The Synthesis of Methyl 2-(Benzyloxycarbonyl)amino-3-dimethylaminopropenoate. The Synthesis of Trisubstituted Pyrroles, 3-Amino-2*H*-pyran-2-ones, Fused 2*H*-Pyran-2-ones and 4*H*-Pyridin-4-ones

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Received April 24, 1998

Methyl 2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2**) was prepared from methyl *N*-(benzyloxycarbonyl)glycinate (**1**) and *t*-butoxybis(dimethylamino)methane, and used as a reagent for preparation of substituted 3-(benzyloxycarbonyl)amino-4*H*-quinolizin-4-ones **5** and **6**, -2*H*-pyran-2-ones **17-19**, -2*H*-1-benzopyran-2-ones **28-31**, and -naphthopyrans **32-35**, -2*H*-pyrano[3,2-*c*]pyridine-2,5-dione **46**, -pyrano[4,3-*b*]pyran-2,5-dione **47**, -pyrano[3,2-*c*]benzopyran-2,5-dione **48**, -pyrano[2,3-*c*]pyrazol-6-ones **49** and **50**, -pyrano[2,3-*d*]pyrimidin-7-ones **51** and **52** derivatives. In the reaction of **2** with 1,3-diketones trisubstituted pyrroles **14-16** were formed. Selective removal of benzyloxycarbonyl group was achieved by catalytic transfer hydrogenation with Pd/C in the presence of cyclohexene to afford free 3-amino compounds **7**, **8**, **20**, **36-38** and **53-57** in yields better than 80%.

J. Heterocyclic Chem., **36**, 225 (1999).

Recently, a group of alkyl 2-acylamino-3-dimethylaminopropenoates and related compounds [1-9] have been prepared and used as reagents for preparation of various heterocyclic systems, such as pyranones, pyridines, pyrimidines and fused systems, azolo- and azinopyrimidines, azolopyranones and pyranoazines, with an acylamino or a 2,2-disubstituted-1-ethenylamino group attached at position 3 of the newly formed pyrimidinone [6,8,10], pyridinone [10,11] or pyranone ring [2,4,5,6].

2,2-Disubstituted 1-ethenyl, such as 2-benzoyl-2-ethoxycarbonyl-1-ethenyl and 2-benzoyl-2-methoxycarbonyl-1-ethenyl groups can be used as *N*-protecting groups in the synthesis of didehydro peptide derivatives containing *N*-terminal 3-heteroarylamino-2,3-didehydroalanine moiety, since they can be easily removed with hydrazine or hydroxylamine under mild conditions [12].

Recently, the synthesis of various pyran-2-ones and fused pyran-2-ones has attracted an interest, since many of them have been found as nonpeptide HIV protease inhibitors [13,14]. 3-Amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been recently studied as candidate fluorescent probes for hypoxic cells in solid tumors. They have been prepared from the corresponding 3-nitro derivatives by reduction [15] or by hydrolysis of benzoylamino group [16].

Deprotection of 3-acylamino-2*H*-pyran-2-one and 3-acylamino-2*H*-1-benzopyran derivatives can not be easily achieved. The removal of the benzoyl group in basic media results, in addition to the expected amino compound, in formation of the corresponding hydroxy compound [17], while in concentrated sulfuric acid under gentle heating the amino compounds were obtained in good yields [18]. Recently, removal of 2,2-disubstituted 1-ethenyl group was achieved with hydrazine hydrate or hydroxylamine under mild conditions [12], and with diethylamine in ethanol [5], while in quinolizine series, free 3-amino compounds were prepared either by reduction of the corresponding nitro derivative [19] or by removal of (2-benzoyl-2-ethoxycarbonyl)-1-ethenyl group with hydrazine hydrate [20]. Analogously, 3-amino substituted fused pyrimidinones have been prepared in high yields [2,4,5,6,21]. On the other hand deprotecting of substituted 3-aminopyran-2-one derivatives and fused analogues with diethylamine was less successful to give the corresponding free 3-amino derivatives in modest yields [5,22].

In this paper, we report on the synthesis of methyl (*Z*)-2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2**), which turned out to be a good C_3 synthon for the construction of pyran, pyridine and pyrimidine systems.

Compound **2** was prepared from methyl *N*-(benzyloxycarbonyl)glycinate (**1**) and *t*-butoxybis(dimethylamino)-methane by heating in toluene for one hour in 96% yield (Scheme 1). The structure of the compound was established on the basis of ^{1}H nmr spectrum in deuteriochloroform, which shows only one set of peaks: a singlet at δ = 3.01 ppm for NMe_2 group, a singlet at δ = 3.66 ppm for COOMe, a singlet at δ = 5.16 ppm for CH_2 group, a broad singlet at δ = 5.26 ppm for NH, and multiplet at δ = 7.26-7.37 ppm for phenyl group and C=CH structural element,

while in dimethyl-d_6 sulfoxide solution two sets of peaks were observed, indicating the existence of two isomers or rotamers. The orientation of groups around the double bond was established on the basis of NOESY experiment, which shows in dimethyl-d_6 sulfoxide solution that two isomers or rotamers, **A** and **B**, are present in ratio 10:3. The orientation around double bond is in both rotamers (*Z*) confirmed by coupling constant $^3J_{(H,CO)}$ = 3.0 Hz and NOE. They differ only in the orientation of benzyloxycarbonyl group around the single N-C bond. The orientation in conformer **A** was confirmed with NOE (Figures 1 and 2).

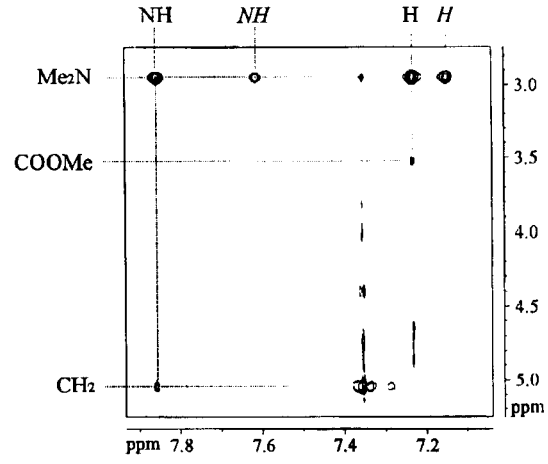
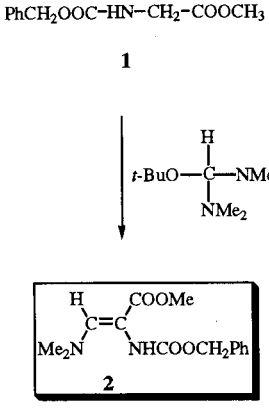
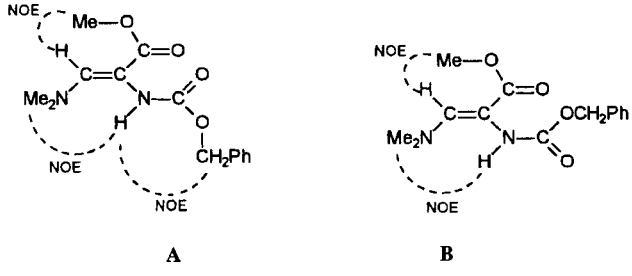


Figure 2. Partial NOESY spectrum of compound **2** measured in dimethyl-d_6 sulfoxide at 302 K. Minor isomer is marked in italics.

