Preparation of Some Acylated Methylhydrazines

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During an investigation on thiosemicarbazides, it was desired to use some derivatives of methylhydrazine which had been acylated at the methyl-bearing nitrogen with a group which could easily be split off. For this purpose the reaction of methylhydrazine with ethyl formate, ethyl trifluoroacetate, isopentyl nitrite, and some alkyl carbonates, was investigated.

The methylhydrazinolysis of esters of carboxylic acids has been studied in detail by Hinman and Fulton, They found that both isomers were formed, but the symmetrical isomer was the predominant product. The yield of the unsymmetrical isomer decreased when the size of the acyl group increased. They found the greatest yield (23%) of the unsymmetrical isomer in the case of methyl acetate. A greater yield of unsymmetrical isomer should be expected in the case of esters of formic acid, as in this case the unsymmetrical isomer should be favoured by both sterical and inductive effects. In agreement with this, we found this isomer to be the predominant product in the reaction with ethyl formate. This predominance was shown by infrared spectroscopy, paper chromatography according to Hinman, and the ability to form a benzylidene compound with benzaldehyde or p-nitrobenzaldehyde (Table 1). These benzylidene compounds were isolated in all cases and their IR spectra recorded. Except for the nitroso compound, they all show a strong absorption band around 1700 cm⁻¹, showing that the carbonyl group in the ester has not reacted.

Also in the reaction with ethyl trifluoroacetate, diethyl carbonate and diphenyl carbonate only the 1-substituted 1-methylhydrazine was isolated. From dibenzyl carbonate, however, both 1-benzyloxyacetyl-1-methylhydrazine and the isomer could be isolated, the latter as the predominant reaction product.

We did not succeed in preparing a benzylidene or p-nitrobenzylidene derivative of 1-trifluoroacetyl-1-methylhydrazine. However the IR and NMR spectra of this compound indicated with certainty that it is a 1,1-substituted hydrazine.

The nitroso compound was also prepared by Thiele, but the method described in this paper shows definite advantages over Thiele's method.

Experimental. N¹-Formyl-N¹-methylhydrazine Methylhydrazine (9.0 g) and ethyl formate (14.2 g) were mixed in ethanol (15 ml) (a slightly exothermic reaction took place) and the mixture refluxed for 6 h. The reaction mixture was evaporated on a water bath at

Table 1. Benzylidene- and p-nitrobenzylidene derivatives, CH₂NR¹N₂ = CHR².

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Yield</th>
<th>M.p.</th>
<th>Formula</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%</td>
<td>°C</td>
<td></td>
<td>C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Found</td>
</tr>
<tr>
<td>Formyl</td>
<td>p-Nitrophenyl</td>
<td>78</td>
<td>221-222</td>
<td>C₁₂H₁₄N₃O₁₂</td>
<td>52.35</td>
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<tr>
<td>Ethoxycarbonyl</td>
<td>p-Nitrophenyl</td>
<td>66</td>
<td>155-56</td>
<td>C₁₁H₁₄N₃O₁₂</td>
<td>52.60</td>
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<tr>
<td>Phenoxycarbonyl</td>
<td>Phenyl</td>
<td>80</td>
<td>99-100</td>
<td>C₁₄H₁₄N₃O₁₂</td>
<td>70.80</td>
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<tr>
<td>Benzylxycarbonyl</td>
<td>p-Nitrophenyl</td>
<td>95</td>
<td>131-32a</td>
<td>C₁₄H₁₄N₃O₁₂</td>
<td>61.14</td>
</tr>
</tbody>
</table>

Solvents used for recrystallisation: a) ethanol; b) 50% ethanol.

