Reaction of 2-Dimethylaminomethylene-1,3-diones with Dinucleophiles. V. Synthesis of 5-Acyl-1,2-dihydro-2-oxo-3-pyridinecarbonitriles and 1,2,5,6,7,8-Hexahydro-2,5-dioxo-3-quinolinecarboxamides

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The reaction of open-chain *sym*-2-dimethylaminomethylene-1,3-diones Ia-d with sodium cyanoacetamide gave, generally in good yields, 6-substituted 5-acyl-1,2-dihydro-2-oxo-3-pyridinecarbonitriles IIa-d, whereas cyclohexane *sym*-2-dimethylaminomethylene-1,3-diones Ie-h afforded in general a mixture of 1,2,5,6,7,8-hexahydro-2,5-dioxo-3-quinolinecarbonitriles and 5,6,7,8-tetrahydro-2,5-dioxo-2*H*-1-benzopyran-3-carboxamides, the latter being isolated in two cases. The reaction of Ie-h with cyanoacetamide in refluxing anhydrous ethanol gave 1,2,5,6,7,8-hexahydro-2,5-dioxo-3-quinolinecarboxamides IIIe-h in excellent yields, whereas Ia-d did not react with the exception of Ia which afforded in good yield 3-pyridinecarboxamide IIIa. Other 3-pyridinecarboxamides were obtained by partial hydrolysis of nitriles IIb,d. 3-Pyridine and 3-quinoline carboxamides were hydrolyzed in satisfactory yields with hydrochloric acid to the corresponding carboxylic acids, which were decarboxylated in good yields to 5-acyl-2(1*H*)-pyridinones and 7,8-dihydro-2,5(1*H*,6*H*)-quinolinediones, respectively, by reflux in quinoline containing a catalytic amount of copper powder.

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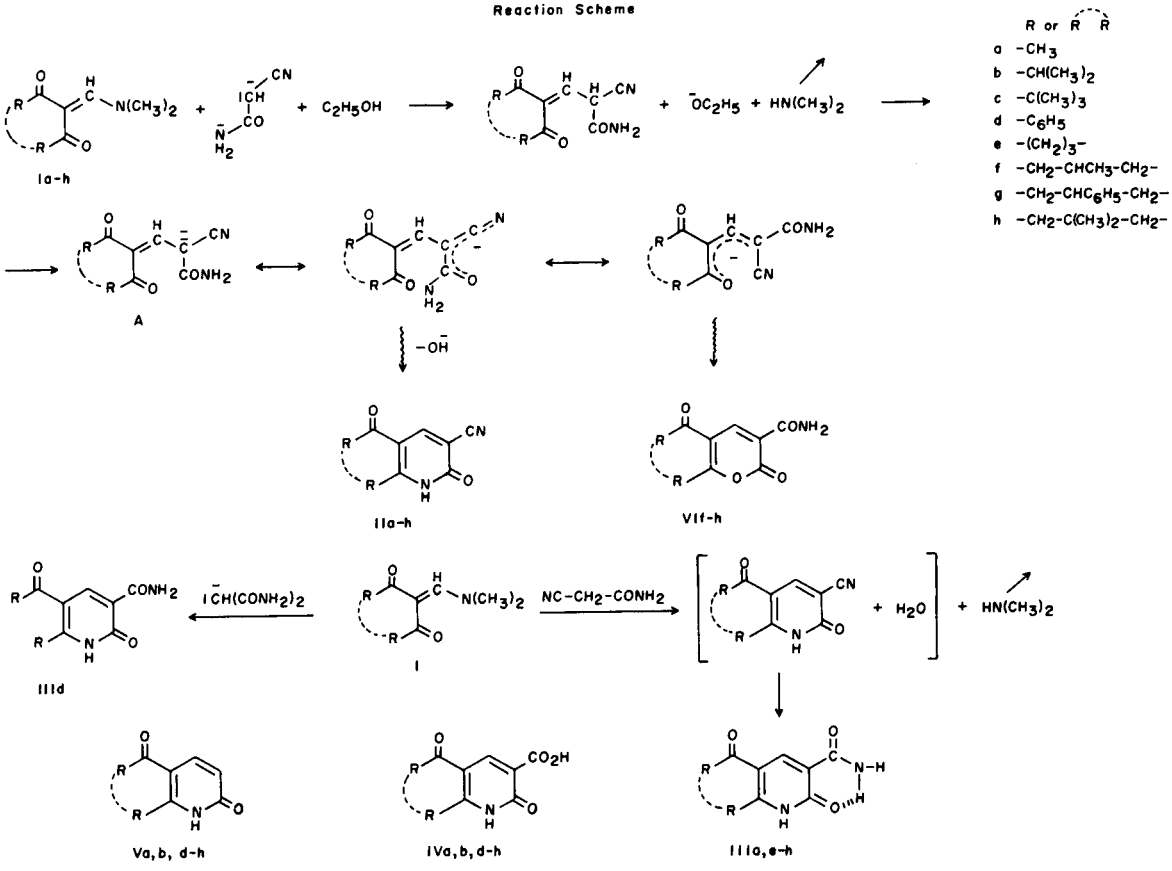
In the preceding papers of the series [1-4] we reported the facile reaction of open-chain and cyclic *sym*-2-dimethylaminomethylene-1,3-diones I with *N-N*, *N-O* and *N*-C-*N* dinucleophiles to give 1,5-disubstituted 4-acylpyrazoles, 5-substituted 4-acylisoxazoles and 5-acylpyrimidines, respectively.