Scheme 1





A:**B** = 10:3

Figure 1.

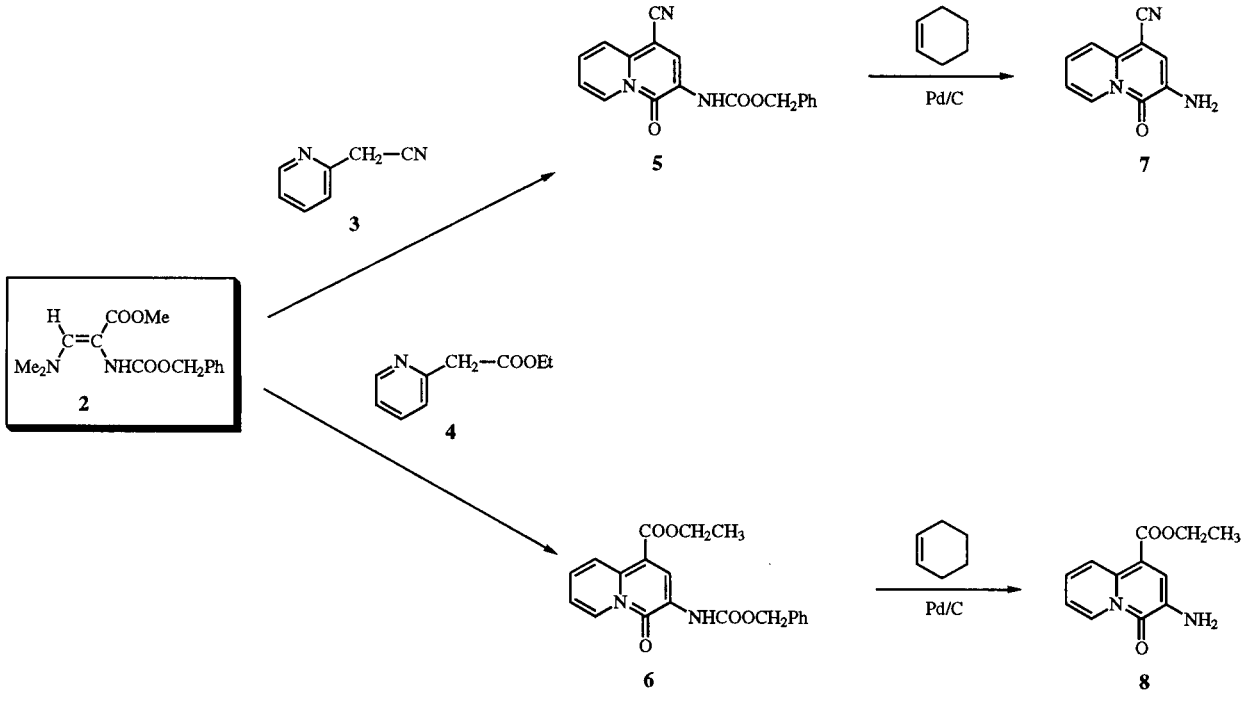
Compounds with an active methylene group at α-position in respect to ring nitrogen atom, such as 2-pyridylacetonitrile (**3**) and ethyl 2-pyridylacetate (**4**), were transformed into 3-(benzyloxycarbonyl)amino-1-cyano-4*H*-quinolizin-4-one (**5**) and the corresponding 1-ethoxycarbonyl derivative **6** (Scheme 2).

Compound **2** reacts with other *C*-nucleophiles, such as methyl acetoacetate (**11**), benzyl acetoacetate (**13**) and ethyl benzoylacetate (**12**) by heating in acetic acid to give 3-(benzyloxycarbonyl)amino-2*H*-pyran-2-one derivatives **17**, **19** and **18**, while acetylacetone (**9**) and benzoylacetone (**10**) were transformed into 3-acetyl-5-methoxycarbonyl-2-methylpyrrole (**14**) and its 1-benzyloxycarbonyl derivative **15**, and 3-benzoyl-5-methoxycarbonyl-2-methylpyrrole (**16**), respectively (Scheme 3).

Cyclic 1,3-diketones, such as cyclohexan-1,3-dione (**21**) and its 5,5-dimethyl derivative **22**, and aromatic hydroxy compounds, such as 1,3-dihydroxybenzene (**24**), 2,6-dihydroxytoluene (**23**) and 1-naphthol (**25**), 2-naphthol (**27**) afforded 5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one derivatives **28** and **29**, 2*H*-1-benzopyran-2-one derivatives **31** and **30**, and 2*H*-naphtho[1,2-*b*]pyran-2-one (**32**) and 3*H*-naphtho[2,1-*b*]pyran-3-one (**35**) derivatives, while 2,3-dihydronaphthalene (**26**) formed a mixture of 3*H*-naphtho[2,1-*b*]pyran-3-one (**33**) and 2*H*,11*H*-naphtho[2,1-*b*:3,4-*b*]dipyran-2,11-dione **34** derivative (Scheme 4).

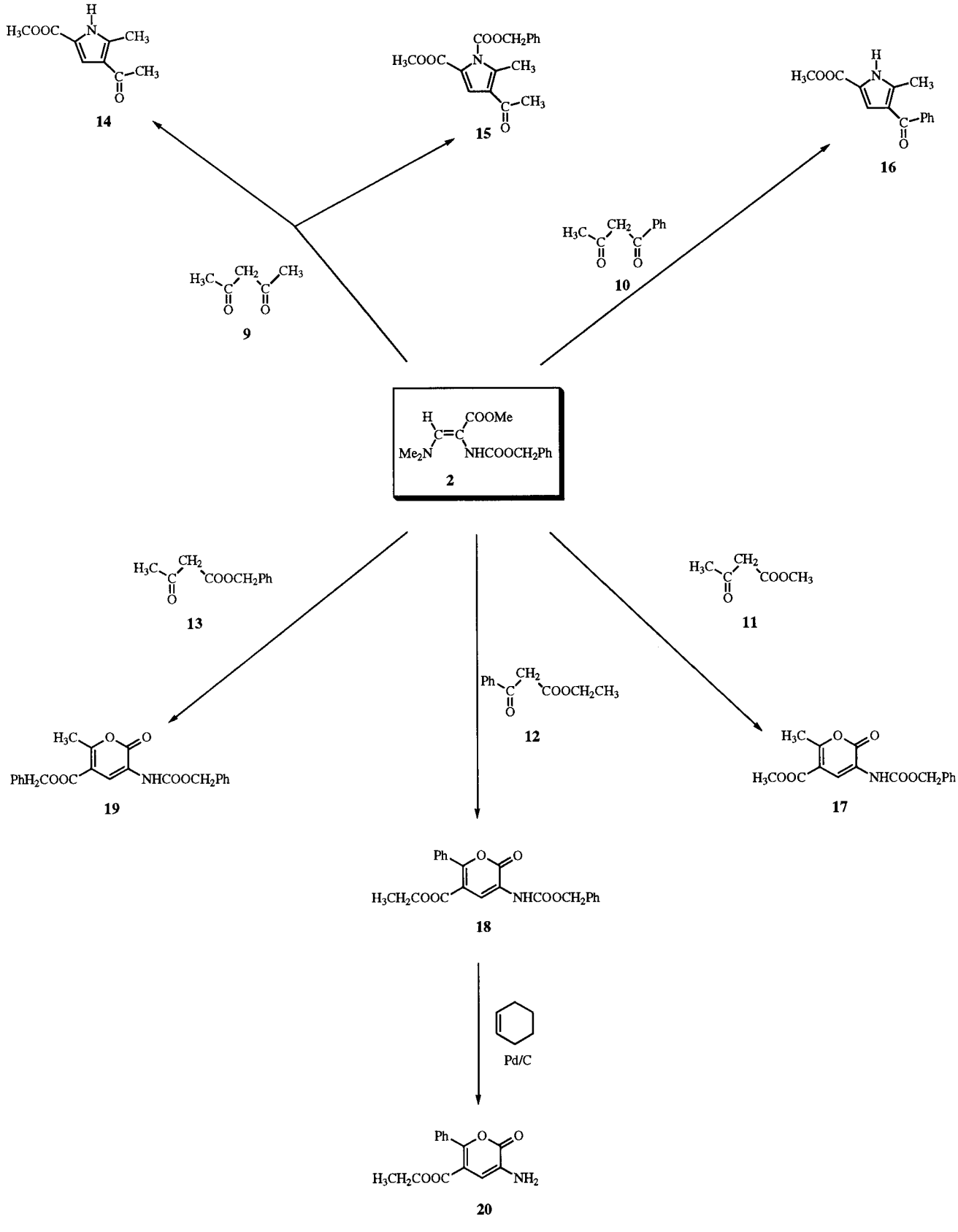
Heterocyclic hydroxy compounds give azolopyran-2-ones and pyranoazines. 4-Hydroxypyridin-2(1*H*)-one (**39**) was transformed into 2*H*-pyrano[3,2-*c*]pyridine-2,5-dione **46**, 4-hydroxy-6-methylpyran-2-one (**40**) into 2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione **47**, 4-hydroxycoumarin (**41**) into 2*H*,5*H*-pyrano[3,2-*c*]benzopyran-2,5-dione **48**, 3-methyl-1-phenylpyrazol-5(1*H*)-one (**42**) and 1,3-diphenylpyrazol-5(1*H*)-one (**43**), into 1*H*,6*H*-pyrano[2,3-*c*]-pyrazol-6-ones **49** and **50**, barbituric acid (**44**) and its 1,3-dimethyl derivative **45** into 2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimin-7-ones **51** and **52** (Scheme 5).

