α-Pyrones. II [1]. Synthesis of Tetrahydroquinoline Derivatives of 4-Aminobutanoic and 2-Amino-2-pentenedioic Acids

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Ethyl 3-benzoylamino-2-oxo-6-triphenylphosphoranylidenemethyl-2*H*-pyran-5-carboxylate (**1**) reacts with 2-nitrobenzaldehydes (**2**) to give 6-(2-nitrostyryl)-2*H*-pyran-2-ones (**3**), as the *E* stereoisomers, in good yields. The reduction of compounds **3**, performed with hydrogen over Pd/C at room temperature and 1 atmosphere, leads to a mixture of 2-amino-4-tetrahydroquinolinylidene-2-pentenedioic acid derivatives **5a-d** as the main products, the corresponding 3-butenoic acid derivatives **6** and a minor amount of pyrano[2,3-*c*]benzazocines **9a-c**. At 40 atmospheres and 90°, the reduction gives 4-amino-2-tetrahydroquinolinylbutanoic acid derivatives **8a-d** as the main products and their precursors **7a,b,d** as the minor ones. Amines **4c,d** are isolated by stopping the reduction after the uptake of 3 equivalents of hydrogen.

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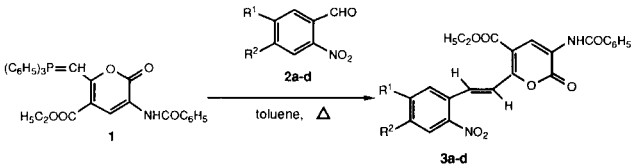
In a previous paper we described the preparation of the versatile synthon ethyl 3-benzoylamino-2-oxo-6-triphenylphosphoranylidenemethyl-2*H*-pyran-5-carboxylate (**1**) from 4-ethoxymethylene-2-phenyloxazol-5(4*H*)-one and ethyl 3-oxo-4-triphenylphosphoranylidene butyrate [1] and discussed its reactivity with aliphatic and aromatic aldehydes. In fact such reactions proved to lead the way to the preparation of 6-(1-alkenyl)-2-pyrones. In line with our program towards the development of synthetic paths to heterocycles from pyrones, we investigated the possibility to extend the reaction of synthon **1** to 2-nitrobenzaldehydes, the aim being to obtain *ortho*-nitrostyrylpyrones **3**. These compounds represent synthetic intermediates as they have a chain with a precursor for an amino group which can give intramolecular addition to the pyrone system and thus produce a functionalized nitrogen heterocycle. Despite the fact that intramolecular reactions involving the α-pyrone ring provide an interesting path to heterocyclic compounds, due to straightforward course, they are, to the best of our knowledge, generally neglected. In fact the simple addition of nitrogen nucleophiles to the 2-pyrone ring may occur competitively both on the carbonyl group and to C(6) as a conjugate addition. Only in some favorable instances is a nitrogen-containing heterocycle produced, in most cases ring opening is observed [2]. Clearly, the existing steric restraints in intramolecular reactions eliminate the dualism of the nucleophilic addition.

Thus, this synthetic path was used for the preparation of derivatives of 4-aminobutanoic (GABA) and 2-amino-2-pentenedioic acids with, as substituent, a tetrahydroquinoline ring starting from 6-(2-nitrostyryl)-2*H*-pyran-2-ones **3**.

The new 6-(2-nitrostyryl)-2*H*-pyran-2-ones **3a-d** were produced by reacting **1** with 2-nitrobenzaldehydes **2a-d** in refluxing toluene, through Wittig reaction (Scheme 1). Compounds **3a,b,d** were produced as a single stereoisomer in the *E* form as is usual for alkenes produced from stabilized ylides [3]. This is confirmed by the ^{1}H nmr coupling constant of the vinyl hydrogens of 15-16 Hz. Only in the case of **3c** was a mixture of the *E* (major) and *Z* (minor) isomers obtained. The *E* isomer was isolated in pure form since it crystallized out directly from the reaction mixture. The separation of a second crop of *E*/*Z* mixture was not attempted.

