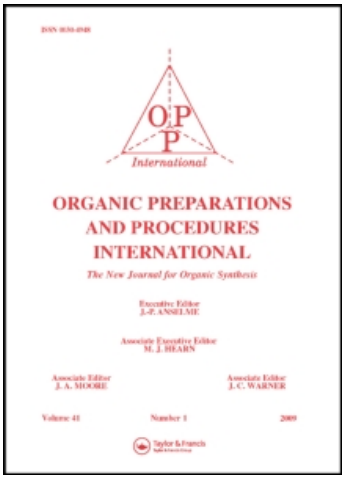

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ACETYLATION OF 4-AMINO-44-DIHYDRO-1H-1,2,4-TRIAZOL-5-ONES

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OPPI BRIEFS

ACETYLATION OF 4-AMINO-4,5-DIHYDRO-1H-1,2,4-TRIAZOL-5-ONES

Submitted by (06/04/92)

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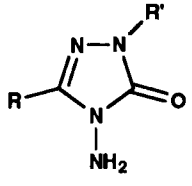
A number of studies involving the acetylation of 1,2,4-triazole derivatives with acetic anhydride have been reported.[1,2] The present work describes the acetylation of compounds **1a-d** with acetic anhydride at different temperatures to afford acetylated products **2-5**. Furthermore, the acetylation of **6a-c** with acetic anhydride gave the diacetyl derivatives **7**.

IR and ^{1}H NMR spectra were useful for the structural elucidation of the acetylated products. The δ values of NH_2 and CONH groups and ring NH were in conformity with reported values.[3-5]



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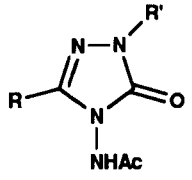

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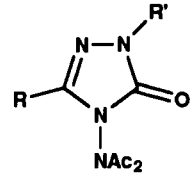

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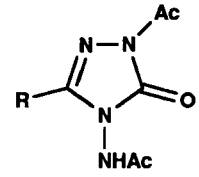

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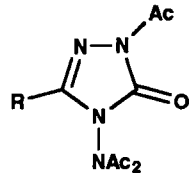

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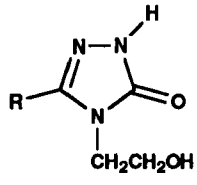

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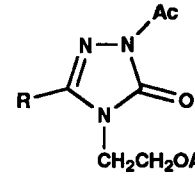

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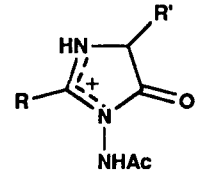

8

a) R = *p*-$MeC_6H_4CH_2$, R' = H b) R = *p*-$ClC_6H_4CH_2$, R' = H

c) R = *p*-$NO_2C_6H_4CH_2$, R' = H d) R = *p*-$ClC_6H_4CH_2$, R' = CH_3

In this connection, structures **3** and **4** could be assigned for the diacetyl derivatives of compound **1**; however, structures **3** were supported by the ^{1}H NMR spectra. The ^{1}H NMR spectra of compounds **2**, **3** and **4** were recorded in DMSO-d_6 and TFA, as a neutral and an acidic solvent, respectively. By comparison of the spectral data given in the Experimental Section, it was clearly seen that the signals from CH_2 groups attached to C-3 positions of the triazole rings were shifted downfield in TFA. Protonation shifts, obtained by comparison of spectra run in DMSO-d_6 and TFA, observed for compounds of type **2**, **3** and **4** are in agreement with stabilization of the resulting cations in acidic medium by an

amidinium type resonance, which, for protonated compounds **2**, can be represented by **8**, for example.