Scheme 2

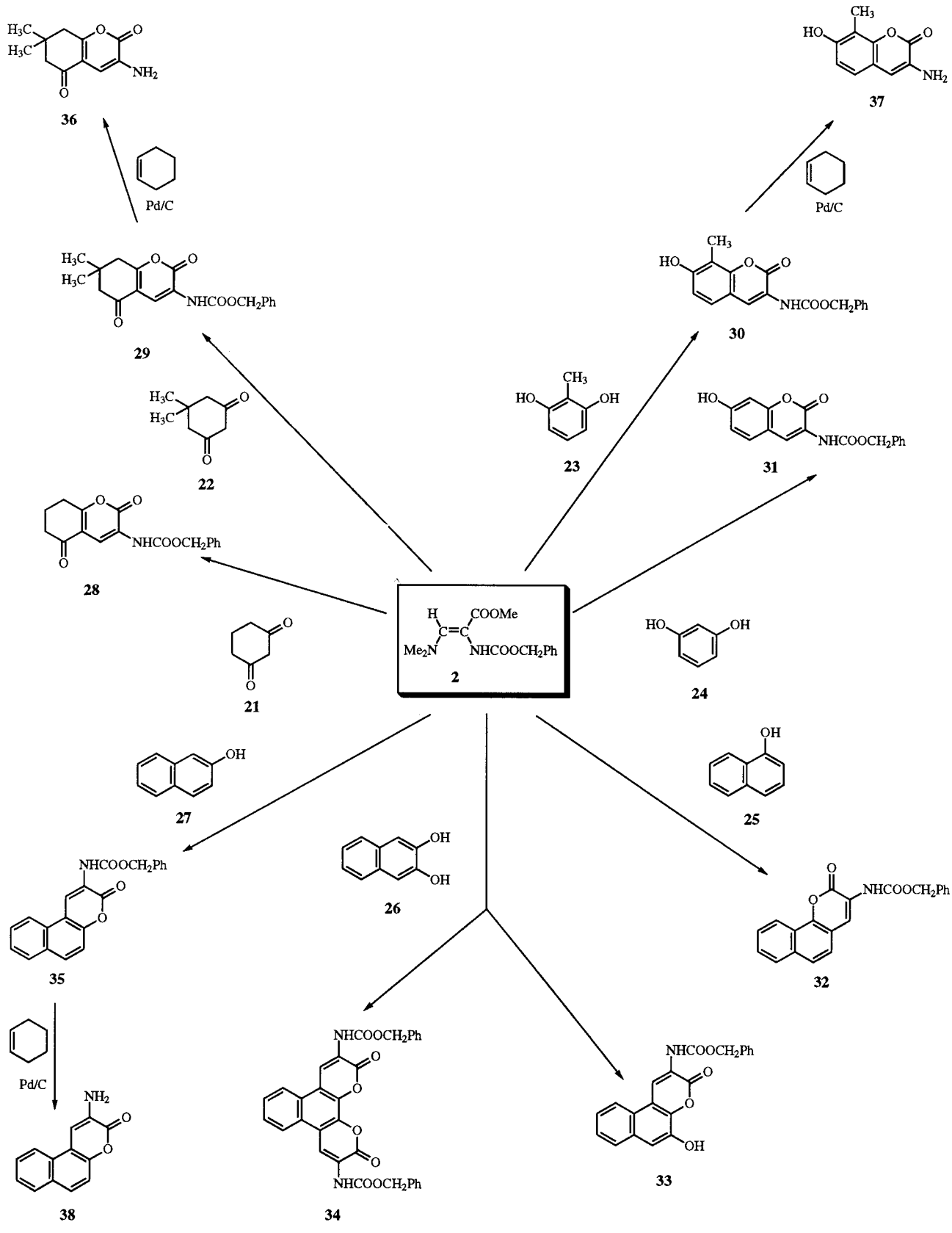


Removal of benzyloxycarbonyl group by catalytic transfer hydrogenation with Pd/C in the presence of cyclohexene turned out to be selective [23,24], since no hydrogenation of heterocyclic systems was observed, to give unsubstituted amino compounds in over 80% yields in most cases. In this manner 3-amino-1-cyano-4*H*-quinolizin-4-one (**7**), 3-amino-1-ethoxycarbonyl-4*H*-quinolizin-4-one (**8**) (Scheme 2), 3-amino-5-ethoxycarbonyl-6-phenyl-2*H*-pyran-2-one (**20**) (Scheme 3), 3-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**36**), 3-amino-7-hydroxy-8-methyl-2*H*-1-benzopyran-2-one (**37**), 2-amino-3*H*-naphtho[3,2-*c*]pyran-3-one (**38**) (Scheme 4), 3-amino-5,6-dihydro-2*H*-pyrano[2,1-*b*]pyridine-2,5-dione (**53**), 3-amino-7-methyl-2*H*,5*H*-pyrano-[4,3-*b*]pyran-2,5-dione (**54**), 3-amino-2*H*,5*H*-pyrano[3,2-*c*]-benzopyran-2,5-dione (**55**), 5-amino-1,3-diphenyl-1*H*,6*H*-pyrano[2,3-*c*]pyrazol-6-one (**56**), and 6-amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]-pyrimin-7-one **57** (Scheme 5).