We wish to report now the reaction of I with cyanoacetamide, namely a 1-3 dinucleophile with *C*-C-*N* structure, as



an useful method to obtain 5-acyl-1,2-dihydro-2-oxo-3-pyridinecarbonitriles IIa-d and 1,2,5,6,7,8-hexahydro-2,5-dioxo-3-quinolinecarboxamides IIIe-h.

Recently, compounds like II became important as cardiotonic agents [5,7], and a survey of the literature revealed that only few 6-substituted 5-acyl-1,2-dihydro-2-oxo-3-pyridinecarbonitriles have been prepared in low yield by reaction of the corresponding I (prepared *in situ*) with sodium cyanoacetamide [6]. Among other open-chain synthons, once more Claisen's 3-ethoxymethylene-2,4-pentanedione [19] was the sole partner employed in the reaction with cyanoacetamide to give 2-pyridone IIa [8,9], whereas in the case of 1,2,5,6,7,8-hexahydro-2,5-dioxo-3-quinolinecarbonitriles the synthons employed were 2-formyl-1,3-cyclohexanediones [10].

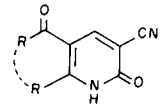
The reaction of I with cyanoacetamide was carried out in two different ways. In the first, a solution of sodium cyanoacetamide in anhydrous ethanol reacted at room temperature with open-chain synthons Ia-d and cyclohexane synthon Ie to afford nitriles IIa-e (Tables I and II) in high or acceptable yields, with the exception of IIc which was obtained in low yield owing to the steric hindrance of Ic. In the case of 2-dimethylaminomethylene-1,3-cyclohexanediones If-h, the reaction was complicated by the formation of tetrahydrocoumarin 3-carboxamides VIf-h, which were difficult to separate from nitriles IIf-h. The yields of nitriles were therefore poor; on the other hand, the isolation of VI was possible in the case of VIf,h, the presence of VIg being inferred only from the ir spectrum of the mixture.

When l were reacted with cyanoacetamide simply by refluxing for a long time a solution of both reagents in anhydrous ethanol, a different result was achieved. Open-chain synthons Ib-d did not react and were recovered from the reaction mixture, whereas Ia and cyclohexane synthons Ie-h gave in excellent yields carboxamides IIIa,e-h (Tables III and IV) instead of the expected nitriles. Carboxamides IIIb,d (also IIIa,e) were obtained by sulfuric acid hydrolysis of the corresponding nitriles II; this hydrolysis was not attempted with nitrile IIc. Carboxamide IIId was also obtained in moderate yield by reaction of Id with sodium malonodiamide in anhydrous ethanol, namely in nearly the same conditions of the reaction of I with sodium cyanoacetamide.

Nitriles II and carboxamides III showed nmr and ir spectral data (Tables II and IV) in agreement with the proposed structures (in particular, see reference [11] for the ir assignments). Carboxamides III seem to form an intramolecular hydrogen bond between 3-amide and 2-carbonyl groups, as can be seen from the two nmr signals for the amide protons at δ 6.9-7.5, 7.7-9.0 for IIIa,b,d and δ 7.7,

Table I

6-Substituted 5-Acyl-1,2-dihydro-2-oxo-3-pyridinecarbonitriles IIa-d and 1,2,5,6,7,8-Hexahydro-2,5-dioxo-3-quinolinecarbonitriles IIe-h



Formula Number	R or R---R	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IIa	-CH_3	91	237 [b]	$C_9H_8N_2O_2$	61.36	4.58	15.90
					61.17	4.55	16.11
IIb	-$CH(CH_3)_2$	90	215	$C_{13}H_{16}N_2O_2$	67.22	6.94	12.06
					67.05	6.73	11.94
IIc	-$C(CH_3)_3$	21	222	$C_{15}H_{20}N_2O_2$	69.20	7.74	10.76
					69.48	7.78	10.79
IId	-C_6H_5	80	284	$C_{19}H_{12}N_2O_2$	75.99	4.03	9.33
					76.10	4.04	9.48
IIe	-$(CH_2)_3$-	48	311 dec	$C_{10}H_8N_2O_2$	63.82	4.28	14.89
					63.76	4.36	14.79
IIf	-CH_2-$CHCH_3$-CH_2-	12	285	$C_{11}H_{10}N_2O_2$	65.34	4.98	13.85
					65.59	4.91	13.73
IIg	-CH_2-CHC_6H_5-CH_2-	18	306 dec [c]	$C_{16}H_{12}N_2O_2$	72.72	4.58	10.60
					72.48	4.66	10.53
IIh	-CH_2-$C(CH_3)_2$-CH_2-	14	298 dec [d]	$C_{12}H_{12}N_2O_2$	66.65	5.59	12.95
					66.41	5.67	12.74