EXPERIMENTAL SECTION

Melting points were determined on a Büchi oil heated melting point apparatus and are uncorrected. Infrared spectra were run as potassium bromide pellets using a Perkin-Elmer 377 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian A60 spectrometer. The ultraviolet absorption spectra were measured between 210 and 350 nm on a Varian spectrophotometer, using 10 mm quartz cells. Combustion analyses were performed on a Carlo Erba 1106 Elemental Analyzer. The starting compounds **6** were synthesized by the treatment of ester ethoxycarbonylhydrazones with ethanolamine.[6]

Synthesis of 1,2,4-Triazol-5-one Derivatives 1

Method A.- The new 3-substituted-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-ones (**1a-c**) were synthesized by the treatment of corresponding ester ethoxycarbonylhydrazones with an aqueous solution of hydrazine hydrate (100%), according to the route previously reported.[3]

Method B.- The same compounds were also obtained from the reactions of corresponding alkyl imidate hydrochlorides with carbohydrazide, by a route similar to the method described earlier.[4]

3-*p*-Methylbenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (1a).- 94% yield (Method A) and 65% yield (Method B) as colorless crystals, mp. 185° (ethanol); IR (KBr): 3298, 3198 (NH_2, NH), 1720 (C=O), 1630 (C=N), 800 (1,4-disubstituted benzenoid ring) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.24 (s, 3H, CH_3), 3.76 (s, 2H, CH_2), 4.80 (s, 2H, NH_2), 7.08 (s, 4H, aromatic H), 11.34 (s, 1H, NH),

Anal. Calcd for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.44. Found: C, 58.95; H, 5.88; N, 27.14

3-*p*-Chlorobenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (1b).- 91% yield (Method A) and 63% yield (Method B) as colorless crystals. mp. 181° (ethanol); IR (KBr): 3298, 3198 (NH_2, NH), 1720 (C=O), 1630 (C=N), 820 (1,4-disubstituted benzenoid ring) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.86 (s, 2H, CH_2), 5.04 (s, 2H, NH_2), 7.26 (s, 4H, aromatic H), 11.36 (s, 1H, NH).

Anal. Calcd for $C_9H_9ClN_4O$: C, 48.12; H, 4.04; N, 24.94. Found: C, 48.29; H, 4.17; N, 24.79

3-*p*-Nitrobenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (1c).- 71% yield (Method A) and 57% yield (Method B) as yellowish crystals, mp. 220° (ethanol); IR (KBr): 3338, 3210 (NH_2, NH), 1690 (C=O), 1615 (C=N), 855 (1,4-disubstituted benzenoid ring) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 4.00 (s, 2H, CH_2), 5.10 (s, 2H, NH_2), 7.54 (d, 2H, aromatic H), 8.12 (d, 2H, aromatic H), 11.40 (s, 1H, NH).

Anal. Calcd for $C_9H_9N_5O_3$: C, 45.96; H, 3.86; N, 29.78. Found: C, 45.78; H, 4.01; N, 29.48

1-Methyl-3-*p*-chlorobenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (1d).- Compound **1b** (2.24 g, 0.005 mol) was dissolved in 8 mL of 2N NaOH and treated with 0.52 mL of dimethyl sulphate. After stirring of the mixture at room temperature for 2 hrs, the solid formed was collected, washed with 10 mL of cold water and dried *in vacuo*. Several recrystallizations of the crude product from water gave 1.24 g (52%) of pure **1d** as colorless crystals, mp. 143° (water); IR (KBr): 3295, 3195 (NH_2), 1695 (C=O), 1635 (C=N), 800 (1,4-disubstituted benzenoid ring) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.24 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 5.20 (s, 2H, NH_2), 7.32 (s, 4H, aromatic H).

Anal. Calcd for $C_{10}H_{11}ClN_4O$: C, 50.32; H, 4.65; N, 23.47. Found: C, 50.62; H, 4.66; N, 23.74

Synthesis of Acetyl Derivatives 2. General Procedure.- Compound **1** (0.005 mol) dissolved in 10 mL of acetic anhydride was stirred at room temperature for 2 hrs. After addition of 30 mL of absolute ethanol, the mixture was stirred for one more hr. Evaporation of the resulting solution at 25-30° under reduced pressure and several recrystallizations of the residue from an appropriate solvent gave pure compound **2**.