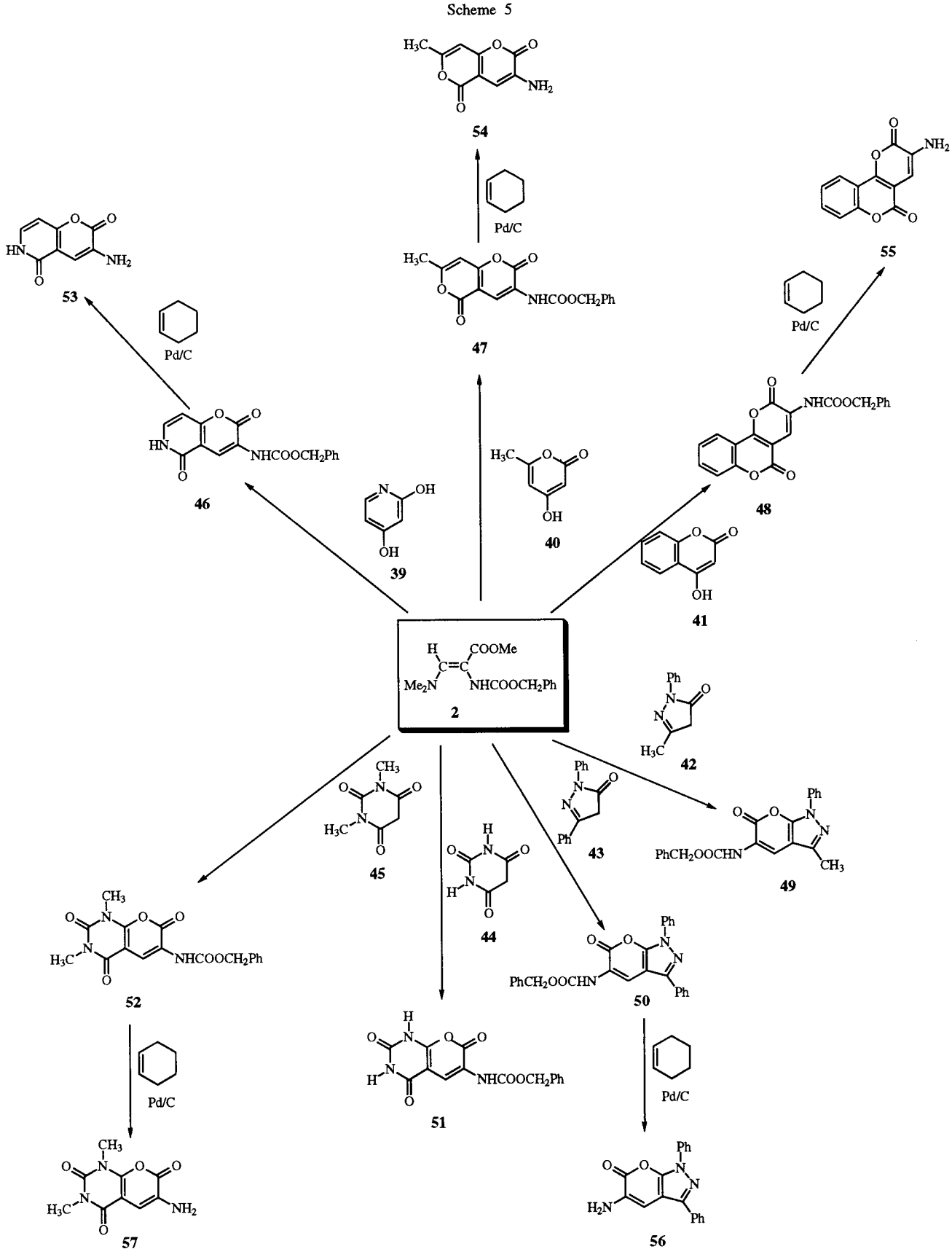
Scheme 3



Scheme 4



Scheme 5


54
55
Pd/C
47
53
Pd/C
Pd/C
46
39
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51
Pd/C
Pd/C
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56

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on Bruker Advance DPX 300 spectrometer, ir spectra on Perkin-Elmer 1310 instrument and micro analyses for C, H and N on Perkin-Elmer Analyzer 2400.

The Synthesis of Methyl *N*-(Benzyloxycarbonyl)glycinate (**1**).

The methyl *N*-(benzyloxycarbonyl)glycinate was prepared according to the modified procedure described in the literature [25].

A solution of (benzyloxycarbonyl)glycine (20.900 g, 100 mmoles) in 500 ml of methanol was stirred at 0°. Ten ml of thionyl chloride was added dropwise and stirred for additional 2 hours. After the reaction was completed, the volatile components were evaporated *in vacuo* to give oily residue **1** in 94% yield, lit [25]; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 3.64 (s, 3H, COOCH_3), 3.78 (d, 2H, CH_2NH), 5.05 (s, 2H, CH_2Ph), 7.28-7.40 (m, 5H, Ph), 7.68 (br t, 1H, N*H*).

The Synthesis of Methyl 2-(Benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2**).

To a solution of methyl *N*-(benzyloxycarbonyl)glycinate (**1**) (2.230 g, 10 mmoles) in toluene (15 ml) *t*-butoxybis(dimethylamino)methane (3.1 ml, 15 mmoles) was added and the mixture was heated in an oil bath at 100° for 1 hour. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and ethyl acetate/heptane, 2:1 as the solvent). After reaction was completed, the volatile components were evaporated *in vacuo*. The solid residue was recrystallized from a mixture of ethyl acetate and heptane to give **2** in 96% yield, mp 107-109°; ^{1}H nmr (deuteriochloroform): δ 3.01 (s, 6H, N(CH_3)$_2$), 3.66 (s, 3H, COOCH_3), 5.16 (s, 2H, CH_2), 5.26 (br s, 1H, N*H*), 7.26-7.37 (m, 6H, Ph, C*H*); ^{1}H nmr (dimethyl-d_6 sulfoxide): 2.95 (s, 6H, N(CH_3)$_2$), 3.50, 3.52 (2s, 3H, COOCH_3, **B**-rotamer, **A**-rotamer), 5.03, 5.05 (2s, 2H, CH_2, **B**-rotamer, **A**-rotamer), 7.14, 7.23 (2s, 1H, C*H*, **B**-rotamer, **A**-rotamer), 7.26-7.39 (m, 5H, Ph), 7.61, 7.85 (2br s, 1H, N*H*, **B**-rotamer, **A**-rotamer), ratio A:B = 10:3.

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.48; H, 6.60; N, 9.88.

The Synthesis of 4*H*-Quinolizin-4-one, 5-Methoxycarbonyl-2-methylpyrrole, 2*H*-Pyran-2-one and Fused 2*H*-Pyran-2-one Systems.

General Procedure.

To a solution of the compound with an active methylene group (1.0 mmole) in the acetic acid (5 ml) methyl 2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2**) (1.0 mmole) was added and the mixture was heated under reflux for several hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol, 25:1 as solvent). After the reaction was completed, acetic acid was evaporated *in vacuo* and the solid residue was recrystallized from an appropriate solvent. The following compounds were prepared in this manner:

3-(Benzyloxycarbonyl)amino-1-cyano-4*H*-quinolizin-4-one (**5**).