[a] From 95% ethanol. [b] Reference [9], mp 231°, 69% yield; reference [16], mp 232°, 48% yield; reference [6], mp 227-230°, 28% yield. This compound has also been prepared by Sen-Gupta procedure [8] in 84% yield (see Experimental). [c] Reference [15], mp 280-284°. [d] Reference [15], mp 310°.

Table II

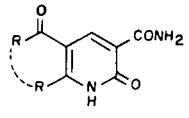
UV, IR and NMR Spectral Data of Compounds IIa-h

Compound	UV, λ max nm (log ε)	IR, cm^{-1}	NMR, δ
IIa	212 (4.21), 276.5 (4.13), 329 (3.98)	3200-2400, 2228, 1693, 1663	2.47 (s, CH_3-6), 2.57 (s, CH_3CO), 8.68 (s, CH-4), ~12.5 (very broad s, NH, disappears with deuterium oxide)
IIb	215.5 (4.10), 219.5 sh (4.07), 270.5(3.95), 333 (3.92)	3200-2500, 2227, 1680, 1655	1.06 (d, J = 6.6, $(CH_3)_2C$-6), 1.25 (d, J = 6.6, $(CH_3)_2CCO$), 3.42 (h, J = 6.6, 2 $CHMe_2$), 8.59 (s, CH-4), 12.65 (broad s, NH, disappears with deuterium oxide)
IIc	216 (3.97), 260 sh (3.52), 340 (3.85)	3250-2500, 2235, 1702, 1655	[a]
IId	218 (4.21), 251 (4.17), 290 sh (3.83), 344 (4.04)	3200-2500, 2228, 1653, 1640	7.2-7.8 (m, 2 C_6H_5), 8.34 (s, CH-4), ~12.5 (very broad s, NH, disappears with deuterium oxide)
IIe	213 (3.97), 217 (3.96), 278 (4.03), 329 (3.95), 341 sh (3.86)	3200-2400, 2230, 1685, 1655	1.8-2.3 (m, CH_2-7), 2.50 (near t, J = 6, CH_2-6), 2.90 (near t, J = 6, CH_2-8), 8.47 (s, CH-4), 12.90 (broad s, NH, disappears with deuterium oxide)
IIf	213.5 (3.97), 217 (3.97), 278 (4.02), 328 (3.93), 341 sh (3.83)	3200-2400, 2230, 1682, 1650	1.11 (near s, CH_3-7), 2.41 (mc, CH_2-6 + CH-7), 2.82 (mc, CH_2-8), 8.31 (s, CH-4), 12.85 (broad s, NH, disappears with deuterium oxide)
IIg	208 (4.44), 281 (4.17), 329 (4.14)	3300-2400, 2230, 1680, 1660	2.6-3.8 (m, CH_2-6 + CH_2-8 + CH-7), 7.34 (s, C_6H_5), 8.42 (s, CH-4), 13.12 (broad, s, NH, disappears with deuterium oxide)
IIh	213 (3.84), 217 (3.82), 281 (3.84), 329 (3.795), 341 sh (3.68)	3200-2500, 2225, 1690, 1655	1.05 (s, $(CH_3)_2C$-7), 2.41 (near s, CH_2-6), 2.81 (near s, CH_2-8), 8.37 (s, CH-4), ~12.7 (very broad s, NH, disappears with deuterium oxide)

[a] The product was insufficiently soluble in the common solvents employed for nmr measurement.

Table III

6-Substituted 5-Acyl-1,2-dihydro-2-oxo-3-pyridinecarboxamides IIIa,b,d and 1,2,5,6,7,8-Hexahydro-2,5-dioxo-3-quinolinecarboxamides IIIe-h



