Amidrazones. 12. Formation of 3-Acylamino-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium Salts by Acid-Promoted Cyclization of N^3-Acylated Derivatives of Acrylamide Dimethylhydrazone and (*E*)-Cinnamamide Dimethylhydrazone [1]

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N^3-Acylated derivatives of acrylamide dimethylhydrazone **3a,b** and (*E*)-cinnamamide dimethylhydrazone **3c,d** cyclized, on treatment with hydriodic acid or *p*-toluenesulfonic acid, to give 3-acylamino-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium salts **4a-d**.

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We recently reported [3] efficient syntheses of acrylamide dimethylhydrazone (**1**) and (*E*)-cinnamamide dimethylhydrazone (**2**). In this paper we report that N^3-acylated derivatives of these amidrazones **3a-d** undergo facile acid-promoted cyclizations to give 3-acylamino-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium salts **4a-d**.

Acylation of **2** with acetyl chloride and *p*-toluyl chloride afforded crystalline N^3-acylated products **3c,d**. However, acylation of **1** with acetyl chloride and benzoyl chloride afforded the N^3-acylated products **3a,b** as oils that could not be obtained analytically pure by either vacuum distillation or chromatography on silica gel.

The reaction of **3a** with hydriodic acid gave the cyclized product, 3-(acetylamino)-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium iodide (**4a**). In similar fashion, treatment of the

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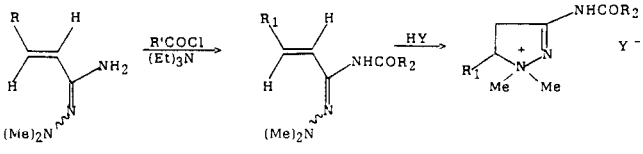
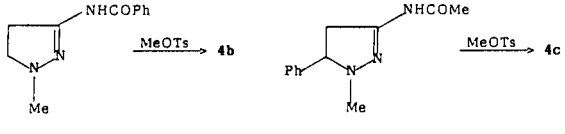


1, R = H
2, R = Ph

3	R_1	R_2
a	H	Me
b	H	Ph
c	Ph	Me
d	Ph	p-tolyl

4	R_1	R_2	Y^-
a	H	Me	I^-
b	H	Ph	TsO^-
c	Ph	Me	TsO^-
d	Ph	p-tolyl	TsO^-



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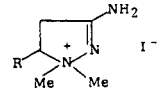
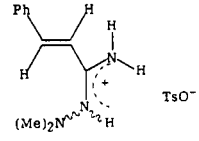


7a, R = H
b, R = Ph



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N^3-acylated amidrazones **3b-d** with ethanolic *p*-toluenesulfonic acid afforded 3-acylamino-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium *p*-toluenesulfonates **4b-d**.

Salts **4b** and **4c** were also prepared by quaternization of the corresponding 3-acylamino-1-methyl-4,5-dihydro-1*H*-pyrazoles **5** [4] and **6** [5] with methyl *p*-toluenesulfonate.

In contrast to the results described above, protonation of amidrazones **1** and **2** gave acylic conjugate acids. The ^{1}H-nmr spectra of the protonated species obtained from **1** and **2** established that cyclization to give cations identical to those present in the previously reported iodide salts **7a,b** [3] did not occur. The reaction of **2** with ethanolic *p*-toluenesulfonic acid afforded a crystalline salt **8**. The assignment of the amidinium-type structure to the cation in **8** is based on its ^{1}H-nmr spectrum which displayed three deshielded NH signals at δ 6.7, 9.6 and 11.0 [6]. Crystalline salts could not be obtained from **1**. However, the ^{1}H-nmr spectrum of the cation generated by protonation of **1** in trifluoroacetic acid clearly supported an acylic structure. The spectrum showed a vinyl multiplet at δ 5.5-6.0, a singlet at δ 2.19 [$(CH_3)_2N$] and broad NH resonance at δ 7.3.

EXPERIMENTAL

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Infrared spectra were obtained from tetrachloroethylene mulls on a Perkin-Elmer 710B instrument. The ^{1}H-nmr spectra were recorded on a Hitachi-Perkin-Elmer 60 MHz instrument employing hexamethyldisiloxane as the internal standard. The ^{13}C-nmr spectra were recorded on an IBM-Bruker WP 100 SY instrument.

*N*³-Acetylacrylamide Dimethylhydrazone (**3a**).

