tert-Amino effect in heterocyclic chemistry. Synthesis of hydrogenated spiro derivatives of quinolines*

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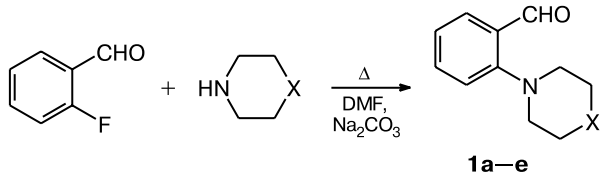
A new method was developed for the one-step synthesis of spiro derivatives of fused quinolines by the reactions of *ortho*-amino derivatives of benzaldehyde with Meldrum's acid, cyclohexane-1,3-dione, or *N,N´*-disubstituted barbituric acids.

Key words: *tert*-amino effect, cyclization, nitrogen-containing heterocycles, spiro derivatives, quinoline.

The term "*tert*-amino effect" was proposed by Meth-Cohn and Suschitzky[1] to generalize cyclization reactions of certain derivatives of *ortho*-substituted *N,N*-dialkylanilines.[2] Cyclizations occurring at the α-carbon atom in the dialkylamino group were described for compounds with an unsaturated *ortho*-substituent including at least one heteroatom (nitroso, nitro, azo, azomethino, imino, or carbonyl groups).[3—9] It was found that *N,N*-dialkylanilines containing vinyl substituents in the *ortho* position also undergo cyclization.[10] These reactions provide an original way of forming C—C bonds with the practically nonactivated NCH_2 group.[11,12]

The aim of the present study was to develop a method for the synthesis of spiro derivatives of heterocycles based on the reactions proceeding by the mechanism of the "*tert*-amino effect". Earlier, we have proposed[13] to use the strategy of the "*tert*-amino effect" for the synthesis of spiro compounds starting from *o*-aminobenzaldehyde and cyclic CH-active compounds, *viz.*, cyclic β-diketo compounds, such as cyclohexane-1,3-dione, Meldrum's acid, and barbituric acid derivatives.

Scheme 1

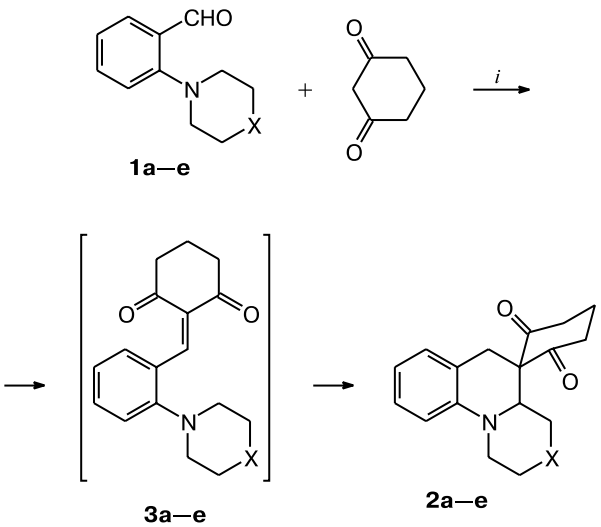


X = O (**a**); NMe (**b**); $(CH_2)_n$ (**c—e**), *n* = 1 (**c**), 2 (**d**), 0 (**e**)

The starting aminobenzaldehydes **1a—e** were prepared in 60—80% yields by the replacement of the fluorine atom in 2-fluorobenzaldehyde with cyclic amines as nucleophiles (Scheme 1).

Knoevenagel condensation of 2-dialkylaminobenzaldehydes **1a—e** with cyclohexanedione (refluxing in toluene for 15 h) afforded individual compounds **2a—e** (Scheme 2).

Scheme 2



i. Toluene, Δ.

The mass spectra of the reaction products (Table 1) have a peak corresponding to the calculated weight of

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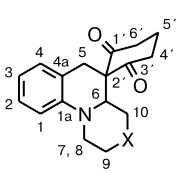
Table 1. Physicochemical characteristics of fused quinolines **2**, **4**, **6**, and **7a—e**