Formula Number	R or R---R	Reflux Time (hours)	Yield %	Mp °C	Molecular Formula	Analyses % Calcd./Found C	H	N
IIIa	$-CH_3$	10	75	330 dec [a] [c]	$C_9H_{10}N_2O_3$	55.67	5.19	14.43
						55.44	5.24	14.39
IIIb	$-CH(CH_3)_2$	—	33	258 [b] [d]	$C_{13}H_{18}N_2O_3$	62.38	7.25	11.19
						62.46	7.32	11.42
IIId	$-C_6H_5$	—	76	334 dec [a] [e]	$C_{19}H_{14}N_2O_3$	71.69	4.43	8.80
						71.40	4.46	8.87
IIIe	$-(CH_2)_3-$	144	82	340 dec [a] [f]	$C_{10}H_{10}N_2O_3$	58.25	4.89	13.58
						58.01	4.60	13.67
IIIf	$-CH_2-CHCH_3-CH_2-$	144	87	318 dec [a]	$C_{11}H_{12}N_2O_3$	59.99	5.49	12.72
						60.02	5.60	12.51
IIIg	$-CH_2-CHC_6H_5-CH_2-$	144	81	316 dec [a]	$C_{16}H_{14}N_2O_3$	68.07	5.00	9.92
						68.27	5.00	10.02
IIIh	$-CH_2-C(CH_3)_2-CH_2-$	144	71	340 dec [a] [g]	$C_{12}H_{14}N_2O_3$	61.53	6.02	11.96
						61.42	6.04	12.12

[a] From dimethyl sulfoxide-95% ethanol 1:1. [b] From 95% ethanol. [c] Reference [9], mp 312°, 51% yield; reference [6], mp >320°. This compound has also been prepared in 75% yield by hydrolysis of IIa (see Experimental). [d] Prepared by hydrolysis of IIb (see Experimental). [e] Prepared by hydrolysis of IId and by reaction of malonodiamide with Id in 42% yield (see Experimental). [f] Reference [10] gave mp 189-191°, but the described compound appears to be a tetrahydrocoumarin derivative VI rather than IIIe. This compound has also been obtained by hydrolysis of IIe in 81% yield (see Experimental). [g] Reference [10], mp 290°.

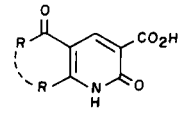
Table IV

UV, IR and NMR Spectral Data of Compounds IIIa,b,d-h

Compound	UV, λ max nm (log ε)	IR, cm^{-1}	NMR, δ
IIIa	215.5 (4.08), 276.5 (4.07), 326 (3.92)	3385, 3200-2300, 1682, 1655 broad	2.31 (s, CH_3-6), 2.44 (s, CH_3CO), 7.45 and 7.68 (2 broad s, 3-$CONH_2$, disappear with deuterium oxide), 8.18 (s, CH-4), 12.23 (broad s, NH-1, disappears with deuterium oxide)
IIIb	270.5 (4.04), 329 (3.98)	3370, 3300-2500, 1685 broad, 1637	1.09 (d, J = 6.6, $(CH_3)_2$C-6), 1.28 (d, J = 6.6, $(CH_3)_2CCO$), 3.1-3.8 (m, 2 $CHMe_2$), 7.72 and 8.88 (2 broad s, 3-$CONH_2$, disappear with deuterium oxide), 8.63 (s, CH-4), 12.47 (broad s, NH-1, disappears with deuterium oxide)
IIId	249 (4.27), 295 sh (3.97), 339 (4.125)	3355, 3300-2400, 1678, 1660, 1638	6.94 and 8.96 (2 broad s, 3-$CONH_2$, disappear with deuterium oxide), 7.1-7.9 (m, 2 C_6H_5), 8.46 (s, CH-4), 12.95 (broad s, NH-1, disappears with deuterium oxide)
IIIe	277 (4.19), 322 (4.05),	3400, 3300-2400, 1685, 1663, 1640	2.04 (mc, CH_2-7), 2.50 (near t, J = 6, CH_2-6), 2.90 (near t, J = 6, CH_2-8), 7.64 (broad s, 3-CONH, disappear with deuterium oxide), 8.67 (near s, CH-4 + 3-CONH which disappears with deuterium oxide), 12.77 (broad s, NH-1, disappears with deuterium oxide)
IIIf	214 (4.02), 277.5 (4.06), 321.5 (3.96)	3350, 3300-2300, 1677, 1655 broad	1.09 (near s, CH_3-7), 2.40 (mc, CH_2-6 + CH-7), 2.80 (mc, CH_2-8), 7.64 (broad s, 3-CONH, disappears with deuterium oxide), 8.67 (mc, CH-4 + 3-CONH which disappears with deuterium oxide), 12.85 (broad s, NH-1, disappears with deuterium oxide)
IIIg	214 (4.22), 279.5 (4.10) 322.5 (4.01)	3600-2400, 1685, 1665 broad	2.5-3.8 (m, CH_2-6 + CH_2-8 + CH-7), 7.41 (s, C_6H_5), 7.76 (broad s, 3-CONH, disappears with deuterium oxide), 8.73 (near s, CH-4 + 3-CONH which disappears with deuterium oxide)
IIIh	214 (4.08), 278.5 (4.07) 323 (3.96)	3350, 3200-2400, 1710, 1678, 1625	1.06 (s, $(CH_3)_2$C-7), 2.42 (near s, CH_2-6), 2.83 (near s, CH_2-8), 7.72 (broad s, 3-CONH, disappears with deuterium oxide), 8.67 (near s, CH-4 + 3-CONH which disappears with deuterium oxide), 12.90 (broad s, NH-1, disappears with deuterium oxide)

