Reaction of Ketenes with *N,N*-Disubstituted α-Aminomethyleneketones. XVIII. Synthesis of *N,N*-Disubstituted 4-Amino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones

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1,4-Cycloaddition of phenylchloroketene to *N,N*-disubstituted 2-aminomethylene-3,4-dihydro-1(2*H*)naphthalenones gave the corresponding adducts, namely *N,N*-disubstituted 4-amino-3-chloro-3,4,5,6-tetrahydro-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones II, in the case of aliphatic *N,N*-disubstitution or aromatic *N*-monosubstitution. Apart from IIf (NR_2 = NMePh), adducts II were unstable and were dehydrochlorinated *in situ* with DBN to give *N,N*-disubstituted 4-amino-5,6-dihydro-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones III in fair overall yields. Compounds III were dehydrogenated with Pd/C in boiling *p*-cymene to afford the title compounds generally in high yields.

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Some years ago we described the polar 1-4 cycloaddition of dichloroketene to *N,N*-disubstituted 2-aminomethylene-3,4-dihydro-1(2*H*)naphthalenones I, which was successful only in the case of hindered aliphatic or aromatic *N*-substitution [NR_2 = $N(CHMe_2)_2$, NMePh, NPh_2] [1].

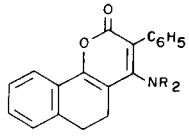
Our recent work on the cycloaddition of *N,N*-disubstituted 2-aminomethylenecyclohexanones to phenylchloroketene, namely a ketene bearing two substituents with different electronegativity [2], prompted us to study the reaction of this ketene with enaminones I.

The reaction of phenylchloroketene (prepared *in situ* from α-chlorophenylacetyl chloride and triethylamine) with Ia-g occurred both in the case of aliphatic *N,N*-disubstitution and aromatic *N*-monosubstitution (Ig did not react) to give cycloadducts IIa-f. These compounds were in general unstable and difficult to obtain pure; isolation (in high yield) was possible only in the case of IIf. This cycloadduct is a mixture of two stereoisomers in the ratio 57:43, as it was shown in nmr spectrum by two singlets at δ 2.72 and 2.89 for CH_3N, and two singlets at δ 4.69 and 5.15 for CH-4. We were unable to resolve this mixture by chromatography on neutral alumina.

The crude cycloadducts IIa-e were therefore dehydrochlorinated directly in benzene solution with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) to afford *N,N*-disubstituted 4-amino-5,6-dihydro-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-

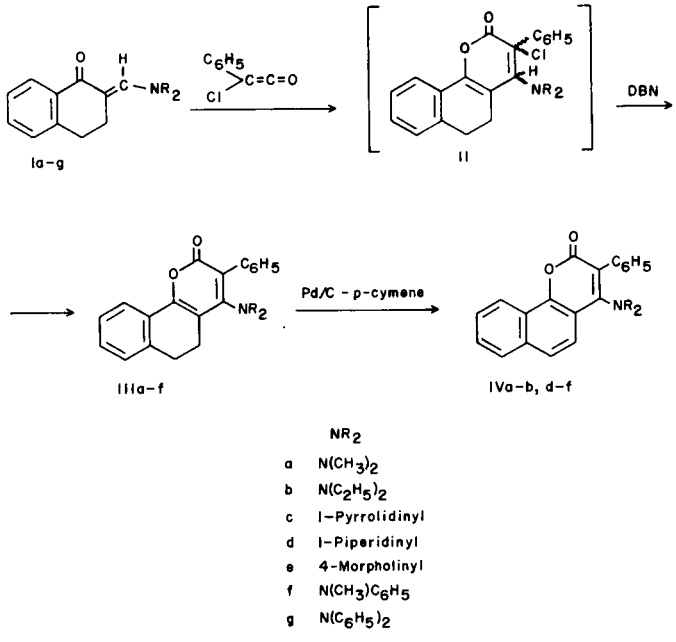
Table I

N,N-Disubstituted 4-Amino-5,6-dihydro-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones IIIa-f



Formula Number	NR_2	Yield %	Mp °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIIa	$N(CH_3)_2$	40	198 [a]	$C_{21}H_{19}NO_2$	79.47	6.03	4.41
					79.30	5.95	4.65
IIIb	$N(C_2H_5)_2$	36	194 [a]	$C_{23}H_{23}NO_2$	79.97	6.71	4.05
					80.21	6.60	4.31
IIIc	1-Pyrrolidinyl	49	200 [b]	$C_{23}H_{21}NO_2$	80.44	6.16	4.08
					80.47	6.18	3.84
IIId	1-Piperidinyl	49	197 [a]	$C_{24}H_{23}NO_2$	80.64	6.49	3.92
					80.81	6.50	3.75
IIIe	4-Morpholinyl	42	217 [a]	$C_{23}H_{21}NO_3$	76.86	5.89	3.90
					77.03	5.95	3.73
IIIf	$N(CH_3)C_6H_5$	80 [c]	216 [b]	$C_{26}H_{21}NO_2$	82.30	5.58	3.69
					82.13	5.58	3.49

[a] From diethyl ether-acetone 2:1. [b] From acetone-chloroform 2:1. [c] Obtained by dehydrochlorination with DBN of pure IIf (see Experimental).



ones IIIa-e (Table I) in fair overall yields. Compound IIIf was obtained in high yield by dehydrochlorination of pure IIf under the above conditions. The structure of 2-pyranones III was proven by their ir and nmr spectral data (Table II).