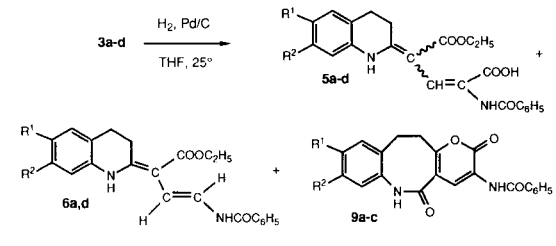
Scheme 1



a, $R^1 = R^2 = H$; b, $R^1 = OCH_3$ $R^2 = H$; c, $R^1 = R^2 = OCH_3$; d, R^1-$R^2 = OCH_2O$

Reduction of compounds **3a-d** was performed by catalytic hydrogenation (10% palladium on charcoal in tetrahydrofuran) at both room temperature and atmospheric pressure (Method A) and at a higher temperature and pressure (90° and 40 atmospheres) (Method B). Under the milder reaction conditions of Method A compounds **3a-d** afforded as the main reaction products the corresponding 2-amino-4-tetrahydroquinolinylidene-2-pentenedioic acid derivatives **5a-d**. In some cases minor amounts of tetrahydroquinoline derivatives **6a,d** and pyrano[2,3-*c*]-benzazocines **9a-c**, besides **5**, were isolated (Scheme 2).

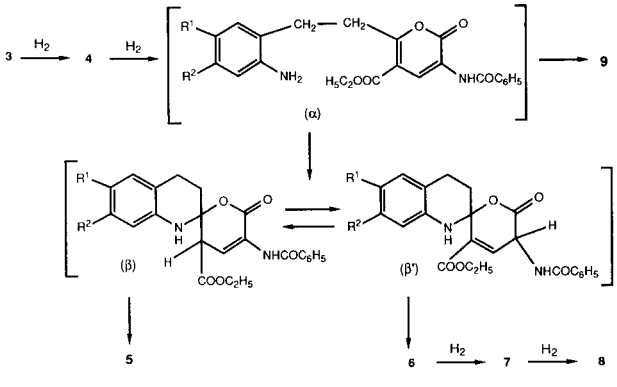
Scheme 2



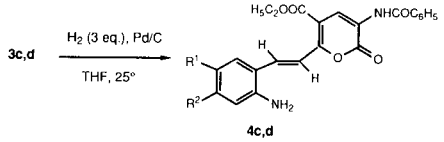
a, $R^1 = R^2 = H$; b, $R^1 = OCH_3$ $R^2 = H$; c, $R^1 = R^2 = OCH_3$; d, R^1-$R^2 = OCH_2O$

The foregoing results can be rationalized by the reaction path depicted in Scheme 3. Hydrogenation of **3** affords intermediate α through reduction of both the nitro group and the double bond. This reduction occurs *via* styryl amines **4** since the reduction rate of the nitro group is greater than that of the hindered double bond [4]. Indeed, in the case of starting materials **3c,d** the corresponding partially reduced compounds **4c,d**, could be obtained by stopping the catalytic hydrogenation after 3 equivalents of hydrogen had been consumed (Scheme 4). The amino group in intermediate α reacts with the ester function linked to C(5) of the pyrone moiety affording **9** through amidation or, preferably, adds intramolecularly to the reactive C(6) position of the pyrone ring forming the tautomeric spiranic intermediates β and β'. Ring opening of β leads to acid **5**. Alternatively, in the tautomeric form β' carbon dioxide elimination is preferred, thus directing the reaction toward the formation of **6**. It is worth noting that two different reaction paths should be postulated for the formation of **5** or **6**. In fact acids **5** were demonstrated to be thermally stable (at least until 100°) thus ruling out the formation of **6** *via* decarboxylation of **5**. It could be that the elimination process would be favored by an increase of the reaction temperature. The reduction of **3a-d** under the stronger conditions of Method B led to the main reaction products, compounds **8a-d**, accompanied by minor amounts of the less reduced substances **7a,b,d** (Scheme 5). These results confirm the favorable effect of a temperature increase on carbon dioxide elimination: only further hydrogenation products deriving from **6** are formed.