This compound was prepared from 2-pyridylacetonitrile (**3**) (0.118 g), 2 hours of reflux, in 96% yield, mp 212-214° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 5.25 (s, 2H, CH_2), 7.15 (ddd, 1H, H_7), 7.36-7.42 (m, 5H, Ph), 7.51 (ddd, 1H, H_8), 7.82 (s, 1H, N*H*), 7.95 (dd, 1H, H_9), 8.77 (s, 1H, H_2), 9.05 (dd, 1H, H_6), $J_{H6,H7}$ = 7.4 Hz, $J_{H7,H8}$ = 6.7 Hz, $J_{H8,H9}$ = 9.1 Hz, $J_{H6,H8}$ = 1.3 Hz, $J_{H7,H9}$ = 1.4 Hz.

Anal. Calcd. for $C_{18}H_{13}N_3O_3$: C, 67.71; H, 4.10; N, 13.16. Found: C, 67.47; H, 3.85; N, 13.23.

3-(Benzyloxycarbonyl)amino-1-ethoxycarbonyl-4*H*-quinolizin-4-one (**6**).

This compound was prepared from ethyl 2-pyridylacetate (**4**) (0.165 g), 4 hours of reflux, in 46% yield, mp 177-179° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, 3H, CH_2CH_3), 4.41 (q, 2H, CH_2CH_3), 5.27 (s, 2H, CH_2), 7.12 (ddd, 1H, H_7), 7.32-7.45 (m, 5H, Ph), 7.47 (ddd, 1H, H_8), 7.79 (s, 1H, N*H*), 9.13 (dd, 1H, H_6), 9.22 (dd, 1H, H_9), 9.24 (s, 1H, H_2), J_{CHCH} = 7.1 Hz, $J_{H6,H7}$ = 6.3 Hz, $J_{H7,H8}$ = 6.7 Hz, $J_{H8,H9}$ = 9.4 Hz, $J_{H6,H8}$ = 1.1 Hz, $J_{H7,H9}$ = 1.3 Hz.

Anal. Calcd. for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.66; H, 4.90; N, 7.92.

3-Acetyl-5-methoxycarbonyl-2-methylpyrrole (**14**) and 3-Acetyl-1-benzyloxycarbonyl-5-methoxycarbonyl-2-methylpyrrole (**15**).

A mixture of these compounds was prepared from acetylacetone (**9**) (0.100 g), 3 hours of reflux. The solvent was evaporated *in vacuo* and the oily residue separated by radial chromatography by chromatotron (Silica gel 60 PF_{254} containing gypsum, Merck, and chloroform as eluent) to give **14** in 17% and **15** in 33% yield. Compound **14** had mp 171-174° (from a mixture of ethyl acetate and heptane); ^{1}H nmr (deuteriochloroform): δ 2.42 (s, 3H, CH_3), 2.59 (s, 3H, COCH_3), 3.87 (s, 3H, COOCH_3), 7.21 (d, 1H, H_3), 9.39 (d, 1H, N*H*), J_{CHNH} = 2.5 Hz.

Anal. Calcd. for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.39; H, 6.07; N, 7.43.

Compound **15** had mp 81-82° (from a mixture of methanol and water); ^{1}H nmr (deuteriochloroform): δ 2.41 (s, 3H, CH_3), 2.60 (s, 3H, COCH_3), 3.77 (s, 3H, COOCH_3), 5.41 (s, 2H, CH_2), 7.19 (s, 1H, H_3), 7.32-7.43 (m, 5H, Ph).

Anal. Calcd. for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.75; H, 5.44; N, 4.30.

3-Benzoyl-5-methoxycarbonyl-2-methylpyrrole (**16**).

This compound was prepared from benzoylacetone (**10**) (0.162 g), 4 hours of reflux, in 29% yield, mp 145-148° (from a mixture of methanol and water); ^{1}H nmr (deuteriochloroform): δ 2.64 (s, 3H, CH_3), 3.86 (s, 3H, COOCH_3), 7.09 (d, 1H, H_3), 7.44-7.55, 7.77-7.81 (2m, 5H, Ph), 9.21 (br s, 1H, N*H*), J_{CHNH} = 2.6 Hz.

Anal. Calcd. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.75; H, 5.54; N, 5.59.

3-(Benzyloxycarbonyl)amino-5-methoxycarbonyl-6-methyl-2*H*-pyran-2-one (**17**).

This compound was prepared from methyl acetoacetate (**11**) (0.116 g), 2 hours of reflux, in 16% yield, mp 138-140° (from a mixture of methanol and water); ^{1}H nmr (deuteriochloroform): δ 2.64 (s, 3H, Het-CH_3), 3.86 (s, 3H, CH_3), 5.22 (s, 2H, CH_2), 7.32-7.39 (m, 6H, Ph, N*H*), 8.34 (s, 1H, H_4).

Anal. Calcd. for $C_{16}H_{15}NO_6$: C, 60.57; H, 4.76; N, 4.41. Found: C, 60.90; H, 4.82; N, 4.17.

3-(Benzyloxycarbonyl)amino-5-ethoxycarbonyl-6-phenyl-2*H*-pyran-2-one (**18**).

This compound was prepared from ethyl benzoylacetate (**12**) (0.192 g), 3 hours of reflux, in 34% yield, mp 132-134° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 1.14 (t, 3H, CH_2CH_3), 4.18 (q, 2H, CH_2CH_3), 5.24 (s, 2H, CH_2), 7.36-7.53 (m, 11H; Ph x 2, N*H*), 8.35 (s, 1H, H_4), J_{CHCH} = 7.1 Hz.

Anal. Calcd. for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87; N, 3.56. Found: C, 67.48; H, 4.84; N, 3.44.

3-(Benzyloxycarbonyl)amino-5-benzyloxycarbonyl-6-methyl-2*H*-pyran-2-one (**19**).

This compound was prepared from benzyl acetoacetate (**13**) (0.192 g), 4 hours of reflux, in 32% yield, mp 110-112° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 2.62 (s, 3H, CH_3), 5.21 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 7.31-7.43 (m, 11H, Ph x 2, N*H*), 8.38 (s, 1H, H_4).

Anal. Calcd. for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87; N, 3.56. Found: C, 66.94; H, 5.02; N, 3.56.

3-(Benzyloxycarbonyl)amino-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**28**).

This compound was prepared from cyclohexane-1,3-dione (**21**) (0.112 g), 2 hours of reflux, in 85% yield, mp 143-144° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 2.16 (tt, 2H, 7-CH_2), 2.56, 2.84 (2t, 4H, 6-CH_2, 8-CH_2), 5.22 (s, 2H, CH_2), 7.32-7.41 (m, 6H, Ph, N*H*), 8.31 (s, 1H, H_4), J_{CHCH} = 6.4 Hz.

Anal. Calcd. for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 65.35; H, 4.90; N, 4.58.

3-(Benzyloxycarbonyl)amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**29**).

This compound was prepared from 5,5-dimethylcyclohexane-1,3-dione (**22**) (0.140 g), 2 hours of reflux, in 89% yield, mp 149-151° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 1.14 (s, 6H, 7,7-CH_3), 2.42, 2.70 (2s, 4H, 6-CH_2, 8-CH_2), 5.22 (s, 2H, CH_2), 7.32-7.61 (m, 6H, Ph, N*H*), 8.30 (s, 1H, H_4).