Table V

6-Substituted 5-Acyl-1,2-dihydro-2-oxo-3-pyridinecarboxylic Acids IVa,b,d and 1,2,5,6,7,8-Hexahydro-2,5-dioxo-3-quinolinecarboxylic Acids IVe-h



Formula Number	R or R---R	Reflux Time (hours)	Yield %	Mp °C [a]	Molecular Formula	Analyses % Calcd./Found C	H	N
IVa	-CH_3	10	70	225 [b]	$C_9H_9NO_4$	55.39	4.65	7.18
						55.15	4.46	7.19
IVb	-$CH(CH_3)_2$	48	40	185	$C_{13}H_{17}NO_4$	62.14	6.82	5.57
						61.98	6.74	5.42
IVd	-C_6H_5	48	50	273 [c]	$C_{19}H_{13}NO_4$	71.47	4.10	4.39
						71.65	4.01	4.58
IVe	-$(CH_2)_3$-	10	89	298	$C_{10}H_9NO_4$	57.97	4.38	6.76
						57.81	4.12	6.43
IVf	-CH_2-$CHCH_3$-CH_2-	20	92	267 [d]	$C_{11}H_{11}NO_4$	59.73	5.01	6.33
						59.75	4.88	6.13
IVg	-CH_2-CHC_6H_5-CH_2-	20	74	302	$C_{16}H_{13}NO_4$	67.84	4.63	4.94
						67.67	4.56	5.20
IVh	-CH_2-$C(CH_3)_2$-CH_2-	20	89	299	$C_{12}H_{13}NO_4$	61.27	5.57	5.95
						61.54	5.44	5.97

[a] From 95% ethanol. [b] Reference [6], mp 241-243°, yield 43%. This compound was also obtained in 60% yield by refluxing a solution of IIa (1.76 g, 10 mmoles) in 6*N* hydrochloric acid (60 ml) for 8 hours; the precipitate was purified as described in the general procedure (see Experimental). [c] This compound was also obtained in 68% yield by refluxing a solution of IId (3.0 g, 10 mmoles) in a mixture of water (5 ml), concentrated sulfuric acid (8 ml) and acetic acid (20 ml) for 48 hours. The solution was evaporated and the residue was treated with water (30 ml) to give a solid which was purified as described in the general procedure (see Experimental). [d] This compound crystallized with a molecule of water (elemental analysis), which was eliminated by drying *in vacuo* (20 mm) at 110° for 24 hours.

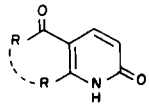
Table VI

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

Compound	UV, λ max nm (log ε)	IR, cm^{-1}	NMR, δ
IVa	215.5 (4.01), 271 (4.00), 327 (3.77)	3500-2300, 1740, 1685, 1625	2.54 (s, CH_3-6), 2.63 (s, CH_3CO), 8.70 (s, CH-4), 13.68 (broad s, NH + CO_2H, disappears with deuterium oxide)
IVb	216.5 (4.03), 265.5 (3.90), 331 (3.71)	3600-2500, 1720, 1685, 1627	1.08 (d, J = 6.6 $(CH_3)_2C$-6), 1.29 (d, J = 6.6, $(CH_3)_2CCO$), 3.0-4.0 (m, 2 $CHMe_2$), 8.61 (near s, CH-4), 13.30 (broad s, NH + CO_2H, disappears with deuterium oxide)
IVd	214 (4.08), 251 (4.08), 305 (3.85), 340 (3.77)	3600-2300, 1737, 1650, 1625	7.40 (mc, 2 C_6H_5), 8.44 (near s, CH-4), 13.50 (broad s, NH + CO_2H, dis appears with deuterium oxide)
IVe	214 (3.95), 270.5 (4.02), 325 (3.84)	3600-2300, 1725, 1665, 1625	2.13 (mc, CH_2-7), 2.55 (near t, J = 6, CH_2-6), 2.97 (near t, J = 6, CH_2-8), 8.55 (s, CH-4), 13.40 (broad s, NH + CO_2H, disappears with deuterium oxide)
IVf	213.5 (3.95), 271 (4.05), 324 (3.89)	3600-2300, 1740, 1670, 1627	1.13 (near s, CH_3-7), 2.46 (mc, CH_2-6 + CH-7), 2.87 (mc, CH_2-8), 8.54 (s, CH-4) ~13 (very broad s, NH + CO_2H, disappears with deuterium oxide)
IVg	215 (4.21), 275 (3.82), 303 sh (3.76), 325 sh (3.59)	3600-2300, 1737, 1672, 1642	2.4-3.9 (m, CH_2-6 + CH_2-8 + CH-7), 7.40 (s, C_6H_5), 8.62 (s, CH-4), ~13 (very broad s, NH + CO_2H, disappears with deuterium oxide)
IVh	214 (4.03), 272.5 (4.04), 324 (3.88	3300-2300, 1745, 1667, 1637	1.09 (s, $(CH_3)_2C$-7), 2.47 (near s, CH_2-6), 2.89 (near s, CH_2-8), 8.58 (s, CH-4), 13.55 (broad s, NH + CO_2H, disappears with deuterium oxide)