Compound	Yield (%)	M.p. /°C	Found / Calculated N (%)	Molecular formula	IR (KBr), ν/cm^{-1}		MS, *m/z* (I_{rel} (%))
					CH	C=O	
1,2,4,4a,5,6-Hexahydrospiro[[1,4]oxazino[4,3-*a*]-quinoline-5,2′-cyclohexane]-1′,3′-dione (**2a**)	73	100	5.00 4.91	$C_{17}H_{19}NO_3$	3010, 2910	1740, 1725	285 (90)
2,3,4,4a,5,6-Hexahydro-6*H*-spiro[benzo[*c*]quinolizine-5,2′-cyclohexane]-1′,3′-dione (**2c**)	66	150	5.08 4.94	$C_{18}H_{21}NO_2$	3010, 2915	1735, 1725	283 (85)
5,6,6a,7,8,9,10,11-Octahydro-5*H*-spiro[azepino[1,2-*a*]quinoline-6,2′-cyclohexane]-1′,3′-dione (**2d**)	73	149—150	4.70 4.71	$C_{19}H_{23}NO_2$	3010, 2910	1740, 1725	297 (95)
1,2,3,3a,4,5-Hexahydrospiro[pyrrolo[1,2-*a*]-quinoline-4,2′-cyclohexane]-1′,3′-dione (**2e**)	60	100—102	5.26 5.20	$C_{17}H_{19}NO_2$	3000, 2915	1740, 1725	175 (96)
2,2-Dimethyl-1′,2′,4′,4a′,5′,6′-hexahydrospiro-[[1,3]dioxane-5,5′-[1,4]oxazino[4,3-*a*]quinoline]–4,6-dione (**4a**)	36	130	4.60 4.41	$C_{17}H_{19}NO_5$	3000, 2915	1740, 1725	317 (64)
2,2,3′-Trimethyl-2′,3′,4′,4a′-tetrahydro-6*H*-spiro[[1,3]dioxane-5,5′-pyrazino[1,2-*a*]quinoline]–4,6-dione (**4b**)	32	170	8.09 8.48	$C_{18}H_{22}N_2O_4$	3000, 2940	1740, 1725	330 (100)
2′,2′-Dimethyl-2,3,4,4a,5,6-hexahydro-6*H*-spiro[benzo[*c*]quinolizine-5,5′-[1,3]dioxane]-4′,6′-dione (**4c**)	68	150	4.82 4.44	$C_{18}H_{21}NO_4$	3010, 2915	1735, 1725	315 (95)
2′,2′-Dimethyl-5,6,6a,7,8,9,10,11-octahydro-5*H*-spiro[azepino[1,2-*a*]quinoline-6,5′-[1,3]dioxane]-4′,6′-dione (**4d**)	53	170	4.40 4.25	$C_{19}H_{23}NO_4$	3000, 2940	1740, 1725	329 (100)
2,2-Dimethyl-1′,2′,3′,3a′,4′,5′-hexahydrospiro-[[1,3]dioxane-5,4′-pyrrolo[1,2-*a*]quinoline]-4,6-dione (**4e**)	56	139—141	5.12 4.65	$C_{17}H_{19}NO_4$	2975, 2940	1780, 1730	301 (81)
1′,3′-Dimethyl-1,2,4,4a,5,6-hexahydrospiro-[[1,4]oxazino[3,4-*a*]quinoline-5,5′-pyrimidine]-2′,4′,6′-trione (**6a**)	36	130	4.60 4.41	$C_{17}H_{19}NO_5$	3000, 2915	1740, 1725, 1680	317 (64)