Scheme 3

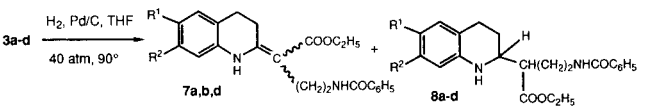


Scheme 4



c, $R^1 = R^2 = OCH_3$; **d**, $R^1\text{-}R^2 = OCH_2O$

Scheme 5



a, $R^1 = R^2 = H$; **b**, $R^1 = OCH_3$ $R^2 = H$; **c**, $R^1 = R^2 = OCH_3$; **d**, $R^1\text{-}R^2 = OCH_2O$

The formation of the tetrahydroquinoline ring in compounds **5-8** is demonstrated from ^1H nmr data showing as significant features the presence of a multiplet (2.2-2.8 δ) associated with the CH_2-CH_2 group and an exchangeable singlet (NH). Compounds **5** are characterized by a singlet in the aromatic region associated with -CH= and by three exchangeable hydrogens related to the NH, NHCO and COOH groups. The configuration of the diene system in compounds **5** could not be defined. According to ^1H nmr recorded on freshly prepared solutions, these compounds were isolated as a single stereoisomer, but underwent a partial isomerization when kept in solution for some time, thus preventing an accurate study. Compounds **6** are characterized by an ^1H nmr spectrum related to that of **5**. A typical feature was an AB pattern associated with the -CH=CH- group. The coupling constant of 14-15 Hz confirms the *E* configuration. A NOESY experiment allowed the demonstration of the spatial proximity of the hydrogens in the -N*H*-C=C-C*H*- chain, thus confirming the *E* configuration of both double bonds. Identification of both **7** and **8** was easy, their ^1H nmr spectra being compared with those of **5** and **6**. A clear splitting of all signals in the spectra of products **8** (perdeuteriobenzene) is strong evidence of the presence of two diastereoisomers. The ^1H nmr spectra of compounds **9** maintain the characteristic signals associated with the starting pyrone structure, *i.e.* two singlets at about 8.4 and 8.8-8.9 δ, associated with $-NHCOC_6H_5$ and H(4). Moreover, a multiplet in the 2.8-3.0 δ region and an exchangeable signal at about 12.4-12.6 δ correspond to the $-CH_2CH_2-$ and -NHCO- bridges, respectively.

In conclusion, the intramolecular ring closure of 6-(2-nitrostyryl)-2*H*-pyran-2-ones, following the reduction of both the nitro group and the double bond, is a satisfactory entry to 2-tetrahydroquinoline substituted derivatives of 4-aminobutanoic acid (GABA), and of 2-amino-2-pentenedioic acid from readily accessible precursors. It is worth noting the ease in directing the reaction toward compounds **5** or **8**, simply changing the reaction conditions changes the final product.

EXPERIMENTAL

Melting points were detected with Büchi 510 (capillary) apparatus. The ir spectra were recorded on a PYE UNICAM SP3-200S Philips spectrophotometer. Nmr experiments were performed on Bruker AC 200 instrument with the solvent indicated.

Ethyl 3-benzoylamino-2-oxo-6-triphenylphosphoranylidenemethyl-2*H*-pyran-5-carboxylate (**1**) is a known compound [1].