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50°C in vacuo, the residue being a yellow oil, b.p. 80°C at 0.8 mm Hg. Yield 10 g (68%)
(C). Found: C 33.08; H 8.27; N 37.62. Calc. for
C₃H₅N₂O: C 32.42; H 8.16; N 37.82.
N³-Methyl-N³-trifluoroacetylhydrazine. Methyl-
hydrazine (11.5 g) and ethyl trifluoroacetate (35.5 g) were mixed in ethanol (30 ml) as
described for the formyl compound. Yield after distillation in vacuo 16 g (45%), b.p.
at 1 mm Hg 110—111°C. The compound
crystallised on cooling, and was recrystallised
from a mixture of butanol and cyclohexane,
m.p. 65—66°C. (Found: C 25.45; H 3.88;
Calc. for C₄H₁₂F₃N₂O: C 25.36; H 3.55).
N³-Ethoxy carbonyl-N³-methylhydrazine. Methyl-
hydrazine (13.6 g) and diethyl carbonate (35.4 g) were mixed, and the solution was
refluxed for 24 h. The mixture was distilled in vacuo, and the fraction boiling at 80—84°C
at 14 mm Hg was collected. Yield 10 g (30%)
(Found: C 40.60; H 8.72; N 23.58. Calc. for
C₃H₁₂N₂O: C 40.68; H 8.53; N 23.71).
N³-Phenoxy carbonyl-N³-methylhydrazine.
Methylhydrazine (9.3 g) and diphenyl carbonate (42.4 g) were dissolved in ethanol (50 ml)
and the mixture refluxed for 11 h. The ethanol
was distilled in vacuo at 70°C, and the residue
dissolved in dry ether (0.5 l) and then dry
hydrogen chloride was bubbled through until no
further precipitation occurred. The hydro-
chloride was recrystallised from propanol
m.p. 165—67°C. Yield 19 g (47%). (Found: C
47.30; H 5.31; N 13.90. Calc. for C₃H₁₈N₂O₂Cl: C 47.46; H 5.49; N 13.87).
N³-Benzoyloxycarbonyl-N³-methylhydrazine.
Methylhydrazine (4.6 g) and dibenzyl carbonate (24.2 g) were dissolved in ethanol (25 ml)
and refluxed for 26 h. Ethanol and benzyl-
alkohol were removed in vacuo at 1 mm Hg at
90°C. On cooling, the product settled to a
semisolid mass which became crystalline after
washing with 3 portions of hexane each of 25
ml. The product was recrystallised from
cyclohexane, m.p. 81—82°C. Yield 5 g (31%)
(Found: C 59.90; H 6.79; N 15.50. Calc.
for C₁₆H₁₈N₂O₂: C 59.98; H 6.91; N 15.55).
Hydrochloride, recrystallised from abs. ethanol
m.p. 167—69°C. (Found: C 49.85; H 6.16; N
13.07. Calc. for C₁₆H₁₂N₂O₂Cl: C 49.86; H 6.07;
N 12.93).
N³-Benzoyloxycarbonyl-N³-methylhydrazine.
The hexane solution from N³-benzoyloxycar-
bonyl-N³-methylhydrazine was evaporated. To
the oily residue 10 ml of 4 N hydrochloric
acid were added, and the acidic solution
extracted with 40 ml of ether to remove ben-
yzalcohol. After removing the dissolved ether, the solution was made basic with sodium
hydroxide, when an oil separated, which was
extracted twice with 25 ml of ether. The
etheral solution was first dried over sodium
sulfate and then evaporated, leaving 2 g of
an oil. By making the p-nitrobenzylidene
 derivative it could be concluded that the oil
contained at least 95 % of the isomer with
a free NH₂ group. The oil was dissolved in 25
ml of dry ether and dry hydrogen chloride
bubbled through. The hydrochloride was
recrystallised from butanol. M.p. 161.0—
162.5°C. (Found: C 50.05; H 6.08; N 12.95.
Calc. for C₁₆H₁₈N₂O₂Cl: C 49.86; H 6.07; N 12.93.
N³-Nitroso-N³-methylhydrazine. To methyl-
hydrazine (4.6 g), cooled in water, was added
isopentyl nitrite (16 ml, calc. amount 14 ml)
during a period of ½ h, and a very vigorous
reaction took place. The mixture was extracted
with 100 ml of light petroleum (b.p. 30—60°C)
to remove isopentylalcohol and unreacted
isopentyl nitrite. This left a yellow oil which
solidified on cooling. The petroleum ether
contained a little of the nitroso compound
which could be removed on cooling. The
compound was purified by dissolving in ether
and precipitating with light petroleum, m.p.
44—45°C (Ref.◦, 45°C). Yield 4 g (55%)
The benzylidene compound was also prepared.
M.p. recryst. from methanol 77—78°C (Ref.◦
78°C).

Benzylidene and p-nitrobenzylidene deriva-
tives (Table 1) were prepared by condensation
of the hydrazines with aldehydes in ethanolic
solution.

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