After unsuccessful trials with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), compounds III were dehydrogenated with palladium on carbon in refluxing *p*-cymene (see [1]) to give, with the exception of IIIc, *N,N*-disubstituted 4-amino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones IVa-b,d-f (Tables III, IV) in good yields. Compoud IIIc did not react or decomposed with a more prolonged reaction time.

In conclusion, phenylchloroketene seems to offer, in comparison with dichloroketene in the cycloaddition to the same enaminones, the advantage of no limitation due to aliphatic *N,N*-disubstitution. This is probably due to a decreased electrophilicity of the carbonyl group in comparison with dichloroketene (compare [1]), and therefore phenylchloroketene appears to be an attractive synthon for the building-up in one step of systems containing the 4-amino-3-phenyl-2-pyranone moiety.

EXPERIMENTAL

The uv spectra were measured in 95% ethanol with a Perkin-Elmer Model 550S spectrophotometer. The ir spectra were taken in chloroform on a Perkin-Elmer Model 398 spectrophotometer; the nmr spectra were recorded in deuteriochloroform on a Perkin-Elmer Model R-100 instrument (60 MHz, TMS as internal standard, J in Hz). Melting points were determined with a Mettler FP1 apparatus.

N,N-Disubstituted 4-Amino-5,6-dihydro-3-phenyl-2*H*-naphtho[1,2-*b*]-pyran-2-ones IIIa-e.

These compounds were prepared from *N,N*-disubstituted 2-aminomethylene-3,4-dihydro-1(2*H*)-naphthalenones Ia-e [1,3] (30 mmoles), α-chlorophenylacetyl chloride and triethylamine in anhydrous benzene solution, followed by DBN treatment of the crude adducts, according to the general procedure already described [2]. Enaminone Ig did not react and was recovered from the reaction mixture before DBN treatment. The crude compounds IIIa-e were purified by chromatography on neutral alumina, using as eluant diethyl ether-acetone 2:1 in the case of IIIa,b,d,e and acetone-chloroform 2:1 in the case of IIIc, followed by recrystallization from the same mixtures (Table I).

3-Chloro-3,4,5,6-tetrahydro-4-methylphenylamino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-one (IIf).

The filtered benzene solution obtained in the reaction of If before DBN treatment was evaporated under reduced pressure and the solid residue was recrystallized from diethyl ether-acetone 2:1, yield, 89%, mp 122°; ir (chloroform): ν max 1768, 1688 cm^{-1}. The nmr spectrum (deuteriochloroform) displayed the presence of two stereoisomers in the ratio 57:43, as it resulted from two singlets at δ 2.72 and 2.89 for CH_3N, and two singlets at δ 4.69 and 5.15 for CH-4. Attempts to resolve the mixture by chromatography on neutral alumina were unsuccessful.

Anal. Calcd. for $C_{26}H_{22}ClNO_2$: C, 75.08; H, 5.33; N, 3.37. Found: C, 75.28; H, 5.28; N, 3.36.

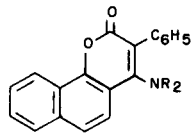
Table II

IR and NMR Spectral Data of Compounds IIIa-f

Compound	IR, cm^{-1} C=O	IR, cm^{-1} C=C	NMR, δ
IIIa	1675	1623 1525	2.48 [s, $(CH_3)_2N$], 2.80 (mc, CH_2-5 + CH_2-6), 7.32 (mc, C_6H_5 + CH-7 + CH-8 + CH-9), 7.87 (mc, CH-10)
IIIb	1678	1622 1518	0.99 (t, J = 7.2, 2 CH_3), 2.80 (mc, 2 CH_2N + CH_2-5 + CH_2-6), 7.36 (mc, C_6H_5 + CH-7 + CH-8 + CH-9), 7.90 (mc, CH-10)
IIIc	1677	1625 1518	1.65 (mc, 2 CH_2 pyr), 2.80 (mc, 2 CH_2N + CH_2-5 + CH_2-6), 7.20 (mc, C_6H_5 + CH-7 + CH-8 + CH-9), 7.75 (mc, CH-10)
IIId	1679	1627 1523	1.47 (mc, 3 CH_2 pip), 2.59 (mc, 2 CH_2N), 2.80 (mc, CH_2-5 + CH_2-6), 7.33 (mc, C_6H_5 + CH-7 + CH-8 + CH-9), 7.8 9 (mc, CH-10)
IIIe	1688	1626 1527	2.74 (mc, 2 CH_2N + CH_2-5 + CH_2-6), 3.61 (mc, 2CH_2O), 7.33 (mc, C_6H_5 + CH-7 + CH-8 + CH-9), 7.90 (mc, CH-10)
IIIf	1693	1625 1528	2.1-2.4 (m, CH_2-5), 2.6-2.9 (m, CH_2-6), 2.76 (s, CH_3N), 6.6-7.5 (m, 2 C_6H_5 + CH-7 + CH-8 + CH-9), 7.90 (mc, CH-10)