Table VII

5-Acyl-2(1*H*)-pyridinones Va,b,d and 7,8-Dihydro-2,5(1*H*,6*H*)-quinolinediones Ve-h



Formula Number	R or R---R	Reflux Time (minutes)	Yield %	Mp °C	Molecular Formula	Analyses % Calcd./Found C	H	N
Va	-CH_3	60	60	204 [a] [d]	$C_6H_5NO_2$	63.56	6.00	9.27
						63.50	6.04	9.20
Vb	-$CH(CH_3)_2$	90	61	157 [b]	$C_{13}2_{17}NO_2$	69.54	8.27	6.76
						69.51	8.12	6.78
Vd	-C_6H_5	120	82	250 [a]	$C_{18}H_{13}NO_2$	78.53	4.76	5.09
						78.45	4.84	5.04
Ve	-$(CH_2)_3$-	75	54	294 [c] [e]	$C_9H_9NO_2$	66.25	5.56	8.58
						66.33	5.66	8.41
Vf	-CH_2-$CHCH_3$-CH_2-	75	52	279 [c]	$C_{10}H_{11}NO_2$	67.78	6.26	7.90
						67.68	6.19	7.90
Vg	-CH_2-CHC_6H_5-CH_2-	90	60	275 [c] [f]	$C_{15}H_{13}NO_2$	75.30	5.48	5.85
						75.10	5.40	5.88
Vh	-CH_2-$C(CH_3)_2$-CH_2-	75	54	289 [c] [g]	$C_{11}H_{13}NO_2$	69.09	6.85	7.32
						68.85	6.84	7.30

[a] From ethyl acetate. [b] From diethyl ether. [c] From 95% ethanol. [d] Reference [6], mp 193-195°, 55% yield; reference [12], mp 196-198°. [e] Reference [13], mp 289-291°. [f] Also obtained in 55% yield by heating IVg (1.41 g, 5 mmoles) at 320-325° (0.4 mm) for 1 hour and collecting the sublimated product. [g] Reference [18], mp 276°; reference [14], mp 290°.

8.7 for IIIe-h (Table IV). This feature was lacking in the nmr spectra of tetrahydrocoumarin 3-carboxamides VIf,h.

A further structural proof for nitriles II and carboxamides III was given by their conversion *via* carboxylic acids IV into compounds V, whose structure was unequivocally proven (see later).

A tentative explanation of the above results is depicted in the reaction scheme, where tetrahydrocoumarins VI could be formed starting from the carbanion intermediate A, which could evolve both to give only nitriles in the case of Ia-e and also tetrahydrocoumarins in the case of If-h. Also in the absence of a strong base such as sodium ethoxide, the methylene group of cyanoacetamide appears to be enough nucleophilic to react with the strong electrophilic

Table VIII

UV, IR and NMR Spectral Data of Compounds Va,b,d-h

Compound	UV, λ max nm (log ε)	IR, cm^{-1}	NMR, δ
Va	280 (4.075), 305 sh (3.81)	3200-2300, 1682, 1640	2.42 (s, CH_3-6), 2.51 (s, CH_3CO), 6.24 (d, J = 9.6, CH-3), 7.95 (d, J = 9.6, CH-4), 12.05 (broad s, NH, disappears with deuterium oxide) (*cf* [12])
Vb	275 (4.05), 305 sh (3.79)	3250-2500, 1677, 1637	1.06 (d, J = 7.2, $(CH_3)_2$C-6), 1.24 (d, J = 7.2, $(CH_3)_2CCO$), 3.40 (h, J = 7.2, 2 $CHMe_2$), 6.28 (d, J = 9.6, CH-3), 7.85 (d, J = 9.6, CH-4), 11.80 (broad s, NH, disappears with deuterium oxide)
Vd	215 (4.15), 243 (4.08), 302 (4.05)	3200-2500, 1655, 1640	6.48 (d, J = 9.6, CH-3), 7.29 (mc, 2 C_6H_5), 7.65 (d, J = 9.6, CH-4), 12.14 (broad s, NH, disappears with deuterium oxide)
Ve	281 (4.09), 303 sh (3.92), 318 sh (3.58)	3200-2400, 1698, 1667	2.04 (mc, CH_2-7), 2.44 (mc, CH_2-6), 2.80 (near t, J = 6, CH_2-8), 6.24 (d, J = 9.6, CH-3), 7.78 (d, J = 9.6, CH-4), 12.10 (broad s, NH, disappears with deuterium oxide) (*cf.* [13])
Vf	282.5 (4.13), 304 sh (3.96), 317 sh (3.65)	3200-2400, 1682, 1665	1.04 (near d, J = 5.6, CH_3-7), 2.3-2.8 (m, CH_2-6 + CH_2-8 + CH-7), 6.23 (d, J = 9.6, CH-3), 7.75 (d, J = 9.6, CH-4), 12.09 (broad s, NH, disappears with deuterium oxide)
Vg	284.5 (4.17), 304 sh (4.01), 318 sh (3.66)	3100-2400, 1668, 1640	2.3-3.7 (m, CH_2-6 + CH_2-8 + CH-7), 6.28 (d, J = 9.6, CH-3), 7.36 (s, C_6H_5), 7.82 (d, J = 9.6, CH-4), 12.28 (broad s, NH, disappears with deuterium oxide)
Vh	283.5 (4.15), 306 sh (3.94), 318 sh (3.62)	3200-2400, 1665, 1645	1.01 (s, $(CH_3)_2$C-7), 2.33 (s, CH_2-6), 2.70 (s, CH_2-8), 6.24 (d, J = 9.6, CH-3), 7.76 (d, J = 9.6, CH-4), 12.10 (broad, s, NH, disappears with deuterium oxide)