Table I

Spectroscopic Data for Compounds **3-9**

No.	Ir (Nujol; cm^{-1}) NH and/or COOH	Ir (Nujol; cm^{-1}) C=O	^1H NMR (δ) (deuteriochloroform)
3a	3390	1730, 1700 1670	1.4 (t, J = 7.0 Hz, 3H, CH_3), 4.4 (q, J = 7.0 Hz, 2H, CH_2), 7.3-8.0 (m, 11H, aromatic H and CH=CH), 8.7 (s, 1H, NH), 8.9 (s, 1H, 4-H)
3b	3410	1730, 1705 1670	1.2 (t, J = 7.0 Hz, 3H, CH_3), 3.8 (s, 3H, OCH_3), 4.2 (q, J = 7.0 Hz, 2H, CH_2), 6.8-8.0 (m, 10H, aromatic H and CH=CH), 8.6 (s, 1H, NH), 8.7 (s, 1H, 4-H)
3c	3400	1730, 1710 1670	[a] 1.4 (t, J = 7.0 Hz, 3H, CH_3), 3.9, 4.0 (two s, 6H, OCH_3), 4.4 (q, J = 7.0 Hz, 2H, CH_2), 7.0, 7.2, 7.4-8.0 (two s and m, 8H, aromatic H and CH=), 8.2 (d, J = 15.7 Hz, 1H, CH=), 8.7 (s, 1H, NH), 9.0 (s, 1H, 4-H)
3d	3350	1720, 1690 1670	1.4 (t, J = 7.0 Hz, 3H, CH_3), 4.4 (q, J = 7.0 Hz, 2H, CH_2), 6.2 (s, 2H, OCH_2O), 7.1, 7.3, 7.4-7.9 (two s and m, 8H, aromatic H and CH=), 8.0 (d, J = 15.7 Hz, 1H, CH=), 8.7 (s, 1H, NH), 8.9 (s, 1H, 4-H)
4c	3560, 3400 3320	1700, 1670	1.3-2.1 (s br, 2H, NH_2), 1.4 (t, J = 7.1 Hz, 3H, CH_3), 3.8 (s, 6H, OCH_3), 4.4 (q, J = 7.1 Hz, 2H, CH_2), 6.2, 7.0, 7.4-7.9 (two s and m, 7H, aromatic H), 7.75, 7.85 (AB system, J = 16.0 Hz, 2H, CH=CH), 8.6 (s, 1H, NH), 8.9 (s, 1H, 4-H)
4d	3420, 3350 3250	1690, 1680	[b] 1.3 (t, J = 7.2 Hz, 3H, CH_3), 4.3 (q, J = 7.2 Hz, 2H, CH_2), 5.7-5.8 (s, br, 2H, NH_2), 5.9 (s, 2H, OCH_2O), 6.4, 6.9, 7.5-8.0 (two s and m, 7H, aromatic H), 7.6, 7.8 (AB system, J = 15.6 Hz, 2H, CH=CH), 8.5 (s, 1H, 4-H), 9.7 (s, 1H, NH)
5a	3700-3000	1710, 1680 1640	[b] 1.2 (t, J = 7.0 Hz, 3H, CH_3), 2.4-2.6 (m, 4H, CH_2CH_2), 4.1 (q, J = 7.0 Hz, 2H, CH_2), 6.8-7.9 (m, 10H, aromatic H and CH=), 9.6 (s, 1H, NHCO), 11.4 (s, 1H, NH), 12.4 (s, 1 H, COOH)
5b	3600-3000	1710, 1690 1640	1.3 (t, J = 7.0 Hz, 3H, CH_3), 2.6-2.8 (m, 4H, CH_2CH_2), 3.7 (s, 3H, OCH_3), 4.2 (q, J = 7.0 Hz, 2H, CH_2), 4.5-5.6 (s, br, 1H, COOH), 6.5-7.8 (m, 9H, aromatic H and CH=), 8.0 (s, 1H, NHCO), 11.7 (s, 1H, NH)
5c	3380-3000	1710, 1690 1680	[b] 1.2 (t, J = 7.1 Hz, 3H, CH_3), 2.2-2.6 (m, 4H, CH_2CH_2), 3.5, 3.6 (two s, 6H, OCH_3), 4.1 (q, J = 7.1 Hz, 2H, CH_2), 6.6, 6.7, 7.4-7.9 (two s and m, 7H, aromatic H), 7.0 (s, 1H, CH=). 9.5 (s, 1H, NHCO), 11.4 (s, 1H, NH), 12.4 (s, 1H, COOH)