3-*p*-Nitrobenzyl-4-acetylamino-4,5-dihydro-1H-1,2,4-triazol-5-one (2c).- Yield 1.32 g (95%) of yellowish crystals, mp. 176° (ethanol/water,1:1); IR (KBr): 3342, 3280 (NH), 1722, 1686 (C=O), 1585 (C=N), 806 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) λ_{max} (ε): 318 nm (480), 276 (8100), 266 (9050), 220 (5000); ^1H NMR (DMSO-d_6): δ 2.40 (s, 3H, CH_3), 4.10 (d, 2H, CH_2), 7.60 (d, 2H, aromatic H), 8,22 (d, 2H, aromatic H), 9.76 (s, 1H, NH), 11.60 (s, 1H, NH); ^1H NMR (TFA): δ 2.80 (s, 3H, CH_3), 4.38 (s, 2H, CH_2), 7.70 (d, 2H, aromatic H), 8.44 (d, 2H, aromatic H).

Anal. Calcd for $C_{11}H_{11}ClN_5O_4$: C, 47.65; H, 4.00; N, 25.26. Found: C, 47.47; H, 4.05; N, 25.05

1-Methyl-3-*p*-chlorobenzyl-4-acetylamino-4,5-dihydro-1H-12,4-triazol-5-one (2d).- Yield 1.03 g (73%) of colorless crystals, mp. 116° (benzene/cyclohexane, 1:1); IR (KBr): 3225 (NH), 1718, 1685 (C=O), 1570 (C=N), 800 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) λ_{max} (ε): 225 nm (6150); ^1H NMR (DMSO-d_6): δ 2.00 (s, 3H, CH_3), 3.32 (s, 3H, CH_3), 3.90 (d, 2H, CH_2), 7.26 (s, 4H, aromatic H), 10.06 (s, 1H, NH); ^1H NMR (TFA): δ 2.32 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 4.20 (d, 2H, CH_2), 7.44 (s, 4H, aromatic H).

Anal. Calcd for $C_{12}H_{13}ClN_4O_2$: C, 51.34; H, 4.67; N, 19.96. Found: C, 51.05; H, 4.78; N, 19.78

Synthesis of Diacetyl Derivatives (3 or 4). General Procedure.- Compound **1** (0.005 mol) dissolved in 10 mL of acetic anhydride was stirred at 85-90° for 2 hrs. After addition of 30 mL of absolute ethanol, the mixture was stirred at the same temperature for one more hr. Evaporation of the resulting solution at 40-45° under reduced pressure and several recrystallizations of the residue from an appropriate solvent gave pure compound **3** or **4**.

Diacetyl Derivative of 3-*p*-Methylbenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (3a or 4a).- Yield 1.20 g (83%) of colorless crystals,mp. 143° (ethyl acetate/petroleum ether, 1:1); IR (KBr): 3298 (NH), 1780, 1705, 1685 (C=O), 1592 (C=N), 806 (1,4-disubstituted benzenoid ring)cm^{-1}; UV (ethanol) λ_{max} (ε): 241 nm (3700); ^1H NMR (DMSO-d_6): δ 2.00 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.76 (s, 2H, CH_2), 7.10 (s, 4H, aromatic H), 11.10 (s, 1H, NH). ^1H NMR (TFA): δ 2.28 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.84 (s, 3H, CH_3), 4.10 (s, 2H, CH_2), 7.32 (s, 4H, aromatic H).