carbon atom of dimethylaminomethylene group in Ia,e-h; the slowly forming dimethylamine could catalyze the addition to the nitrile group of the water produced in the reaction, with formation of the corresponding carboxamide.

Carboxylic acids IVa,b,d-h (Tables V and VI) were routinely prepared, generally in good yields, by refluxing a solution of amides IIIa,b,d-h in hydrochloric acid. Two compounds (IVa,d) were also prepared in satisfactory yields by sulfuric acid hydrolysis of nitriles IIa,d.

The best way to decarboxylate IV to 5-acyl-2(1*H*)-pyridinones Va,b,d and 7,8-dihydro-2,5(1*H*,6*H*)-quinolinediones Ve-h (Table VII) in moderate to satisfactory yields was to reflux a solution of IV in quinoline containing a catalytic amount of copper powder. Heating *in vacuo* at temperatures higher than 300° or refluxing in concentrated hydrobromic acid gave poorer results.

The structure of compounds V was clearly proven by their nmr spectra (Table VIII), in which were present two doublets centered at δ 6.2-6.5 and 7.6-7.9 (J = 9.6 Hz), due to C-3 and C-4 protons, respectively, in full agreement with the values found for compounds Va,e,g already known but prepared by other routes [12-14].

In conclusion, this seems to be another useful application of *sym*-2-dimethylaminomethylene-1,3-diones as synthons for building-up of functionalized heterocyclic systems.

EXPERIMENTAL

The uv spectra were measured in 95% ethanol with a Hitachi-Perkin-Elmer Model EPS-3T spectrophotometer. The ir spectra were taken in potassium bromide on a Perkin-Elmer Model 398 spectrophotometer; the nmr spectra were recorded in DMSO-d_6 on a Perkin-Elmer Model R-100 instrument (60 MHz, TMS as internal standard, J in Hz). Melting points were determined with a Fisher-Johns apparatus.

General Procedure for Nitriles IIa-h.

Compounds Ia-h [1] (20 mmoles) were added at room temperature to a solution of sodium cyanoacetamide in anhydrous ethanol, prepared by adding a solution of sodium ethoxide [from sodium (0.48 g, 21 mmoles) and anhydrous ethanol (15 ml)] to cyanoacetamide (1.77 g, 21 mmoles) dissolved in warm anhydrous ethanol (20 ml). The mixture was stirred at room temperature for 24 hours, the precipitate was filtered, washed thoroughly with anhydrous diethyl ether and dissolved in water (30-40 ml). The aqueous solution was acidified with 6*N* hydrochloric acid at *p*H ~ 1, the precipitate was filtered, washed with water, dried and recrystallized from a suitable solvent (Table I).

In the case of If,g,h, anhydrous diethyl ether (50 ml) was added to the clear solution obtained after 24 hours stirring; the precipitate was filtered, washed with anhydrous diethyl ether and treated as described above. The final product was a mixture of nitriles IIf,g,h and tetrahydrocoumarins VIf,g,h (ir spectra), from which the latter could be obtained pure in the case of If,h by repeated recrystallizations from the proper solvent.

5,6,7,8-Tetrahydro-7-methyl-2,5-dioxo-2*H*-1-benzopyran-3-carboxamide VIf.

