Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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To cite this article: Helmut Egg, Josef Hauzinger, Klemens Kraus & Elisabeth Spanyar (1992) Synthesis of 1,1-Diacetyl-2-arylhydrazines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 22:8, 1199-1203, DOI: 10.1080/00397919208021106

To link to this article: http://dx.doi.org/10.1080/00397919208021106

SYNTHETIC COMMUNICATIONS, 22(8), 1199-1203 (1992)

SYNTHESIS OF 1,1-DIACETYL-2-ARYLHYDRAZINES

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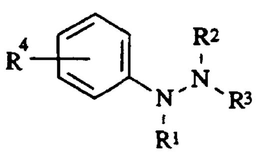
ABSTRACT. The reaction of arylhydrazines **1** with acetic anhydride in the presence of a catalytic amount of 4-(dimethylamino)pyridine leads to 1,1-diacetyl-2-arylhydrazines **4**.

1-Acyl-2-arylhydrazines **2** and 1,2-diacyl-1-arylhydrazines **3** are well studied compounds, which can be prepared by established procedures[1,2,3].



1 $R^1 = R^2 = R^3 = H$
2 $R^1 = H$ $R^2 = RCO$ $R^3 = H$
3 $R^1 = R^2 = RCO$ $R^3 = H$
4 $R^1 = H$ $R^2 = R^3 = RCO$
5 $R^1 = R^2 = R^3 = RCO$

In contrast, 1,1-diacyl-2-arylhydrazines **4** not derived from dicarboxylic acids,

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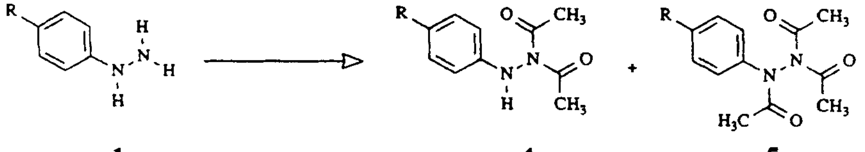
which are of interest in connection with conformational studies, are unknown with one single exception described by Veibel and Lillelund[4]. Presumably because of steric hindrance, they obtained 2-(2,2-diacetylhydrazino)benzoic acid (**4a**) by heating 2-hydrazinobenzoic acid (**1a**) with an excess of acetic anhydride in acetic acid.

In the course of our studies on acylations catalyzed by 4-(dimethylamino)pyridine (DMAP) we found a simple one-step method for the synthesis of **4**. Treatment of solutions of arylhydrazines (**1b-f**) in pyridine with 2 equivalents of acetic anhydride in the presence of 0.1 equivalents of DMAP at room temperature leads in good to moderate yields to the title compounds **4b-f** accompanied by small amounts of the corresponding triacetyl derivatives **5b-f**.



1 **4** **5**

R: b H, c CH_3, d OCH_3, e Cl, f Br

A different behaviour is shown by 4-nitrophenylhydrazine (**1g**) which, under these conditions, yields acetic acid 2-acetyl-1-(4-nitrophenyl)hydrazide (**3g**) exclusively. When the reaction of **1b-f** is carried out without the catalyst, usually mixtures of 2 and 3 are obtained.

The isomeric compounds 3 and 4 can be distinguished by their ^{1}H-NMR spectra. Whereas the spectra of 4 display only one sharp singlet at 2.4-2.5 ppm for the two acetyl groups due to rapid chemical exchange, the spectra of the isomeric 3 are more complex due to hindered rotation about the N-CO bonds[5]. At standard conditions (303 K) partially coalescent spectra with all signals broadened are obtained. Especially the two acetyl groups give rise to two broad singlets with different halfwidth at 2.15-2.05 and 2.0-1.9 ppm.

EXPERIMENTAL

Melting points were determined on a Reichert-Kofler hot stage microscope and are uncorrected. IR spectra were recorded on Shimadzu IR-470 (KBr; cm^{-1}). NMR spectra were recorded on Bruker AM 300 or Jeol JMN-PMX 60 (δ-values in ppm using TMS as internal standard or solvent signals as indirect internal standard).

General Procedure

0.02 mol of acetic anhydride are added to a solution of 0.01 mol. of **1** and 0.001 mol of DMAP in 10 ml dry pyridine with external ice cooling and stirring. The clear solution is kept at room temperature for 12 h, then poured into 100 ml 2N HCl and extracted three times with 50 ml portions of methylene chloride. On evaporation, the combined methylene chloride solution yields an oily residue, which is purified by preparative medium pressure LC[6] on silica (Kieselgel Merck, corn size 0.040-0.063 mm) using ether as eluting agent.