Acetyl chloride (3.5 g, 0.044 mole) was added over 15 minutes to a stirred solution containing 5.0 g (0.044 mole) of **1** [3] and 4.5 g of triethylamine in 150 ml of dry benzene. After stirring for 30 minutes the reaction mixture was filtered. After removal of the solvent at reduced pressure, 6.0 g of the crude product was obtained as a yellow oil which could not be obtained analytically pure by either vacuum distillation or column chromatography on silica gel. The crude material was used for the preparation of **4a**; ^{1}H-nmr (DMSO-d$_6$): δ 2.05 (s, C-CH$_3$), 2.38 (s, (CH$_3$)$_2$N), 5.3 (dd, 1H, *cis*-CH$_2$=CH, J_{cis} = 8 HZ, J_{gem} = 2 HZ), 5.8 (dd, 1H, *trans*-CH$_2$=CH, J_{trans} = 16 HZ, J_{gem} = 2 HZ), 6.8, (dd, 1H, CH$_2$=CH-, J_{trans} = 16 HZ, J_{cis} = 8 HZ), 8.7 (bd s, NH). Minor impurity signals were observed as singlets at δ 1.95, 2.30 and 2.75.

*N*³-Benzoylacrylamide Dimethylhydrazone (**3b**).

Benzoyl chloride (1.3 g, 0.0090 mole) was added over 10 minutes to a stirred solution of 1.00 g (0.0090 mole) of **1** and 3.8 ml of triethylamine in 20 ml of methylene chloride. After stirring for 10 minutes the reaction mixture was filtered and the filtrate washed with three 10 ml portions of 5% sodium carbonate solution. The organic layer was dried over magnesium sulfate. Removal of the solvent at reduced pressure gave a yellow oil that was treated with *ca.* 50 ml of pentane. The pentane-insoluble material was filtered off and the filtrate evaporated at reduced pressure. The crude product was obtained as a yellow oil (0.56 g) which decomposed on attempted vacuum distillation. The crude material was used for the preparation of **4b**; ^{1}H-nmr (deuteriochloroform): δ 2.45 [s, (CH$_3$)$_2$N superimposed on signals (δ 2.3-2.7) due to minor impurities], 5.38 (dd, 1H, *cis*-CH$_2$=CH, J_{cis} = 8 HZ, J_{gem} = 2 HZ), 5.90 (dd, 1H, *trans*-CH$_2$=CH, J_{trans} = 17 HZ, J_{gem} = 2 HZ), 7.05 (dd, 1H, J_{trans} = 17 HZ, J_{cis} = 8 HZ, CH$_2$=CH-R), 7.2-7.9 (m, 5H, ArH), 9.7 (bd s, 1H, NH, deuterium oxide exchangeable).

(*E*)-*N*³-Acetylcinnamamide Dimethylhydrazone (**3c**).

Acetyl chloride (0.80 g, 0.011 mole) was added over 15 minutes to a stirred solution containing 2.0 g (0.011 mole) of **2** [3] and 1.5 ml of triethylamine in 60 ml of dry benzene. After stirring for 2 hours, 20 ml of water was added and the organic layer was separated and dried over magnesium sulfate. After removal of the solvent at reduced pressure the crude product was obtained as a yellow gum that was dissolved in boiling ethanol. On cooling 0.75 g (33%) of product was obtained, mp 95-99°. Further recrystallization from ethanol gave yellow crystals, mp 97-100°; ^{1}H-nmr (deuteriochloroform): δ 2.05 (s, 3H, CH$_3$C), 2.40 (s, 6H, (CH$_3$)$_2$N), 7.1-7.5 (m, 7H, ArH and CH=CH), 9.1 (bd s, 1H, NH exchangeable with deuterium oxide); ir: 1715 and 3300 cm^{-1}.

Anal. Calcd. for C$_{13}$H$_{17}$N$_3$O: C, 67.5; H, 7.4; N, 18.2. Found: C, 67.3; H, 7.4; N, 17.9.

(*E*)-*N*³-(4-Methylbenzoyl)cinnamamide Dimethylhydrazone (**3d**).

This compound was prepared from 2.5 g (0.013 mole) of **2** and *p*-toluyl chloride in a manner analogous to that described for the preparation of **3c**. The crude product was obtained in 99% yield, mp 114-118°. Recrystallization from ethanol gave yellow crystals, mp 123-125°; ^{1}H-nmr (DMSO-d$_6$): δ 2.41 (s, 3H, CH$_3$C), 3.69 (s, 6H, (CH$_3$)$_2$N), 6.8-8.2 (m, 11H, ArH and CH=CH), 9.9 (bd s, 1H, NH); ir: 1680 and 3330 cm^{-1}.