This compound had mp 228° from ethyl acetate, yield ~2%; uv: λ max nm (log ε) 211.5 (3.85), 269 (3.86), 310 (3.81); ir (potassium bromide): ν max 3420, 3160, 1737, 1700, 1690, 1555 cm^{-1}; nmr (DMSO-d_6): δ 1.15 (near s, CH_3-7), 2.48 (mc, CH_2-6 + CH-7), 2.87 (mc, CH_2-8), 7.84 (near s, $CONH_2$, disappears with deuterium oxide), 8.50 (s, CH-4) (*cf.* reference [17] for similar VIe).

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.68; H, 5.14; N, 6.60.

5,6,7,8-Tetrahydro-7,7-dimethyl-2,5-dioxo-2*H*-1-benzopyran-3-carboxamide VIh.

This compound had mp 215° from ethyl acetate (reference [10] mp 207-209° dec), yield 40%; uv: λ max nm (log ε) 205 (4.17), 262 (4.02), 321 (3.97); ir (potassium bromide): ν max 3410, 3180, 1745, 1693, 1555 cm^{-1}; nmr (DMSO-d_6): δ 1.06 (s, $(CH_3)_2$C-7), 2.46 (near s, CH_2-6), 2.86 (near s, CH_2-8), 7.81 (near s, $CONH_2$, disappears with deuterium oxide), 8.47 (s,

CH-4) (*cf.* reference [10] and also [17] for similar VIe).

Anal. Calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.10; H, 5.65; N, 6.18.

Concentration to a small volume of the diethyl ether-ethanol solutions gave a precipitate, from which nitriles IIf,g,h could be obtained by dissolution in water followed by acidification as described above.

Nitrile IIa from 3-Ethoxymethylene-2,4-pentanedione and Sodium Cyanoacetamide (*cf.* [8]).

3-Ethoxymethylene-2,4-pentanedione [19] (3.12 g, 20 mmoles) was reacted with sodium cyanoacetamide using the same general procedure described for nitriles IIa-h, yield, 2.97 g (84%); mp, ir and nmr spectral data were identical with those of compound prepared from Ia.

General Procedure for Amides IIIa,e-h.

A solution of Ia,e-h (20 mmoles) and cyanoacetamide (1.85 g, 22 mmoles) in anhydrous ethanol (150 ml) was refluxed for a certain time (Table III). After cooling, the precipitate was filtered and recrystallized from dimethyl sulfoxide-95% ethanol 1:1. Amide IIIe must be dried *in vacuo* (20 mm) at 120° for 96 hours in order to eliminate a molecule of crystallization water (elemental analysis).

Amides IIIa,b,d,e by Partial Hydrolysis of Nitriles IIa,b,d,e.

A solution of nitriles IIa,b,d,e (10 mmoles) in concentrated sulfuric acid (10 ml) containing water (0.5 ml) was heated at 50° for 2 hours, then poured into cold water (100 ml). The precipitate was filtered, washed with water and recrystallized from a suitable solvent (Table III).

Amide IIId from Id and Sodium Malonodiamide.

A solution of Id (2.79 g, 11 mmoles) in anhydrous ethanol (30 ml) was added dropwise with stirring to a warm solution of sodium malonodiamide in anhydrous ethanol, prepared by dissolving malonodiamide (1.12 g, 11 mmoles) in anhydrous ethanol (80 ml) previously treated with sodium (0.25 g, 11 mmoles). The solution was stirred for 3 hours at 50° and for 2 hours at room temperature, then evaporated under reduced pressure and the residue was dissolved in water (50 ml). The aqueous solution was extracted with diethyl ether and acidified with 6*N* hydrochloric acid ($pH \sim 1$); the precipitate was recrystallized from 95% ethanol and dried at 80° (20 mm) for 24 hours, yield, 1.33 g (42%); mp, ir and nmr spectral data were identical with those of the product prepared by partial hydrolysis of IId.

General Procedure for Carboxylic Acids IVa,b,d-h.

A solution of amides IIIa,b,d-h (10 mmoles) in concentrated (6*N* in the case of IIIa) hydrochloric acid (50-100 ml) was refluxed for a certain time (Table V). After cooling, the precipitate was filtered, washed with water and recrystallized from 95% ethanol.

General Procedure for 5-Acyl-2(1*H*)-pyridinones Va,b,d and 7,8-Dihydro-2,5(1*H*,6*H*)-quinolinediones Ve-h.

A solution of IVa,b,d-h (10 mmoles) in quinoline (14 ml) containing copper powder (0.16 g) was refluxed for a certain time (Table VII). The mixture was filtered hot, the liquid was cooled and chloroform (50-60 ml) was added. In the case of compounds Ve,f,h, the added chloroform caused the immediate precipitation of the product, which was filtered and recrystallized. In the case of Va,b,d,g no precipitate was formed, therefore the solution was extracted two times with 6*N* hydrochloric acid, washed with water and dried (magnesium sulfate). The solid residue obtained after evaporation of chloroform under reduced pressure was recrystallized from a suitable solvent.

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