Acetic Acid 1-Acetyl-2-phenylhydrazide (4b)

Yield 1.38 g (72%); m.p. = 85°C (petrolether). $C_{10}H_{12}N_2O_2$ (192.22). Calcd. C 62.49, H 6.29, N 14.57; found C 62.76, H 6.41, N 14.79. IR: 3295 (N-H), 1726 and 1700 (C=O). ^{1}H-NMR ($CDCl_3$): 7.3-6.7 (m, 5H, aromat.), 6.64 (s, 1H, NH), 2.47 (s, 6H, CH_3CO).

Acetic Acid 1-Acetyl-2-(4-methylphenyl)hydrazide (4c)

Yield 1.28 g (62%); m.p. = 95-98°C (cyclohexane). $C_{11}H_{14}N_2O_2$ (206.25). Calcd. C 64.06, H 6.84, N 13.58; found C 64.11, H 6.92, N 13.78. IR: 3295 (N-H), 1708 and 1697 (C=O). ^{1}H-NMR ($CDCl_3$): 7.12, 6.98, 6.67 and 6.53 (AA'XX', 4H, aromat.), 6.6 (s, 1H, NH), 2.46 (s, 6H, CH_3CO), 2.26 (s, 3H, CH_3-Ar).

Acetic Acid 1-Acetyl-2-(4-methoxyphenyl)hydrazide (4d)

Yield 0.77 g (35%); m.p. = 107°C (cyclohexane). $C_{11}H_{14}N_2O_3$ (222.25). Calcd. C 59.45, H 6.35, N 12.60; found C 59.63, H 6.37, N 12.53. IR: 3310 (N-H), 1696 (C=O). ^{1}H-NMR

($CDCl_3$): 6.86, 6.70, 6.67 and 6.51 (AA'XX', 4H, aromat.), 6.6 (s, 1H, NH), 3.69 (s, 3H, CH_3O), 2.44 (s, 6H, CH_3CO).

Acetic Acid 1-Acetyl-2-(4-chlorophenyl)hydrazide (4e)

Yield 1.59 g (70%); m.p. = 103°C (carbon tetrachloride). $C_{10}H_{11}ClN_2O_2$ (226.66). Calcd. C 52.99, H 4.89, N 12.36; found C 53.03, H 5.33, N 12.49. IR: 3285 (N-H), 1716 and 1700 (C=O). ^1H-NMR ($CDCl_3$): 7.20, 7.07, 6.65 and 6.52 (AA'XX', 4H, aromat.), 6.6 (s, 1H, NH), 2.43 (s, 6H, CH_3CO).

Acetic Acid 1-Acetyl-2-(4-bromophenyl)hydrazide (4f)

Yield 1.98 g (73%); m.p. = 101°C (cyclohexane). $C_{10}H_{11}BrN_2O_2$ (271.12). Calcd. C 44.30, H 4.09, N 10.33; found C 44.27, H 3.95, N 10.22. IR: 3290 (N-H), 1713 and 1700 (C=O). ^1H-NMR ($CDCl_3$): 7.32, 7.17, 6.59 and 6.44 (AA'XX', 4H, aromat.), 6.6 (s, 1H, NH), 2.42 (s, 6H, CH_3CO).

Acetic Acid 2-Acetyl-1-(4-nitrophenyl)hydrazide (3g)

A solution of 1.53 g (0.01 mol) 4-nitrophenylhydrazine (1g), 2 ml (0.021 mol) acetic anhydride and 0.122 g (0.001 mol) DMAP in 10 ml dry pyridine is heated 6 h on a steam bath. After cooling the solution is poured into 100 ml 2N-HCl and kept at 0°C for 30 min. The solid product is collected by filtration and recrystallized from 25% EtOH.
Yield 1.96 g (83%); m.p. = 188°C. $C_{10}H_{11}N_3O_4$ (237.22). Calcd. C 50.63, H 4.67, N 17.71; found C 50.44, H 4.35, N 17.44. IR: 3245 (N-H), 1690 and 1675 (C=O). ^1H-NMR (DMSO-d_6): 10.9 (s, 1H, NH), 8.23, 8.08, 7.82 and 7.67 (AA'XX', 4H, aromat.), 2.12 (s, 3H, 1-CH_3CO), 2.02 (s, 3H, 2-CH_3CO).

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(Accepted in The Netherlands 26 November, 1991)