Anal. Calcd for $C_{14}H_{16}N_4O_3$: C,58.32; H, 5.59; N, 19.44. Found: C, 58.17; H, 5.65; N, 19.15

Diacetyl Derivative of 3-*p*-Chlorobenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (3b or 4b).- Yield 1.17 g (88%) of colorless crystals, mp. 125° (benzene); IR (KBr): 3270 (NH), 1780, 1705, 1685 (C=O), 1590 (C=N), 800 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) λ_{max}(ε): 239 nm (3290); ^1H NMR (DMSO-d_6): δ 2.00 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.80 (s, 2H, CH_2), 7.32 (s, 4H, aromatic H), 11.10 (s, 1H, NH); ^1H NMR (TFA): δ 2.30 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 4.10 (s, 2H, CH_2), 7.44 (s, 4H, aromatic H).

Anal. Calcd for $C_{13}H_{13}ClN_3O$: C, 50.58; H, 4.24; N, 18,14. Found: C, 50.86; H, 4.28; N, 18.28

Diacetyl Derivative of 3-*p*-Nitrobenzyl-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (3c or 4c).- Yield 1.44 g (90%) of yellowish crystals, mp. 152° (benzene); IR (KBr): 3270 (NH), 1776, 1720, 1683 (C=O), 1598 (C=N), 806 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 318 nm (540), 278 (7300), 268 (7500), 222 (3700); ^1H NMR (DMSO-d_6): δ 2.04 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 4.08 (s, 2H, CH_2), 7.68 (d, 2H, aromatic H), 8.36 (d, 2H, aromatic H), 11.20 (s, 1H, NH); ^1H NMR (TFA): δ 2.38 (s, 3H, CH_3), 2.86 (s, 3H, CH_3), 4.32 (s, 2H, CH_2), 7.74 (d, 2H, aromatic H), 8.52 (d, 2H, aromatic H).

Anal. Calcd for $C_{13}H_{13}N_5O_5$: C, 48.90; H, 4,10; N, 21,93. Found: C, 48.62; H, 4.10; N, 21.64

Synthesis of Triacetyl Derivatives 5. General Procedure.- Compound 1 (0.005 mol) was refluxed with 10 mL of acetic anhydride for 0.5 hr and then 30 mL of absolute ethanol was added. After refluxing for 0.5 hr and evaporation of the resulting solution at 40-45° under reduced pressure, the residue was crystallized from an appropriate solvent to afford pure compound **5**.

1-Acetyl-3-*p*-methylbenzyl-4-diacetylamino-4,5-dihydro-1H-1,2,4-triazol-5-one (5a).- Yield 1.44 (87%) of colorless crystals, mp. 110° (acetone/petroleum ether, 1:1); IR (KBr): 1768, 1720, 1695 (C=O), 1605 (C=N), 806 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 236 nm (2790); ^1H NMR (DMSO-d_6): δ 2.14 (s, 6H, $2CH_3$), 2.34 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 3.92 (s, 2H, CH_2), 7.32 (s, 4H, aromatic H); ^1H NMR (TFA): δ 2.36 (s,6H, $2CH_3$), 2,44 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 4.04 (s, 2H, CH_2), 7,40 (s, 4H, aromatic H).

Anal. Calcd for $C_{16}H_{18}N_4O_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.46; H, 5.61; N, 17.15

1-Acetyl-3-*p*-chlorobenzyl-4-diacetylamino-4,5-dihydro-1H-1,2,4-triazol-5-one (5b).- Yield 1.56 g (89%) of colorless crystals, mp. 154° (benzene/petroleum ether, 1:1); IR (KBr): 1780, 1735, 1695 (C=O), 1600 (C=N), 802 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 240 nm (3480); ^1H NMR (DMSO-d_6): δ 2.20 (s, 6H, $2CH_3$), 2.52 (s, 3H, CH_3), 3.96 (s, 2H, CH_2), 7.36 (s, 4H, aromatic H); ^1H NMR (TFA): δ 2.40 (s, 6H, $2CH_3$), 2.90 (s, 3H, CH_3), 4.06 (s, 2H, CH_2), 7.48 (s, 4H, aromatic H).