Anal. Calcd. for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.99; H, 5.84; N, 4.36.

3-(Benzyloxycarbonyl)amino-7-hydroxy-8-methyl-2*H*-1-benzopyran-2-one (**30**).

This compound was prepared from 2,6-dihydroxytoluene (**23**) (0.124 g), 3 hours of reflux, in 39% yield, mp 235-238° (from a mixture of ethanol and water); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.16 (s, 3H, Het-CH_3), 5.17 (s, 2H, CH_2), 6.85 (d, 1H, H_6), 7.31-7.56 (m, 6H, Ph, H_5), 8.28 (s, 1H, H_4), 9.03 (s, 1H, N*H*), 10.23 (br s, 1H, O*H*), $J_{H5,H6}$ = 8.7 Hz.

Anal. Calcd. for $C_{18}H_{15}NO_5$: C, 66.46; H, 4.65; N, 4.31. Found: C, 66.15; H, 4.80; N, 4.40.

3-(Benzyloxycarbonyl)amino-7-hydroxy-2*H*-1-benzopyran-2-one (**31**).

This compound was prepared from 1,3-dihydroxybenzene (**24**) (0.110 g), 3 hours of reflux, in 12% yield, mp 212-215° (from a mixture of methanol and toluene): ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.17 (s, 2H, CH_2), 6.74 (d, 1H, H_8), 6.80 (d, 1H, H_6), 7.29-7.46 (m, 5H, Ph), 7.51 (d, 1H, H_5), 8.13 (s, 1H, H_4), 9.03 (s, 1H, N*H*), 10.36 (br s, 1H, O*H*), $J_{H5,H6}$ = 8.6 Hz, $J_{H6,H8}$ = 2.3 Hz.

Anal. Calcd. for $C_{17}H_{13}NO_5$: C, 65.59; H, 4.21; N, 4.50. Found: C, 65.19; H, 4.12; N, 4.35.

3-(Benzyloxycarbonyl)amino-2*H*-naphtho[1,2-*b*]pyran-2-one (**32**).

This compound was prepared from 1-naphthol (**25**) (0.144 g), 3 hours of reflux, in 14% yield, mp 179-181° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 5.26 (s, 2H, CH_2), 7.33-7.43 (m, 6H, Ph, N*H*), 7.49 (d, 1H, H_6), 7.56-7.70 (m, 2H, H_8, H_9), 7.71 (d, 1H, H_5), 7.87 (dd, 1H, H_7), 8.45 (s, 1H, H_4), 8.47 (dd, 1H, H_{10}), $J_{H5,H6}$ = 8.6 Hz, $J_{H7,H8}$ = 8.5 Hz, $J_{H7,H9}$ = 1.8 Hz, $J_{H8,H10}$ = 1.5 Hz, $J_{H9,H10}$ = 9.7 Hz.

Anal. Calcd. for $C_{21}H_{15}NO_4$: C, 73.04 H, 4.38; N, 4.06; Found: C, 72.89; H, 4.28; N, 3.90.

2-(Benzyloxycarbonyl)amino-5-hydroxy-3*H*-naphtho[2,1-*b*]-pyran-3-one (**33**) and 2-Di(benzyloxycarbonyl)amino-2*H*,11*H*-naphtho[2,1-*b*:3,4-*b*]dipyran-2,11-dione (**34**).

A mixture of these compounds was prepared from 2,3-dihydroxynaphthalene (**26**) (0.160 g), 4.5 hours of reflux. The solvent was evaporated *in vacuo* and the solid residue separated by radial chromatography by chromatotron (Silica gel 60 PF_{254} containing gypsum, Merck, chloroform/methanol, 15:1 as eluent) to give **33** in 49% and **34** in 4% yield. Compound **33** had mp 228-230° (from a mixture of ethanol and toluene); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.25 (s, 2H, CH_2), 7.35-7.52 (m, 8H, Ph, H_6, H_8, H_9), 7.80 (dd, 1H, H_7), 8.13 (dd, 1H, H_{10}), 8.99 (s, 1H, H_1), 9.43 (s, 1H, N*H*), 10.59 (br s, 1H, O*H*) $J_{H7,H8}$ = 6.0 Hz, $J_{H7,H9}$ = 2.9 Hz, $J_{H8,H10}$ = 2.3 Hz, $J_{H9,H10}$ = 6.4 Hz.

Anal. Calcd. for $C_{21}H_{15}NO_5$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.62; H, 4.32; N, 3.95.

Compound **34** had mp 267-270° (from a mixture of ethanol and toluene); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.28 (s, 4H, CH_2 x 2), 7.36-7.52 (m, 10H, Ph x 2), 7.77 (dd, 2H, H_6, H_7), 8.30 (dd, 2H, H_5, H_8), 9.03 (s, 2H, H_4, H_9), 9.68 (s, 2H, N*H* x 2), $J_{H5,H6}$ = 6.0 Hz, $J_{H7,H8}$ = 6.0 Hz, $J_{H5,H7}$ = 3.0 Hz, $J_{H6,H8}$ = 3.0 Hz.

Anal. Calcd. for $C_{32}H_{22}N_2O_8$: C, 68.32; H, 3.94; N, 4.98. Found: C, 68.66; H, 4.18; N, 4.82.

2-(Benzyloxycarbonyl)amino-3*H*-naphtho[2,1-*b*]pyran-3-one (**35**).

This compound was prepared from 2-naphthol (**27**) (0.114 g), 4 hours of reflux, in 19% yield, mp 181-182° (from a mixture of ethanol and toluene); ^{1}H nmr (deuteriochloroform): δ 5.29 (s, 2H, CH_2), 7.34-7.47 (m, 6H, Ph, H_6), 7.57 (ddd, 1H, H_8), 7.64-7.69 (m, 2H, H_9, N*H*), 7.89 (d, 1H, H_5), 7.90 (dd, 1H, H_7), 8.31 (d, 1H, H_{10}), 8.31 (s, 1H, H_1), $J_{H5,H6}$ = 9.0 Hz, $J_{H7,H8}$ = 7.1 Hz, $J_{H8,H9}$ = 6.9 Hz, $J_{H9,H10}$ = 8.2 Hz, $J_{H7,H9}$ = 1.3 Hz, $J_{H8,H10}$ = 1.1 Hz.

Anal. Calcd. for $C_{21}H_{15}NO_4$: C, 73.04 H, 4.38; N, 4.06 Found: C, 72.96 H, 4.54; N, 4.13.

3-(Benzyloxycarbonyl)amino-5,6-dihydro-2*H*-pyrano[3,2-*c*]-pyridine-2,5-dione (**46**).

This compound was prepared from 4-dihydroxypyridin-2(1*H*)-one (**39**) (0.111 g), 1.5 hours of reflux, in 87% yield, mp >280° (from a mixture of methanol and toluene); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.19 (s, 2H, CH_2), 6.35 (d, 1H, H_8),

7.33-7.47 (m, 5H, Ph), 7.51 (d, 1H, H_7), 8.24 (s, 1H, H_4), 9.30 (br s, 1H, N*H*), 11.92 (br s, 1H, OH or NH), $J_{H8,H9}$ = 7.3 Hz.