1′,3,3′-Trimethyl-2,3,4,4a-tetrahydro-6*H*-spiro[pyrazino[1,2-*a*]quinoline-5,5′-pyrimidine]-2′,4′,6′-trione (**6b**)	55	180	16.33 16.37	$C_{18}H_{22}N_4O_3$	3000, 2940	1760, 1700, 1680	342 (100)
1′,3′-Dimethyl-2,3,4,4a,5,6-hexahydro-6*H*-spiro[benzo[*c*]quinolizine-5,5′-pyrimidine]-2′,4′,6′-trione (**6c**)	30	190	12.84 12.84	$C_{18}H_{21}N_3O_3$	3010, 2915	1735, 1725, 1685	327 (100)
1′,3′-Dimethyl-5,6,6a,7,8,9,10,11-octahydro-5*H*-spiro[azepino[1,2-*a*]quinoline-6,5′-pyrimidine]-2′,4′,6′-trione (**6d**)	33	200	12.60 12.31	$C_{19}H_{23}N_3O_3$	3000, 2940	1740, 1725, 1695	341 (100)
1,3-Dimethyl-1′,2′,3′,3a′,4′,5′-hexahydrospiro-[pyrimidine-5,4′-pyrrolo[1,2-*a*]quinoline]-2,4,6-trione (**6e**)	60	160	13.77 13.41	$C_{17}H_{19}N_3O_3$	3020, 2955	1745, 1680, 1660	313 (100)
1′,3′-Diphenyl-1,2,4,4a,5,6-hexahydrospiro-[[1,4]oxazino[3,4-*a*]quinoline-5,5′-pyrimidine]-2′,4′,6′-trione (**7a**)	50	120	9.59 9.27	$C_{27}H_{23}N_3O_4$	3000, 2915	1740, 1725, 1695	453 (100)
3-Methyl-1′,3′-diphenyl-2,3,4,4a-tetrahydro-6*H*-spiro[pyrazino[1,2-*a*]quinoline-5,5′-pyrimidine]-2′,4′,6′-trione (**7b**)	25	150	11.90 12.00	$C_{28}H_{26}N_4O_3$	3060, 3000, 2940	1760, 1700, 1685	466 (100)
1′,3′-Diphenyl-2,3,4,4a,5,6-hexahydro-6*H*-spiro[benzo[*c*]quinolizine-5,5′-pyrimidine]-2′,4′,6′-trione (**7c**)	42	177—180	9.28 9.31	$C_{28}H_{25}N_3O_3$	3090, 3010, 2915	1735, 1725, 1685	451 (100)
1′,3′-Diphenyl-5,6,6a,7,8,9,10,11-octahydro-5*H*-spiro[azepino[1,2-*a*]quinoline-6,5′-pyrimidine]-2′,4′,6′-trione (**7d**)	60	200	9.20 9.03	$C_{29}H_{27}N_3O_3$	3000, 2900, 2750	1740, 1725, 1690	465 (100)
1,3-Diphenyl-1′,2′,3′,3a′,4′,5′-hexahydrospiro-[pyrimidine-5,4′-pyrrolo[1,2-*a*]quinoline]–2,4,6-trione (**7e**)	40	200	9.57 9.60	$C_{27}H_{23}N_3O_3$	3035, 2985, 2920	1750, 1695, 1685	437 (90)