Anal. Calcd for $C_{15}H_{15}ClN_4O_4$: C, 51.37; H, 4.31; N, 15.97. Found: C, 51.49; H, 4.41; N, 16,22

Synthesis of Diacetyl Derivatives 7. General Procedure.- Compound **6** (0.01 mol) was refluxed with 15 mL of acetic anhydride for 0.5 hr. After addition of 50 mL of absolute ethanol, the mixture was refluxed for 1 hr. Evaporation of the resulting solution at 40-45° under reduced pressure gave a viscous residue. The crude product was solidified when allowed to stand in deep-freeze with 4-5 mL of petroleum ether. Several recrystallizations of the crystals from an appropriate solvent afforded pure compound **7**.

1-Acetyl-3-*p*-methylbenzyl-4-(2-acetoxyethyl)-4,5-dihydro-1H-1,2,4-triazol-5-one (7a).- Yield 2.00 g (63%) of colorless crystals, mp. 73° (benzene/petroleum ether, 1:1); IR (KBr): 1730, 1720, 1692 (C=O), 1585 (C=N), 802 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 259 nm (290), 226 (5670), 209 (9020); ^1H NMR ($CDCl_3$): δ 2.06 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 3.72 (t, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.16 (t, 2H, CH_2), 7.20 (s, 4H, aromatic H).

Anal. Calcd for $C_{16}H_{19}N_3O_4$: C, 60.55; H, 6.04; N, 13.24. Found: C, 60.83; H, 6,21; N, 13.48

1-Acetyl-3-*p*-chlorobenzyl-4-(2-acetoxyethyl)-4,5-dihydro-1H-1,2,4-triazol-5-one (7b).- Yield 1.77 g (52%) of colorless crystals, mp. 89° (benzene/petroleum ether, 1:1); IR (KBr): 1750, 1735, 1720 (C=O), 1590 (C=N), 800 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 262 nm (190), 226 (6820), 210 (12750); ^1H NMR (DMSO-d_6): δ 1.98 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.82 (t, 2H, CH_2), 4.02 (s, 2H, CH_2), 4.08 (t, 2H, CH_2), 7.38 (s, 4H, aromatic H).

Anal. Calcd for $C_{15}H_{16}ClN_3O_4$: C, 53.35; H, 4.77; N, 12.44. Found: C, 53.65; H, 4.82; N, 12.39

1-Acetyl-3-*p*-nitrobenzyl-4-(2-acetoxyethyl)-4,5-dihydro-1H-1,2,4-triazol-5-one (7c).- Yield 1.68 g (48%) of yellowish crystals, mp. 134° (benzene); IR (KBr): 1743, 1725, 1705 (C=O), 1585 (C=N), 805 (1,4-disubstituted benzenoid ring) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.96 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.90 (t, 2H, CH_2), 4.12 (t, 2H, CH_2), 4.20 (s, 2H, CH_2), 7.60 (d, 2H, aromatic H), 8.26 (d, 2H, aromatic H).

Anal. Calcd for $C_{15}H_{16}N_4O_6$: C, 51.72; H, 4.63; N, 16.09. Found: C, 51.46; H, 4.60; N, 15.83

Synthesis of Ester Ethoxycarbonylhydrazones.- The new ester ethoxycarbonylhydrazones necessary for the synthesis of compound **1** were obtained by the treatment of corresponding alkyl imidate hydrochlorides with ethyl carbazate, according to a route similar to the methods previously reported.[7,8]

Ethyl *p*-Methylphenylacetate Ethoxycarbonylhydrazone.- Yield 85% of colorless crystals, mp.77° (petroleum ether, 40-60°); IR (KBr): 3165 (NH), 1690 (C=O), 1628 (C=N), 795 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 237 nm (3090); ^1H NMR ($CDCl_3$): δ 1.24 (t, 3H, CH_3), 1.32 (t, 3H, CH_3), 2.36 (s, 3H, CH_3), 3.68 (s, 2H, CH_2), 4.18 (q, 2H, CH_2), 4.34 (q, 2H, CH_2), 7.18 (s, 4H, aromatic H), 8.22 (s, 1H, NH).