Anal. Calcd. for C$_{19}$H$_{21}$N$_3$O: C, 74.2; H, 6.9; N, 13.7. Found: C, 73.9; H, 7.0; N, 13.6.

3-(Acetylamino-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium Iodide (**4a**).

A solution containing 1.0 g (0.0065 mole) of crude **3a** in 10 ml of ethanol was treated with 1.8 ml of 47% hydriodic acid. Addition of ether to the ice cooled reaction mixture precipitated 0.70 g (38%) of the product, mp 240-250°. Recrystallization from ethanol gave colorless crystals, mp 267-271°; ^{1}H-nmr (DMSO-d$_6$): δ 2.10 (s, 3H, CH$_3$C), 3.32 (s, 6H, (CH$_3$)$_2$N$^+$), 3.4-4.1 (m, 4H, 4-CH$_2$ and 5-CH$_2$), 11.4 (bd s, 1H, NH, exchangeable with deuterium oxide); ^{13}C-nmr (DMSO-d$_6$): δ 23.2 (*C*H$_3$CO), 33.1 (C-4), 54.6 [(CH$_3$)$_2$N$^+$], 61.7 (C-5), 165.6 (C-3 or C=O), 169.1 (C-3 or C=O); ir: 1740 cm^{-1}.

Anal. Calcd. for C$_7$H$_{14}$IN$_3$O: C, 29.7; H, 5.0; N, 14.8. Found: C, 29.9; H, 5.0; N, 14.4.

3-(Benzoylamino)-4,5-dihydro-1,1-dimethyl-1*H*-pyrazolium *p*-Toluenesulfonate (**4b**).

A reaction mixture containing 2.9 g (0.013 mole) of crude **3b** and 2.50 g (0.013 mole) of *p*-toluenesulfonic acid monohydrate in 20 ml of ethanol was kept at room temperature for 12 hours. Addition of ether precipitated 1.5 g (30%) of product, mp 230-234°. The product was shown (^{1}H nmr and ir) to be identical with **4b** prepared as follows:

A mixture of 1.5 g (0.0074 mole) of *N*-(4,5-dihydro-1-methyl-1*H*-pyrazol-3-yl)benzamide **5** [4] and 7.4 g of methyl *p*-toluenesulfonate was heated at 110° for 6 hours. Dilution of the cooled reaction mixture with anhydrous ether precipitated 2.7 g (94%) of the solid product, mp 235-244°. Recrystallization from ethanol-ether gave colorless crystals, mp 243-247°; ^{1}H-nmr (DMSO-d$_6$): δ 2.45 (s, 3H, CH$_3$C), 3.1-4.1 (m, 10H, superimposed on a singlet at δ 3.70, 4-CH$_2$, 5-CH$_2$ and (CH$_3$)$_2$N$^+$); 6.8-8.4 (m, 9H, ArH), 11.9 (bd s, 1H, NH, exchangeable with deuterium oxide); ^{13}C-nmr (methanol-d$_1$): δ 19.3 (*C*H$_3$CO), 33.4 (C-4), 54.4 [(CH$_3$)$_2$N$^+$], 61.9 (C-5), 124.9-141.7 (8 signals), 166.7 (C-3 or C=O), 167.8 (C-3 or C=O); ir: 1720 cm^{-1}.

Anal. Calcd. for C$_{19}$H$_{23}$N$_3$O$_4$S: C, 58.6; H, 6.0; N, 10.8. Found: C, 58.8; H, 5.9; N, 10.7.

3-(Acetylamino)-4,5-dihydro-1,1-dimethyl-5-phenyl-1*H*-pyrazolium *p*-Toluenesulfonate (**4c**).