Table 2. ^{1}H NMR spectra of fused quinolines **2**, **4**, **6**, and **7a—e**



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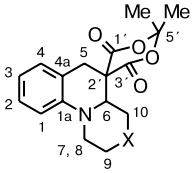

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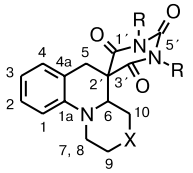


6, **7**

Compound	δ, *J*/Hz									
	H(1)	H(2)	H(3)	H(4)	ArC(5)H	ArC(5)H	NC(6)H	NC(7)H	NC(8)H	Other signals
2a*	6.85 (d, *J* = 8.0)	7.01 (dd, *J* = 8.2, 8.0)	6.66 (dd, *J* = 7.4, 8.2)	7.06 (d, *J* = 7.4)	3.03 (d, *J* = 16.8)	2.69 (d, *J* = 16.8)	4.43 (dm, *J* = 9.6)	3.98 (ddd, *J* = 12.6, 9.1, 1.6)	2.99 (ddd, *J* = 12.6, 8.6, 8.6)	2.00—2.10 (m, 1 H, C(5´)H); 2.40 (dddd, 1 H, C(4´)H, *J* = 15.1, 3.6, 2.1, 4.9); 2.56 (dddd, 1 H, C(6´)H, *J* = 15.0, 3.6, 2.2, 5.6); 3.30—3.40 (m, 6 H, C(9)H, C(6´)H, C(4´)H); 3.57 (ddd, 1 H, C(10)H, *J* = 9.1, 8.4, 2.2)
2c*	6.78 (d, *J* = 8.0)	6.97 (dd, *J* = 8.5, 8.0)	6.62 (dd, *J* = 7.4, 8.5)	7.04 (d, *J* = 7.4)	3.11 (d, *J* = 16.6)	2.66 (d, *J* = 16.6)	4.38 (dm, *J* = 9.9)	3.99 (dm, *J* = 14.2)	3.12 (ddd, *J* = 14.2, 8.6, 2.6)	1.02—1.15 (m, 2 H, 2 C(X)H); 1.25—1.41 (m, 2 H, C(5´)H, C(10)H); 1.48—1.56 (m, 1 H, C(5´)H); 1.65—1.82 (m, 2 H, C(9)H, C(10)H); 2.05—2.15 (m, 1 H, C(5´)H); 2.29 (dm, 1 H, C(4´)H, *J* = 13.7); 2.44 (dm, 1 H, C(6´)H, *J* = 14.6); 3.06 (ddd, 1 H, C(9)H, *J* = 12.0, 5.6, 2.0); 3.30—3.40 (m, 2 H, C(6´)H, C(4´)H)
2d**	6.53 (d, *J* = 8.2)	7.00 (dd, *J* = 8.2, 7.8)	6.67 (dd, *J* = 7.4, 7.4)	7.12 (d, *J* = 7.4)	3.30 (d, *J* = 17.3)	2.92 (d, *J* = 17.3)	4.06 (dd, *J* = 9.1, 5.1)	3.98 (ddd, *J* = 15.2, 5.1, 1.6)	3.03 (ddd, *J* = 14.1, 9.1, 6.4)	1.30—1.70 (m, 8 H, C(10)H, C(9)H, 2 C(X)H_2, C(5´)H_2); 2.05—2.25 (m, 2 H, C(10)H, C(9)H); 2.51 (dddd, 1 H, C(4´)H, *J* = 14.4, 4.4, 2.7, 1.5); 2.62 (dddd, 1 H, C(6´)H, *J* = 14.6, 4.4, 2.8, 1.5); 2.80 (ddd, 1 H, C(6´)H, *J* = 14.1, 14.1, 6.6); 3.06 (ddd, 1 H, C(4´)H, *J* = 15.2, 11.3, 5.6)
2e*	6.40—6.47 (m)	7.00 (dd, *J* = 8.0, 7.3)	6.40—6.47 (m)	6.92 (d, *J* = 7.9)	3.36 (d, *J* = 15.2)	2.85 (d, *J* = 15.2)	3.82 (dd, *J* = 10.1, 5.8)	3.49 (dd, *J* = 7.9, 6.7)	1.50—2.21 (m, 6 H, 3 CH_2); 2.25 (ddd, 1 H, C(4´)H, *J* = 15.2, 5.6, 4.8); 2.54 (ddd, 1 H, C(6´)H, *J* = 15.0, 4.9, 4.3); 2.75—3.10 (m, 3 H, C(6´)H, C(4´)H, NC(8)H)	
4a**	7.01 (d, *J* = 7.4)	7.18 (dd, *J* = 8.0, 7.4)	6.80 (dd, *J* = 8.0, 8.3)	6.89 (d, *J* = 8.3)	3.61 (d, *J* = 16.8)	2.99 (d, *J* = 16.8)	3.92 (dd, *J* = 11.7, 3.2)	3.86 (dm, *J* = 12.2)	3.69 (ddd, *J* = 11.6, 12.2, 2.7)	1.74, 1.77 (both s, 2 H each, Me); 2.70 (ddd, 1 H, C(9)H, *J* = 11.6, 10.2, 3.6); 3.28 (dd, 1 H, C(10)H, *J* = 11.0, 10.6); 3.46 (dd, 1 H, C(9)H, *J* = 10.2, 3.1); 3.77 (ddd, 1 H, C(10)H, *J* = 11.0, 3.1, 2.9)

(*to be continued*)

Table 2 (*continued*)