Anal. Calcd for $C_{14}H_{20}N_2O_3$: C, 63.61; H, 7.63; N, 10.60. Found: C, 63.68; H, 7.86; N, 10.74

Ethyl *p*-Chlorophenylacetate Ethoxycarbonylhydrazone.- Yield 84% of colorless crystals, mp.78° (petroleum ether, 40-60°); IR (KBr): 3223 (NH), 1678 (C=O), 1635 (C=N), 792 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 237 nm (3120); ^1H NMR ($CDCl_3$): δ 1.20 (t, 3H, CH_3), 1.36 (t, 3H, CH_3), 3.78 (s, 2H, CH_2), 4.00 (q, 2H, CH_2), 4.34 (q, 2H, CH_2), 7.30 (s, 4H, aromatic H), 8.24 (s, 1H, NH).

Anal. Calcd for $C_{13}H_{17}ClN_2O_3$: C, 54.84; H, 6.02; N, 9.84. Found: C, 55.08; H, 6.04; N, 9.96

Ethyl *p*-Nitrophenylacetate Ethoxycarbonylhydrazone.- Yield 47% of colorless crystals, mp. 100° (petroleum ether, 40-60°); IR (KBr): 3162 (NH), 1685 (C=O), 1640 (C=N), 845 (1,4-disubstituted benzenoid ring) cm^{-1}; UV (ethanol) $\lambda_{max}(\varepsilon)$: 317 nm (980), 277 (7660), 268 (7570), 231 (5850); ^1H NMR ($CDCl_3$): δ 1.30 (t, 3H, CH_3), 1.40 (t, 3H, CH_3), 3.96 (s, 2H, CH_2), 4.12 (q, 2H, CH_2), 4.28 (q, 2H, CH_2), 7,40 (d, 2H, aromatic H), 7.60 (s, 1H, NH), 8.26 (d, 2H, aromatic H).

Anal. Calcd for $C_{13}H_{17}N_3O_5$: C, 52.87; H, 5.80; N, 14.23. Found: C, 53.17; H, 5.90; N, 14.39

Preparation of Alkyl Imidate Hydrochlorides.- The new alkyl imidate hydrochlorides necessary for the synthesis of ester ethoxycarbonylhydrazones and compounds **1** were prepared by a route similar to Pinner's Method.[9]

Ethyl Imido-*p*-methylphenylacetate Hydrochloride.- Yield 96% of colorless crystals, mp. 181°

(dec.) (absolute ethanol/ethyl ether, 1:4); IR (KBr): 2990, 2850, 770 (NH_2^+), 1632 (C=N), 810 (1,4-disubstituted benzenoid ring) cm^{-1}; ^1H NMR (TFA): δ 1.58 (t, 3H, CH_3), 2,40 (s, 3H, CH_3), 4,06 (s, 2H, CH_2), 4.68 (q, 2H, CH_2), 7.30 (s, 4H, aromatic H), 9.36 (s, 2H, NH_2).

Anal. Calcd for $C_{11}H_{15}NO$•HCl: HCl, 17.06; Cl, 16.59. Found: HCl, 17.01; Cl, 16.38

Ethyl Imido-*p*-chlorophenylacetate Hydrochloride.- Yield 94% of colorless crystals, mp. 179° (dec.) (absolute ethanol/ethyl ether, 1:4); IR (KBr): 2970, 2850, 790 (NH_2^+), 1640 (C=N), 820 (1,4-disubstituted benzenoid ring) cm^{-1}; ^1H NMR (TFA): δ 1.58 (t, 3H, CH_3), 4.10 (s, 2H, CH_2), 4.68 (q, 2H, CH_2), 7.42 (s, 4H, aromatic H), 9.40 (s, 2H, NH_2),