Anal. Calcd. for $C_{16}H_{12}N_2O_5$: C, 61.54; H, 3.87; N, 8.97. Found: C, 61.29; H, 3.77; N, 8.95.

3-(Benzyloxycarbonyl)amino-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]-pyran-2,5-dione (**47**).

This compound was prepared from 4-hydroxy-6-methylpyran-2-one (**40**) (0.126 g), 0.5 hour of reflux, in 80% yield, mp 204-206° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 2.34 (s, 3H, Het-C*H*$_3$), 5.23 (s, 2H, C*H*$_2$), 6.17 (s, 1H, H_8), 7.32-7.41 (m, 6H, Ph, N*H*), 8.39 (s, 1H, H_4).

Anal. Calcd. for $C_{17}H_{13}NO_6$: C, 62.39; H, 4.00; N, 4.28. Found: C, 62.29; H, 3.95; N, 4.21.

3-(Benzyloxycarbonyl)amino-2*H*,5*H*-pyrano[3,2-*c*]benzopyran-2,5-dione (**48**).

This compound was prepared from 4-hydroxycoumarin (**41**) (0.162 g), 1 hour of reflux, in 59% yield, mp 234-237° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 5.26 (s, 2H, C*H*$_2$), 7.37-7.42 (m, 7H, Ph, H_8, H_{10}), 7.52 (s, 1H, N*H*), 7.62 (ddd, 1H, H_9), 8.00 (dd, 1H, H_7), 8.54 (s, 1H, H_4), $J_{H7,H8}$ = 8.3 Hz, $J_{H8,H9}$ = 7.4 Hz, $J_{H9,H10}$ = 9.5 Hz, $J_{H7,H9}$ = 1.7 Hz.

Anal. Calcd. for $C_{20}H_{13}NO_6$: C, 66.12; H, 3.61; N, 3.86. Found: C, 66.17; H, 3.43; N, 3.81.

5-(Benzyloxycarbonyl)amino-3-methyl-1-phenyl-1*H*,6*H*-pyrano[2,3-*c*]pyrazol-6-one (**49**).

This compound was prepared from 3-methyl-1-phenylpyrazol-5(1*H*)-one (**42**) (0.174 g), 2.5 hours of reflux, in 16% yield, mp 166-168° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 2.44 (s, 3H, Het-C*H*$_3$), 5.23 (s, 2H, C*H*$_2$), 7.30-7.51, 7.83-7.86 (2m, 11H, Ph x 2, H_4), 8.36 (s, N*H*).

Anal. Calcd. for $C_{21}H_{17}N_3O_4$: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.00; H, 4.34; N, 11.30.

5-(Benzyloxycarbonyl)amino-1,3-diphenyl-1*H*,6*H*-pyrano[2,3-*c*]-pyrazol-6-one (**50**).

This compound was prepared from 1,3-diphenylpyrazol-5(1*H*)-one (**43**) (0.236 g), 4.5 hours of reflux, in 93% yield, mp 194-196° (from a mixture of methanol and toluene); ^{1}H nmr (deuteriochloroform): δ 5.24 (s, 2H, C*H*$_2$), 7.35-7.42, 7.48-7.53, 7.94-7.98 (3m, 16H, Ph x 3, H_4), 8.71 (s, 1H, N*H*).

Anal. Calcd. for $C_{26}H_{19}N_3O_4$: C, 71.39; H, 4.38; N, 9.61. Found: C, 71.47; H, 4.61; N, 9.71.

6-(Benzyloxycarbonyl)amino-2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimidin-7-one (**51**).

This compound was prepared from barbituric acid (**44**) (0.128 g), 1.5 hours of reflux, in 79% yield, mp >280° (from a mixture of methanol and dimethylformamide); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.15 (s, 2H, C*H*$_2$), 7.30-7.44 (m, 5H, Ph), 7.96 (s, 1H, H_4), 9.20, 11.47, 12.87 (3s, 3H, N*H* x 3).

Anal. Calcd. for $C_{15}H_{11}N_3O_6$: C, 54.72; H, 3.37; N, 12.76. Found: C, 54.68; H, 3.21; N, 12.93.

6-(Benzyloxycarbonyl)amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimidin-7-one (**52**).

This compound was prepared from 1,3-dimethylbarbituric acid (**45**) (0.156 g), 1.5 hours of reflux, in 91% yield, mp 175-177° (from a mixture of ethanol and toluene); ^{1}H nmr (deuteriochloroform): δ 3.42, 3.56 (2s, 6H, Het-C*H*$_3$ x 2), 5.22 (s, 2H, C*H*$_2$), 7.13 (s, 1H, H_4), 7.34-7.42 (m, 5H, Ph), 8.51 (s, 1H, N*H*).

Anal. Calcd. for $C_{17}H_{15}N_3O_6$: C, 57.14; H, 4.23; N, 11.76. Found: C, 56.98; H, 4.16; N, 11.87.

Deprotection of 3-(Benzyloxycarbonyl)amino-4*H*-quinolizin-4-ones and 3-(Benzyloxycarbonyl)amino-2*H*-pyran-2-ones.

General Procedure.

A solution of compounds **5**, **6**, **18**, **29**, **30**, **35**, **46**, **47**, **48**, **50**, **52**, in ethanol was mixed with cyclohexene (in excess of molar proportion required) and commercial 10% Pd/C catalyst (catalyst substrate ratio 1:2 to 1:5 by weight). The mixture was refluxed for 15 minutes to 1.5 hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/ methanol, 5:1 as solvent). The catalyst was removed by filtration of warm mixture. The filtrate was evaporated *in vacuo* and the solid residue was recrystallized from an appropriate solvent. The following compounds were prepared in this manner:

3-Amino-1-cyano-4*H*-quinolizin-4-one (**7**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-1-cyano-4*H*-quinolizin-4-one (**5**) (0.163 g, 0.5 mmole), 30 minutes of reflux, in 88% yield, mp 204-205° (from a mixture of ethanol and *n*-heptane), lit [20] mp 190-192°; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.63 (s, 2H, N*H*$_2$), 7.14 (ddd, 1H, H_7), 7.22 (s, 1H, H_2), 7.38 (ddd, 1H, H_8), 7.68 (dd, 1H, H_9), 8.82 (dd, 1H, H_6), $J_{H6,H7}$ = 7.5 Hz, $J_{H7,H8}$ = 6.8 Hz, $J_{H8,H9}$ = 9.1 Hz, $J_{H6,H8}$ = 1.1 Hz, $J_{H7,H9}$ = 1.5 Hz.

Anal. Calcd. for $C_{10}H_7N_3O$: C, 64.86; H, 3.81; N, 22.69. Found: C, 64.64; H, 4.09; N, 22.87.

3-Amino-1-ethoxycarbonyl-4*H*-quinolizin-4-one (**8**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-1-ethoxycarbonyl-4*H*-quinolizin-4-one (**6**) (0.183 g, 0.5 mmole), 30 minutes of reflux, in 94% yield, mp 136-139°, lit [19] mp 135-136° (from a mixture of ethyl acetate and heptane); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 1.34 (t, 3H, CH_2CH_3), 4.31 (q, 2H, CH_2CH_3), 5.42 (s, 2H, N*H*$_2$), 7.13 (ddd, 1H, H_7), 7.35 (ddd, 1H, H_8), 7.74 (s, 1H, H_2), 8.86 (dd, 1H, H_9), 8.91 (dd, 1H, H_6), J_{CHCH} = 7.2 Hz, $J_{H6,H7}$ = 7.2 Hz, $J_{H7,H8}$ = 6.4 Hz, $J_{H8,H9}$ = 9.4 Hz , $J_{H6,H8}$ = 1.5 Hz, $J_{H7,H9}$ = 1.5 Hz.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.75; H, 5.45; N, 11.88.