5d	3500-3100	1730, 1700 1660	1.2 (t, J = 7.1 Hz, 3H, CH_3), 2.4-2.6 (m, 4H, CH_2CH_2), 3.3-4.0 (s br, 1H, COOH), 4.2 (q, J = 7.1 Hz, 2H, CH_2), 5.8 (s, 2H, OCH_2O), 6.2, 6.4, 7.3-7.8 (two s and m, 7H, aromatic H), 7.2 (s, 1H, CH=), 8.1 (s, 1H, NHCO), 11.5 (s, 1H, NH)
6a	3280	1650	[b] 1.3 (t, J = 7.2 Hz, 3H, CH_3), 2.7-2.9 (m, 4H, CH_2CH_2), 4.2 (q, J = 7.2 Hz, 2H, CH_2CH_3), 6.3 (d, 14.6 Hz, 1H, *CH*=CHN), 6.9-8.0 (m, 10H, aromatic and H and =*CH*NH), 10.3 (d, J = 9.7 Hz, 1H, NHCO), 11.4 (s, 1H, NH)
6d	3230	1650	[b] 1.3 (t, J = 7.0 Hz, 3H, CH_3), 2.6-2.9 (m, 4H, CH_2CH_2), 4.2 (q, J = 7.0 Hz, 2H, CH_2CH_3), 5.9 (s, 2H, OCH_2O), 6.2 (d, J = 14.5 Hz, 1H, *CH*=CHN), 6.71, 6.72, 7.4-8.0 (two s and m, 7H, aromatic H), 6.9 (dd, J = 14.6 Hz, J = 10.0 Hz, 1H, =CHN), 10.3 (d, J = 10.0 Hz, 1H, NHCO), 11.3 (s, 1H, NH)
7a	3240	1660, 1640	1.3 (t, J = 7.1 Hz, 3H, CH_3), 2.7 (t, J = 7.0 Hz, 2H, CH_2CH_2N), 2.7-2.9 (m, 4H, CH_2CH_2), 3.5 (q, J = 7.0 Hz, 2H, CH_2N), 4.2 (q, J = 7.1 Hz, 2H, OCH_2), 6.4 (t, J = 7.0 Hz, NHCO), 6.7-7.8 (m, 9H, aromatic H), 11.3 (s, 1H, NH)
7b	3300	1640, 1630	1.3 (t, J = 7.2 Hz, 3H, CH_3), 2.68 (t, J = 7.0 Hz, 2H, CH_2CH_2N), 2.75-2.85 (m, 4H, CH_2 CH_2), 3.5 (q, J = 7.0 Hz, 2H, CH_2N), 3.8 (s, 3H, OCH_3), 4.2 (q, J = 7.2 Hz, 2H, CH_2CH_3), 6.5 (t, J = 7.0 Hz, NHCO), 6.7-7.8 (m, 8H, aromatic H), 11.3 (s, 1H, NH)
7d	3350	1600, 1630	1.3 (t, J = 7.1 Hz, 3H, CH_3), 2.5-2.8 (m, 6H, CH_2CH_2N and CH_2CH_2), 3.5 (q, J = 7.0 Hz, 2H, CH_2N), 4.2 (q, J = 7.1 Hz, 2H, CH_2CH_3), 5.9 (s, 2H, OCH_2O), 6.3, 6.6, 7.4-7.8 (two s and m, 7H, aromatic H), 6.5 (t, J = 7.0 Hz, 1H, NHCO), 11.2 (s, 1H, NH)
8a	3350	1740, 1650	[c] 1.2 (t, J = 7.1 Hz, 3H, CH_3), 1.7-2.1 (m, 4H, CH_2CH_2N and CH_2CH_2CH), 2.6-2.7 (m, 3H, CHCOO and CH_2CH_2CH), 3.4-3.5 (m, 3H, CH_2NH and *CH*NH), 4.0-4.2 (m, 2H, OCH_2), 4.4-4.5 (m, 1H, NH), 7.1-7.2 (m, 1H, NHCO), 6.4-7.8 (m, 9H, aromatic H)
8b	3350	1730, 1660	[c] 1.2 (t, J = 7.1 Hz, 3H, CH_3), 1.7-2.1 (m, 4H, CH_2CH_2N and CH_2CH_2CH), 2.6-2.8 (m, 3H, CHCOO and CH_2CH_2CH), 3.4-3.6 (m, 3H, CH_2NH and *CH*NH), 3.7 (s, 3H, OCH_3), 4.0-4.2 (m, 2H, OCH_2), 4.4-4.5 (m, 1H, NH), 6.7-6.8 (m, 1H, NHCO), 6.4-7.8 (m, 8H, aromatic H)
8c	3350	1740, 1640	[c] 1.2 (t, J = 7.0 Hz, 3H, CH_3), 1.6-2.2 (m, 4H, CH_2CH_2N and CH_2CH_2CH), 2.5-2.9 (m, 3H, CHCOO and CH_2CH_2CH), 3.3-3.7 (m, 3H, CH_2NH and *CH*NH), 3.8 (s, 6H, OCH_3), 4.1-4.3 (m, 2 H, OCH_2), 4.3-4.4 (m, 1H, NH), 6.5-6.6 (m, 1H, NHCO), 6.10, 6.15, 6.5, 7.3-7.8 (m, 7H, aromatic H)