Anal. Calcd for $C_{10}H_{12}ClNO$•HCl: HCl, 15.57; Cl, 15.14. Found: HCl, 15.51; Cl, 14.95

Ethyl Imido-*p*-nitrophenylacetate Hydrochloride.- Yield 95% of colorless crystals, mp. 191° (dec.) (absolute ethanol/ethyl ether, 1:4); IR (KBr): 2980, 2790, 800 (NH_2^+), 1633 (C=N), 850 (1,4-disubstituted benzenoid ring) cm^{-1}; ^1H NMR (TFA): δ 1.60 (t, 3H, CH_3), 4.40 (s, 2H, CH_2), 4.78 (q, 2H, CH_2), 7.78 (d, 2H, aromatic H), 8.44 (d, 2H, aromatic H), 9.44 (s, 2H, NH_2).

Anal. Calcd for $C_{10}H_{12}N_2O_3$•HCl: HCl, 14.90; Cl, 14.49. Found: HCl, 14.60; Cl, 14.50

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SYNTHESIS OF SOME BENZOTHIAZOLOBENZOTRIAZEPINES

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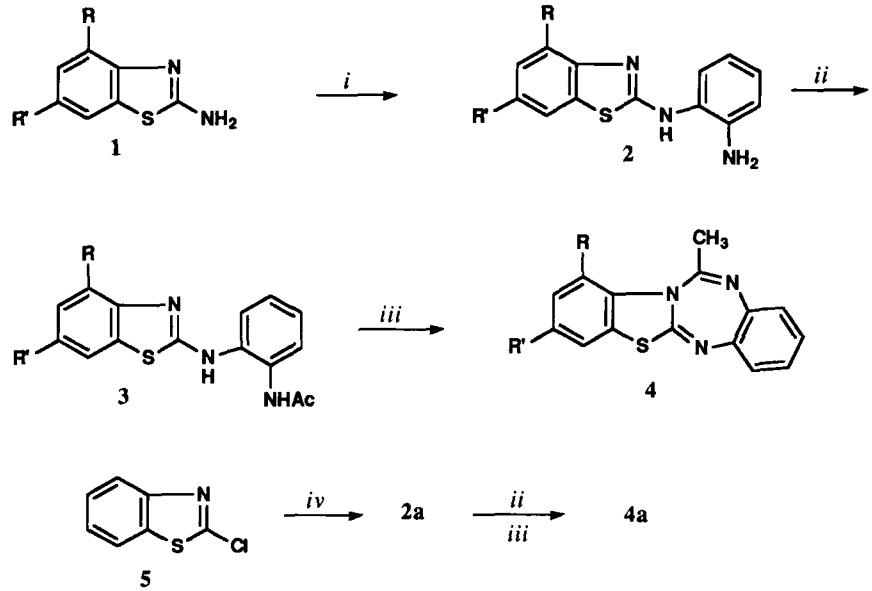
In continuation of our earlier work on 3-substituted[1,2,4]triazepino[3,4-b]benzothiazolone[1] from 2-hydrazinobenzothiazole and ethyl acetoacetate, we now report the synthesis of benzothiazolo[2,3-b][1,3,5]benzotriazepines. Reaction of 2-aminobenzothiazole (1) with *o*-chloroaniline in the presence of pyridine, potassium carbonate and cupric oxide under the conditions of Ullmann reaction gave **2** in fair yields. These N-phenylaminobenzothiazoles were acetylated to give



a) R = R' = H b) R = H, R' = CH_3 c) R = R' = CH_3 d) R = H, R' = OEt e) R = H, R' = NO_2

i) *o*-Chloroaniline, CuO, K_2CO_3; *ii*) Ac_2O; *iii*) $POCl_3$; *iv*) *o*-Phenylenediamine