3-Amino-5-ethoxycarbonyl-6-phenyl-2*H*-pyran-2-one (**20**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-5-ethoxycarbonyl-6-phenyl-2*H*-pyran-2-one (**18**) (0.085 g, 0.2 mmole), 15 minutes of reflux, in 67% yield, mp 97-100° (from a mixture of ethyl acetate and heptane); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 1.01 (t, 3H, CH_2CH_3), 4.07 (q, 2H, CH_2CH_3), 5.75 (s, 2H, N*H*$_2$), 6.66 (s, 1H, H_4), 7.44-7.45 (m, 5H, Ph), J_{CHCH} = 7.1 Hz.

Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 65.05; H, 5.13; N, 5.25.

3-Amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzo-pyran-2-one (**36**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (**29**) (0.156 g, 0.5 mmole), 15 minutes of reflux, in 88% yield, mp 192-195° (from ethanol), lit [18] mp 195.5-196.5°;

^{1}H nmr (dimethyl-d_6 sulfoxide): δ 1.04 (s, 6H, 7,7-CH_3), 2.34, 2.67 (2s, 4H, 6-CH_2, 8-CH_2), 5.43 (s, 2H, NH_2), 6.59 (s, 1H, H_4).

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.61; H, 6.46; N, 6.81.

3-Amino-7-hydroxy-8-methyl-2*H*-1-benzopyran-2-one (**37**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-7-hydroxy-8-methyl-2*H*-1-benzopyran-2-one (**30**) (0.162 g, 0.5 mmole), 15 minutes of reflux, in 85% yield, mp 227-229° (from a mixture of ethanol and ethyl acetate); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.15 (s, 3H, Het-CH_3), 5.17 (s, 2H, NH_2), 6.69 (s, 1H, H_4), 6.74 (d, 1H, H_5), 7.07 (d, 1H, H_6), 9.66 (br s, 1H, O*H*), $J_{H5,H6}$ = 8.5 Hz.

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.44; H, 5.08; N, 7.01.

2-Amino-3*H*-naphtho[2,1-*b*]pyran-3-one (**38**).

This compound was prepared from 2-(benzyloxycarbonyl)-amino-3*H*-naphtho[2,1-*b*]pyran-3-one (**35**) (0.176 g, 0.5 mmole), 30 minutes, in 92% yield, mp 158-160° (from ethanol); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.84 (s, 2H, NH_2), 7.48 (d, 1H, H_6), 7.55 (s, 1H, H_1), 7.56 (ddd, 1H, H_8), 7.64 (ddd, 1H, H_9), 7.80 (d, 1H, H_5), 7.98 (d, 1H, H_7), 8.23 (d, 1H, H_{10}), $J_{H5,H6}$ = 9.0 Hz, $J_{H7,H8}$ = 8.3 Hz, $J_{H8,H9}$ = 7.2 Hz, $J_{H9,H10}$ = 8.3 Hz, $J_{H7,H9}$ = 1.5 Hz.

Anal. Calcd. for $C_{13}H_9NO_2$: C, 73.92; H, 4.29; N, 6.63. Found: C, 73.85; H, 4.51; N, 6.59.

3-Amino-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-2,5-dione (**53**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridine-2,5-dione (**46**) (0.123 g, 0.4 mmole), 20 minutes of reflux, in 82% yield, mp >280° (washed with methanol); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.65 (s, 2H, NH_2), 6.28 (d, 1H, H_8), 6.81 (s, 1H, H_4), 7.23 (d, 1H, H_7), 11.61 (br s, 1H, OH or NH), $J_{H8,H9}$ = 7.2 Hz.

Anal. Calcd. for $C_8H_6N_2O_3$: C, 53.94; H, 3.39; N, 15.72. Found: C, 53.66; H, 3.37; N, 15.53.

3-Amino-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (**54**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (**47**) (0.164 g, 0.5 mole), 15 minutes of reflux, in 37% yield, mp >290° (from a mixture of ethanol and ethyl acetate); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.54 (s, 3H, Het-CH_3), 5.82 (s, 2H, NH_2), 6.52 (s, 1H, H_8), 6.61 (s, 1H, H_4).

Anal. Calcd. for $C_9H_7NO_4$: C, 55.96; H, 3.65; N, 7.25. Found: C, 55.74; H, 3.82; N, 7.08.

3-Amino-2*H*,5*H*-pyrano[3,2-*c*]benzopyran-2,5-dione (**55**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-2*H*,5*H*-pyrano[3,2-*c*]benzopyran-2,5-dione (**48**) (0.110 g, 0.3 mmole), 15 minutes of reflux, in 88% yield, mp 272-275° (washed with methanol); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 6.16 (s, 2H, NH_2), 6.72 (s, 1H, H_4), 7.44 (ddd, 1H, H_8), 7.47 (dd, 1H, H_{10}), 7.60 (dd, 1H, H_9), 7.86 (dd, 1H, H_7), $J_{H7,H8}$ = 7.9 Hz, $J_{H8,H9}$ = 7.2 Hz, $J_{H9,H10}$ = 6.8 Hz, $J_{H7,H9}$ = 1.9 Hz, $J_{H8,H10}$ = 1.1 Hz.

Anal. Calcd. for $C_{12}H_7NO_4$: C, 62.89; H, 3.08; N, 6.11. Found: C, 62.68; H, 3.13; N, 5.79.

5-Amino-1,3-diphenyl-1*H*,6*H*-pyrano[2,3-*c*]pyrazol-6-one (**56**).

This compound was prepared from 5-(benzyloxycarbonyl)-amino-1,3-diphenyl-1*H*,6*H*-pyrano[2,3-*c*]pyrazol-6-one (**50**) (0.226 g, 0.5 mmole), 1.5 hours of reflux, in 91% yield, mp 147-150° (from a mixture of ethanol and ethyl acetate); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 5.24 (s, 2H, NH_2), 7.17 (s, 1H, H_4), 7.42-7.63, 7.83-7.91 (2m, 10H, Ph x 2).

Anal. Calcd. for $C_{18}H_{13}N_3O_2$: C, 71.28; H, 4.32; N, 13.85. Found: C, 70.95; H, 4.37; N, 13.65.

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimidin-7-one (**57**).

This compound was prepared from 6-(benzyloxycarbonyl)-amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-7*H*-pyrano-[2,3-*d*]pyrimidin-7-one (**52**) (0.178 g, 0.5 mmole), 20 minutes of reflux, in 94% yield, mp >290°, (from a mixture of ethanol and toluene), lit [18] mp 239-242°; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 3.23, 3.37 (2s, 6H, Het-CH_3 x 2), 5.23 (s, 2H, NH_2), 6.80 (s, 1H, H_4).

Anal. Calcd. for $C_9H_9N_3O_4$: C, 48.43; H, 4.06; N, 18.83. Found: C, 48.40; H, 4.05; N, 18.76.

Acknowledgement.

The authors wish to express their gratitude to the Ministry of Science and Technology, Slovenia, for financial support.

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