Table I (continued)

8d	3350	1740, 1640	[c] 1.2 (t, J = 7.1 Hz, 3H, CH_3), 1.4-2.1 (m, 4H, CH_2CH_2N and CH_2CH_2CH), 2.6-2.8 (m, 3H, CHCOO and CH_2CH_2CH), 3.3-3.7 (m, 3H, CH_2NH and CHNH), 4.0-4.3 (m, 2H, CH_2CH_3), 4.3-4.4 (m, 1H, NH), 5.8 (s, 2H, OCH_2O), 6.5-6.6 (m, 1H, NHCO), 6.10, 6.18, 6.4, 7.3-7.8 (m, 7H, aromatic H)
9a	3380, 3330	1720, 1650	2.9-3.2 (m, 4H, CH_2CH_2), 7.0-7.9 (m, 9H, aromatic H), 8.4 (s, 1H, NHCO), 8.9 (s, 1H, 4-H), 12.6 (s, 1H, NH ring)
9b	3400	1720, 1660	2.8-3.0 (m, 4H, CH_2CH_2), 3.7 (s, 3H, OCH_3), 6.6-7.8 (m, 8H, aromatic H), 8.4 (s, 1H, NHCO), 8.8 (s, 1H, 4-H), 12.4 (s, 1H, NH ring)
9c	3400	1720, 1650	2.8-3.1 (m, 4H, CH_2CH_2), 3.88, 3.93 (two s, 6H, OCH_3), 6.6, 6.7, 7.6-7.9 (two s and m, 7H, aromatic H), 8.4 (s, 1H, NHCO), 8.9 (s, 1H, 4-H), 12.5 (s, 1H, NH ring)

[a] Z Stereoisomer: 1.4 (t, J = 7 Hz, 3H, CH_3), 3.8, 4.0 (two s, 6H, OCH_3), 4.4 (q, J = 7 Hz, 2H, CH_2), 6.8, 7.4-8.0 (s, and m, 7H, aromatic H), 7.35, 7.83 (AB system, J = 6.4 Hz, 2H, CH=CH), 8.5 (s, 1H, NH), 8.9 (s, 1H, 4-H). [b] DMSO-d_6. [c] Mixture of two diastereoisomers.

Table II

Physical and Analytical Data for Compounds **3, 5-9**

No.	Mp (°C)	Formula (MW)	Calcd./Found C%	H%	N%	No.	Mp (°C)	Formula (MW)	Calcd./Found C%	H%	N%
3a	176-178 [a]	$C_{23}H_{18}N_2O_7$ (434)	63.58 63.28	4.17 4.32	6.45 6.68	**7a**	115-116 [c]	$C_{22}H_{24}N_2O_3$ (364)	72.51 72.26	6.64 6.44	7.69 7.58
3b	205 [b] [a]	$C_{24}H_{20}N_2O_8$ (464)	62.07 61.93	4.34 4.53	6.03 5.82	**7b**	135-136 [c]	$C_{23}H_{26}N_2O_4$ (394)	70.02 70.05	6.64 6.50	7.10 7.33
3c	258-260 [a]	$C_{25}H_{22}N_2O_9$ (494)	60.73 60.76	4.48 4.59	5.67 5.53	**7d**	165-166 [f]	$C_{23}H_{24}N_2O_5$ (408)	67.63 67.88	5.92 5.72	6.86 7.11
3d	242-245 [a]	$C_{24}H_{18}N_2O_9$ (478)	60.25 59.94	3.79 3.86	5.85 5.98	**8a**	[g]	$C_{22}H_{26}N_2O_3$ (366)	72.10 71.98	7.15 7.03	7.64 7.55
5a	202-205 [c]	$C_{23}H_{22}N_2O_5$ (406)	67.96 67.75	5.46 5.49	6.89 6.66	**8b**	[g]	$C_{23}H_{28}N_2O_4$ (396)	69.67 69.44	7.12 7.00	7.07 6.98
5b	143-144 [c]	$C_{24}H_{24}N_2O_6$ (436)	66.04 66.26	5.54 5.65	6.42 6.49	**8c**	[g]	$C_{24}H_{30}N_2O_5$ (426)	67.58 67.34	7.09 7.19	6.57 6.33
5c	150-152 [d]	$C_{25}H_{26}N_2O_7$ (466)	64.36 64.02	5.62 5.64	6.01 5.85	**8d**	[g]	$C_{23}H_{26}N_2O_5$ (410)	67.29 67.00	6.38 6.11	6.83 6.67
5d	208-210 [c]	$C_{24}H_{22}N_2O_7$ (450)	63.99 63.69	4.92 4.91	6.22 6.18	**9a**	231-232 [c]	$C_{21}H_{16}N_2O_4$ (360)	69.99 69.76	4.48 4.63	7.77 7.55
6a	220-230 [e]	$C_{22}H_{22}N_2O_3$ (362)	72.90 72.60	6.12 6.21	7.73 7.68	**9b**	250-251 [c]	$C_{22}H_{18}N_2O_5$ (390)	67.68 67.49	4.71 4.52	7.17 7.37
6d	230-240 [c]	$C_{23}H_{22}N_2O_5$ (406)	67.97 67.78	5.45 5.23	6.89 6.60	**9c**	[h]	$C_{23}H_{20}N_2O_6$ (420)	– –	– –	– –

