C_6H_5CH_2Br$ | 79 | 1 | KBr | 72 – 74 | 50 – 61 [14] |
| $CH_2=CHCH_2Br$ | 79 | 22 | KBr | [a] | |
| $C_2H_5Br$ | 7 | 5 | KBr | 38 – 40 | |
| $C_3H_7Br$ | 13 | 96 | KBr | | |
| $C_2H_5CH(CH_3)Br$ | 0 | 96 | KBr | | |
| $C_6H_5CH_2Cl$ | 0 | 1 | NaCl | | |

[a] Liquid at 0°C, contaminated with azobenzene; boiling point not found.

*Table 5.* $^1H$ Nuclear magnetic resonance at 60 MHz and 98 MHz of the monoalkyl hydrazobenzenes in carbon tetrachloride; chemical shifts in $\tau$ values.




| $R^1$ | | | NH |
|---|---|---|---|
| $CH_3$ | [a] | $CH_3$: 7.00 | 4.89 |
| $C_2H_5$ | [a] | $CH_2$: 6.50, $CH_3$: 8.83 | 4.68 |
| $C_3H_7$ | [a] | $CH_2$: 6.59, 8.30, $CH_3$: 9.03 | 4.42 |
| $C_4H_9$ | [b] | $CH_2$: ~6.64[c] (2H), 8.47 – 8.84[c] (4H), $CH_3$: 9.11 | 4.60 |
| $CH(CH_3)_2$ | [a] | CH: 5.88, $(CH_3)_2$: 8.90 | 4.90 |
| $CH_2CH(CH_3)_2$ | [a] | $CH_2$: 6.74, CH: 8.02, $(CH_3)_2$: 9.03 | 4.62 |
| $CH_2C_6H_5$ | [a] | $CH_2$: 5.34, $C_6H_5$: 2.7 – 3.5 | 4.59 |
| $C_2H_4C_6H_5$ | [a] | $CH_2$: 6.22, 7.06, $C_6H_5$: 2.7 – 3.5 | 4.86 |
| $CH_2CH=CHCH_3$ | [b] | $CH_2$: ~6.64[c], CH: 5.2 – 5.4[c] (2H), $CH_3$: 8.38[d] | 4.49 |
| $CH_2CH=CHC_6H_5$ | [b] | $CH_2$: 5.82[e], CH: 3.85[f], 3.54[g], $C_6H_5$: 2.7 – 3.5 | 4.49 |
| $CH_2CH=CH_2$ | [a] | $CH_2$: 5.98[h,i],  | |



[a] 60 MHz, [b] 98 MHz, [c] Complex. [d] Doublet, $J=4.8$ Hz. [e] Doublet, $J=5.7$ Hz. [f] Two triplets, $J=5.7$ Hz, 15.8 Hz. [g] Doublet, $J=15.8$ Hz. [h] Two doublets. [i] $J_{1,2}=6$ Hz, $J_{1,3}=1.5$ Hz, $J_{1,4}=0$, $J_{2,3}=8$ Hz, $J_{2,4}=12$ Hz, $J_{3,4}\approx 1$ Hz.

This method is useful for alkylation of hydrazobenzene with primary iodides and especially reactive bromides. Organic halides of other types which were tested, gave little or no alkyl hydrazobenzene.

The NMR-data are collected in Table 5.

## EXPERIMENTAL

Melting points were determined on a micro hot-stage. Infra-red spectra were recorded on a Perkin Elmer 457 Grating Infrared Spectrophotometer, NMR-spectra on Varian A – 60 A and HA 100 Spectrometers, and the mass spectra on an AEI/EC MS 902 instrument. TLC was performed with toluene as eluent and iodine vapour as staining reagent.

*The monoacyl hydrazobenzenes* were prepared according to Efimovsky.[15] *General procedure:* To a stirred solution of hydrazobenzene (18.4 g, 0.1 mol) in pyridine (50 ml) and dry ether (300 ml) was added slowly the acid chloride or acid anhydride (0.11 mol). After the reaction was completed, the solution was evaporated *in vacuo* and the pyridine salt removed with 1 N sodium hydroxide. The reaction time and temperature as well as the yields and melting points are collected in Table 6.