This compound was obtained in 79% yield from **3c** in a manner analogous to that described for the preparation of **4b**, mp 183-185°. The salt was identical (ir and ^{1}H-nmr) with that prepared by the following procedure:

A mixture of 10.0 g (0.046 mole) of crude *N*-(4,5-dihydro-1-methyl-5-phenyl-1*H*-pyrazol-3-yl)acetamide **6** (mp 76-82°, lit [5] mp 83°), and 12.9 g of methyl *p*-toluenesulfonate was heated at 105° for 8.5 hours. Dilution of the reaction mixture with ether precipitated 13.5 g (73%) of product, mp 183-185°. Recrystallization from ethanol-ether gave colorless crystals, mp 183-185°; ^{1}H-nmr (DMSO-d$_6$): δ 2.10 (s, 3H, CH$_3$CO), 2.22 (s, 3H, ArCH$_3$), 2.72 (s, 3H, N$^+$CH$_3$), 2.85 (s, 3H, N$^+$CH$_3$), 4.0 (m, 2H, 4-CH$_2$), 5.41 (m, 1H, 5-CH), 6.8-7.8 (m, 9H, ArH), 11.8 (bd s, 1H, NH, exchangeable with deuterium oxide); ^{13}C-nmr (methanol-d$_1$): δ 18.3 (Ar*C*H$_3$), 21.2 (*C*H$_3$CO), 35.5 (C-4), 47.8 (N$^+$CH$_3$), 52.5 (N$^+$CH$_3$), 76.0 (C-5), 123.9-140.8 (8 signals), 164.9 (C-3 or C=O), 168.7 (C-3 or C=O); ir: 1735 cm^{-1}.

Anal. Calcd. for C$_{20}$H$_{25}$N$_3$O$_4$S: C, 59.5; H, 6.3; N, 10.4. Found: C, 59.4; H, 6.1; N, 10.4.

3-(4-Methylbenzoyl)-4,5-dihydro-1,1-dimethyl-5-phenyl-1*H*-pyrazolium *p*-Toluenesulfonate (**4d**).

This compound was obtained in quantitative yield from **3d** by the procedure described for the preparation of **4b**, mp 146-152°. Recrystallization from ethanol-ether afforded colorless crystals, mp 150-153°; ^{1}H-nmr (DMSO-d$_6$): δ 2.22 (s, 3H, *p*-toluyl CH$_3$), 2.39 (s, 3H, tosylate CH$_3$), 2.82 (s, 3H, N$^+$CH$_3$), 3.45 (s, 3H, N$^+$CH$_3$), 4.2 (m, 2H, 4-CH$_2$), 4.52 (m, 1H, 5-CH), 6.8-8.1 (m, 13H, ArH), 11.9 (s, 1H, NH, exchangeable with deuterium oxide); ^{13}C-nmr (methanol-d$_1$): δ 19.2 (C-*C*H$_3$), 19.6 (C-*C*H$_3$), 36.5 (C-4), 48.7 (N$^+$CH$_3$), 53.4 (N$^+$CH$_3$), 76.8 (C-5), 124.7-143.4 (11 signals), 165.7 (C=O or C-3), 166.6 (C=O or C-3); ir: 1710 cm^{-1}.

Anal. Calcd. for C$_{26}$H$_{29}$N$_3$O$_4$S: C, 65.1; H, 8.8; N, 6.1. Found: C, 65.1; H, 8.8; N, 6.0.

(*E*)-Cinnamamide Dimethylhydrazonium *p*-Toluenesulfonate (**8**).

Addition of ether to a solution containing 0.30 g of **2** and 0.30 g of *p*-toluenesulfonic acid monohydrate in 5 ml ethanol precipitated 0.51 g (89%) of **8**, mp 154-157°. Recrystallization from ethanol-ether gave colorless crystals, mp 155-157°; ^{1}H-nmr (deuteriochloroform): δ 2.21 (s, 3H, CCH$_3$), 2.48 (s, 6H, N(CH$_3$)$_2$, 6.6-8.1 (m, 12H, ArH, CH=CH and NH), 9.6

(bd s, 1H, NH, exchangeable with deuterium oxide), 11.0 (bd s, 1H, NH, exchangeable with deuterium oxide). On treatment with deuterium oxide, a shoulder at δ 6.7 in the downfield multiplet was removed and a vinyl doublet δ 6.65 (J = 17 HZ) was observed; ^{13}C-nmr (DMSO-d_6): δ 20.8 (C-CH_3), 45.9 [$N(CH_3)_2$], 113.2-158.7 (11 signals); ir: 1620, 1670, 3080, 3170 and 3330 cm^{-1}.

Anal. Calcd. for $C_{16}H_{23}N_3O_3S$: C, 59.8; H, 6.4; N, 11.6. Found: C, 59.8; H, 6.3; N, 11.5.

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