[a] From toluene. [b] Softening from 175°. [c] From methylene chloride-*iso*-propyl ether. [d] From methylene chloride. [e] From acetone-benzene. [f] From ethyl acetate-benzene. [g] Mixture of two diastereoisomers obtained as sticky products. [h] Obtained only in impure form.

General Procedure for the Reaction of Ylide **1** with 2-Nitrobenzaldehydes **2**: Synthesis of Ethyl 3-Benzoylamino-2-oxo-6-(2-nitrostyryl)-2*H*-pyran-5-carboxylates **3a-d**.

A suspension of ylide **1** (10 mmoles) and aldehyde (11 mmoles) was stirred and refluxed in toluene (150 ml) for 8-36 hours until the starting ylide disappeared. After cooling the yellow solid was filtered off yielding pure **3**. After elimination of the solvent, the mother liquor was recrystallized from methylene chloride/*iso*-propyl ether yielding a further amount of **3**. Total yields were: for **3a**, 95%; **3b**, 95%; **3c**, 91% (76% of the pure *E* stereoisomer crystallized directly from the reaction mixture and 15% of *E* and *Z* stereoisomers from the mother liquor in 1:3 ratio); **3d**, 93%. Analytical and spectroscopic data are given in Tables 1 and 2.

General Procedure for the Reduction of Ethyl 3-Benzoylamino-2-oxo-6-(2-nitrostyryl)-2*H*-pyran-5-carboxylates **3**.

Method A.

Pyrone **3** (2.3 mmoles) was suspended in anhydrous THF (70 ml) and reduced at atmospheric pressure and room temperature with hydrogen over 10% Pd/C (400 mg, 0.35 mmole). The solution became red and then, when the hydrogen uptake was completed (3-7 hours), turned yellow. The hydrogen was eliminated *in vacuo* and stirring was continued for 2 hours. The reaction mixture was quickly worked up because of the easy isomerization of acid **5** in solution. The catalyst was filtered and washed with methylene chloride (2 x 20 ml). After solvent evaporation the crude mixture was recrystallized yielding pure **5**. Total yields were: for **5a**, 54%; **5b**, 53%; **5c**, 53%; **5d**, 32%. By column chromatography with ethyl acetate/toluene (1:4) of the mother liquor benzazocine **9** and tetrahydroquinoline **6** were isolated after crystallization. Total yields were: for **6a**, 7%; **6d**, 30%; **9a**, 8%; **9b**, 9%; **9c**, 7%. Analytical and spectroscopic data are given in Tables 1 and 2.

Method B.

Compound **3** (2.3 mmoles) was suspended in anhydrous THF (70 ml) and reduced with hydrogen over 10% Pd/C (400 mg, 0.35 mmole) at 90° and 40 atmospheres in an autoclave for 8 hours and then left overnight at room temperature. The catalyst was filtered off and washed with methylene chloride (2 x 10 ml). The solvent was evaporated and the crude mixture chromatographed with ethyl acetate/toluene (1:4). From the first fraction, after crystallization, pure compound **7** was isolated (**7a**, 12%; **7b**, 29%; **7d**, 35%); the second fraction contained a mixture of two diastereoisomers **8** (**8a**, 71%; **8b**, 53%; **8c**, 46%; **8d**, 23%) which were obtained as sticky products. Every attempt to separate the two isomers failed. Analytical and spectroscopic data are given in Tables 1 and 2.

Method C.

In the dark, pyrone **3** (2.3 mmoles) was hydrogenated as described in Method A but the reduction was stopped when 3 equivalents of hydrogen were consumed. The red solution was worked up readily because of the unstability of amine **4** in solution and in the light. The catalyst was filtered and washed with a mixture of THF/methylene chloride (1:1) (3 x 10 ml). The solution was evaporated to a volume of 15 ml; red crystals precipitated and were filtered yielding amine **4** which could not be purified further owing to its instability. Total yields were: for compounds **4c**, 72%; **4d**, 70%. Spectroscopic data are given in Table 1.

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