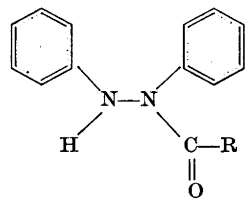



*Table 6.* Data from the preparation of monoacyl hydrazobenzenes

| R | Reaction temp. | Reaction time | Yield % | Recryst. from | Melting point °C | Lit. value °C | *m/e* | Calc. M |
|---|---|---|---|---|---|---|---|---|
| $CH_3$ | 5°C | 20 min | 90 | EtOH | 160 – 163 | 164.5,[15] 160 [16] | | |
| $CH_2CH_3$ | 5°C | 10 min | 96 | EtOH | 141 – 142 | 143,[15] 145 [16] | | |
| $CH(CH_3)_2$ | 25°C | 24 h | 68 | MeOH | 149 – 151 | 152 [15] | | |
| $C(CH_3)_3$ | Reflux | 2 h | 51 | Petrol ether | 144 – 145 | | 254[a] | 268 |
| $C_6H_5$ | 25°C | 30 min | 82 | (100 – 120°C) | 140 – 142 | 136 [15] | | |
| $CH_2C_6H_5$ | 25°C | 2.5 h | 72 | Toluene | 171 – 173 | 169 [15] | | |
| $CH=CHC_6H_5$ | Reflux | 30 min | 95 | PhCN | 225 – 226 | 219 [15] | | |
| $CH=CHCH_3$ | 25°C | 5 h | 84 | EtOH | 149.5 – 151.5 | | 252 | 252 |
| 2,4,6-$C_6H_2(CH_3)_3$ | Reflux | 3 h | 22 | EtOH | 154 – 156 | | 330 | 330 |

[a] M – 14.

*Benzyl hydrazobenzene.* Benzoyl hydrazobenzene (2.88 g, 0.01 mol) in dry ether (150 ml) was added dropwise to a solution of lithium aluminium hydride (0.5 g, 0.013 mol) in dry ether (50 ml) and was refluxed for 5.5 h until the TLC showed no spot corresponding to benzoyl hydrazobenzene. After cooling, water (1 ml) was added very cautiously and then 2 N sodium hydroxide (2 ml) and at last more water (2 ml). After 30 min the mixture was filtered and the precipitate thoroughly washed with ether. The extract was dried with calcium chloride and the ether removed at low pressure leaving a solid residue (1.65 g). Its infra-red spectra showed no carbonyl absorption. Recrystallised from methanol, 1.15 g pale yellow crystals (Table 1).

*Reduction with lithium aluminium hydride in dibutyl ether. General procedure:* In these experiments the solution of the monoacyl hydrazobenzene (4 – 6 g, 0.02 mol) in redistilled dibutyl ether (50 ml) was added dropwise to a stirred dispersion of lithium

aluminium hydride (1.9 g, 0.05 mol) in redistilled dibutyl ether (50 ml). The reaction was followed with TLC and was terminated after 2 – 4 h of refluxing. The mixture was allowed to cool and the excess lithium aluminium hydride was decomposed by the cautious addition of water (2 ml), then 2 N sodium hydroxide (2 ml) and finally more water (3 ml). After 30 min the resulting granular precipitate was filtered off and thoroughly washed with dibutyl ether. The filtrate was dried with calcium chloride, and the solvent was removed at low pressure. The residual mixture (*ca.* 5 g) was separated by column chromatography with toluene as eluent. The alkyl hydrazobenzene emerged first from the column and the alkyl aniline shortly after. When a crystalline product was obtained, it was recrystallized three or four times from petrol ether (40 – 60°C) until it was colourless.

*Alkylation of hydrazobenzene using tetrabutylammonium hydroxide. General procedure:* A solution of tetrabutylammonium hydroxide (7 ml, 40 % in water, 0.01 mol) and the appropriate inorganic halide (0.01 mol) in water (3 ml) was added to a solution of hydrazobenzene (1.84 g, 0.01 mol) and alkyl halide (0.02 mol) in methylene chloride (10 ml) and refluxed with vigorous stirring. When the reaction of the aqueous layer had become neutral or acidic, the mixture was allowed to cool, and the layers were separated. The solvent was removed at low pressure and the residue redissolved in ether. When the halide was an iodide, the insoluble tetrabutylammonium iodide ($\sim$ 3.69 g, 100 %) was filtered off and thoroughly washed with ether. When the halide was a bromide, the ethereal solution was washed thrice with water, dried with calcium chloride, and the ether evaporated. The residue was recrystallised from petrol ether (40 – 60°C) by cooling to – 10°C.

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