Table III

N,N-Disubstituted 4-Amino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones IVa-b,d-f



Formula Number	NR_2	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IVa	$N(CH_3)_2$	87	202	$C_{21}H_{17}NO_2$	79.98	5.43	4.44
					79.86	5.69	4.46
IVb	$N(C_2H_5)_2$	87	197	$C_{23}H_{21}NO_2$	80.44	6.16	4.08
					80.38	6.41	3.94
IVd	1-Piperidinyl	83	209	$C_{24}H_{21}NO_2$	81.10	5.95	3.94
					81.08	6.05	3.89
IVe	4-Morpholinyl	79	231	$C_{23}H_{19}NO_3$	77.29	5.36	3.92
					77.16	5.51	3.77
IVf	$N(CH_3)C_6H_5$	52	218	$C_{26}H_{19}NO_2$	82.74	5.07	3.71
					82.72	5.32	3.66

[a] From acetone.

Table IV

UV, IR and NMR Spectral Data of Compounds IVa-b,d-f

Compound	UV, λ max nm (log ε)	IR, cm^{-1} C=O	C=C	NMR, δ
IVa	217.5 (4.60) 270 sh (4.45) 274.5 (4.48) 298 (4.07) 305.5 (4.06) 347 (4.04)	1695	1635 1554	2.67 [s, $(CH_3)_2N$], 7.38 and 7.66 (2 mc, C_6H_5 + 5 Har), 8.60 (mc, CH-10)
IVb	268.5 (4.41) 276 (4.46) 294 (4.02) 308 (4.09) 349 (4.01)	1690	1635 1548	1.06 (t, J = 7.2, 2 CH_3), 2.99 (q, J = 7.2, 2 CH_2N), 7.42 and 7.68 (2 mc, C_6H_5 + 5 Har), 8.65 (mc, CH-10)
IVd	267.5 (4.40) 275.5 (4.47) 294.5 (3.99) 306 (4.01) 346.5 (3.96)	1695	1635 1552	1.59 (mc, 3 CH_2 pip), 2.81 (mc, 2 CH_2N), 7.39 and 7.68 (2 mc, C_6H_5 + 5 Har), 8.60 (mc, CH-10)
IVe	264.5 (4.36) 273.5 (4.39) 303.5 (4.06) 337 sh (4.09) 345.5 (4.10)	1690	1634 1554	2.85 (mc, 2 CH_2N), 3.77 (mc, 2 CH_2O), 7.40 and 7.69 (2 mc, C_6H_5 + 5 Har), 8.59 (mc, CH-10)
IVf	273 (4.39) 278.5 (4.40) 315 (4.09) 323.5 (4.11) 363 (4.07)	1706	1635 1557	2.90 (s, CH_3N), 6.6-7.9 (m, 2 C_6H_5 + 5 Har), 8.63 (mc, CH-10)

5,6-Dihydro-4-methylphenylamino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-one (IIIf).

A solution of IIf (6.24 g, 15 mmoles) and DBN (2.48 g, 20 mmoles) in anhydrous benzene (50 ml) was refluxed for 1 hour. The crude residue obtained following a described procedure [4] was purified by chromatography on neutral alumina, using acetone - chloroform 2:1 as eluant, followed by recrystallization from the same mixture (Table I).

N,N-Disubstituted 4-Amino-3-phenyl-2*H*-naphtho[1,2-*b*]pyran-2-ones IVa-b,d-f.

A mixture of IIIa-f (2 g) and 10% palladium on carbon (1 g) in *p*-cymene (50 ml) was refluxed with stirring for 3 hours (IIIa-e) or 6 hours (IIIf). After cooling, the mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was purified by chromatography on neutral alumina (acetone), followed by recrystallization from the same solvent (Table III). Compound IIIc was unaffected by 3 hours treatment, whereas a more prolonged reaction time (6 hours) gave only intractable decomposition products.

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REFERENCES AND NOTES

[1] P. Schenone, F. Evangelisti, G. Bignardi and A. Bargagna, *Ann. Chim. (Rome)*, **64**, 613 (1974).

[2] A. Bargagna, P. Schenone and M. Longobardi, *J. Heterocyclic Chem.*, **22**, 1471 (1985), and references cited therein.

[3] P. Schenone, L. Mosti, G. Bignardi and A. Tasca, *Ann. Chim. (Rome)*, **64**, 603 (1974).

[4] L. Mosti, G. Bignardi, F. Evangelisti and P. Schenone, *J. Heterocyclic Chem.*, **13**, 1201 (1976).