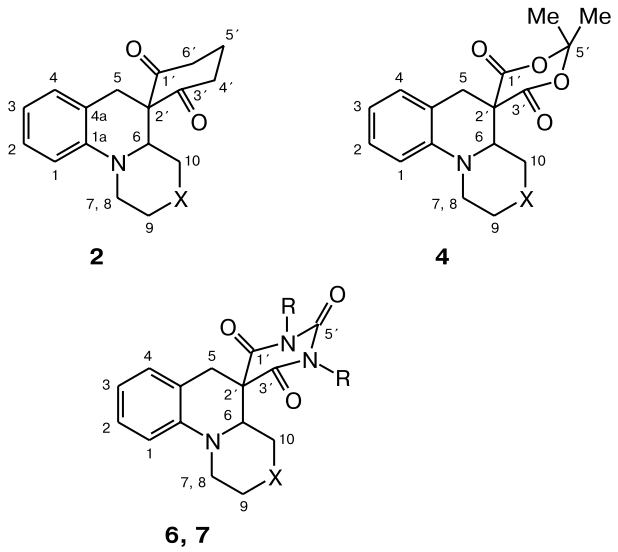
Compound	δ, *J*/Hz									
	H(1)	H(2)	H(3)	H(4)	ArC(5)H	ArC(5)H	NC(6)H	NC(7)H	NC(8)H	Other signals
4b**	7.00 (d, *J* = 7.4)	7.08 (dd, *J* = 8.4, 7.4)	6.70 (dd, *J* = 8.0, 8.4)	6.93 (d, *J* = 8.0)	3.35 (d, *J* = 17.0)	3.29 (d, *J* = 17.0)	3.92 (dd, *J* = 12.4, 4.0)	1.74 (s, 3 H, Me); 1.75 (dd, 1 H, CH, *J* = 10.7, 4.5); 1.77 (s, 3 H, Me); 2.00 (ddd, 1 H, CH, *J* = 11.8, 4.0, 3.1); 2.20 (s, 3 H, NMe); 2.63 (d, 1 H, CH, *J* = 10.8); 2.80 (d, 1 H, CH, *J* = 9.9); 2.82 (dd, 1 H, CH, *J* = 11.2, 3.8); 3.41 (dd, 1 H, CH, *J* = 10.8, 3.1)		
4c*	6.91 (d, *J* = 8.0)	6.66 (ddd, *J* = 8.5, 8.0, 1.2)	7.05 (ddd, *J* = 8.5, 7.8, 1.4)	6.99 (dd, *J* = 7.8, 1.2)	3.30 (d, *J* = 16.9)	3.25 (d, *J* = 16.9)	4.05 (dm, *J* = 12.3)	3.42 (dd, *J* = 12.2, 2.4)	2.78 (ddd, *J* = 12.2, 3.2, 2.9)	1.22 (ddd, 1 H, CH, *J* = 11.7, 5.8, 4.0); 1.38—1.66 (m, 4 H, 4 CH); 1.74—1.78 (m, 1 H, CH); 1.76, 1.77 (both s, 2 H each, Me)
4d**	6.53 (d, *J* = 8.2)	7.00 (dd, *J* = 8.2, 7.8)	6.67 (dd, *J* = 7.4, 7.8)	7.12 (d, *J* = 7.4)	3.25 (d, *J* = 17.3)	3.15 (d, *J* = 17.3)	3.42—3.65 (m)	3.29—3.38 (m)		1.30—1.70 (m, 8 H, C(10)H, C(9)H, 2 C(X)H_2, C(9)H, C(8)H); 1.71, 1.78 (both s, 2 H each, Me); 1.85—2.00 (m, 1 H, C(10)H)
4e*	6.54—6.60, 7.03—7.11 (both m, 2 H each, ArH)				3.33 (s, 2 H)		3.84 (dd, *J* = 8.9, 6.1)	3.58 (dd, *J* = 16.5, 5.8)	3.10 (dd, *J* = 16.5, 8.2)	1.50—1.62 (m, 1 H, CH); 1.72, 1.79 (both s, 2 H each, Me); 1.87—1.98 (m, 2 H, 2 CH); 2.01—2.19 (m, 1 H, CH)
6a*	6.83 (d, *J* = 9.0)	6.68 (dd, *J* = 8.1, 9.0)	7.04 (dd, *J* = 7.9, 8.1)	6.92 (d, *J* = 7.9)	3.33 (d, *J* = 16.8)	3.10 (d, *J* = 16.8)	3.84 (d, *J* = 14.2)	2.93 (ddd, 1 H, CH, *J* = 11.9, 3.6, 3.5); 3.10—3.25 (m, 1 H, CH); 3.13, 3.14, 3.22 (all s, 2 H each, Me); 3.41 (dd, 1 H, CH, *J* = 10.3, 3.2); 3.54 (ddd, 1 H, CH, *J* = 11.4, 2.8, 2.3); 3.63 (dd, 1 H, CH, *J* = 11.0, 2.9); 3.78 (dd, 1 H, CH, *J* = 12.2, 2.3)		
6b**	6.90 (d, *J* = 8.0)	6.67 (ddd, *J* = 7.1, 8.0, 1.4)	7.04 (dd, *J* = 7.1, 7.5)	6.96 (dd, *J* = 7.5, 1.4)	3.24 (d, *J* = 17.0)	3.15 (d, *J* = 17.0)	3.92 (ddd, *J* = 12.7, 2.2, 2.9)	3.48 (dd, *J* = 10.8, 3.1)	2.45—2.55 (m)	1.69 (dd, 1 H, CH, *J* = 11.8, 10.8); 1.98 (ddd, 1 H, CH, *J* = 11.8, 2.9, 3.4); 2.14 (s, 3 H, Me); 2.70 (dm, 1 H, CH, *J* = 9.9); 2.82 (ddd, 1 H, CH, *J* = 12.0, 1.3, 2.5); 3.11, 3.19 (both s, 2 H each, NMe)
6c*	6.83 (d, *J* = 8.1)	6.97—7.05 (m)	6.97—7.05 (m)	6.63 (dd, *J* = 6.3, 0.9)	3.29 (d, *J* = 17.0)	3.00 (d, *J* = 17.0)	3.99 (d, *J* = 13.9)	3.48 (ddd, *J* = 9.2, 7.3, 4.4)	2.81 (ddd, *J* = 9.2, 7.4, 4.4)	1.10—1.17 (m, 1 H, CH); 1.26—1.55 (m, 4 H, 2 CH_2); 1.70 (d, 1 H, CH, *J* = 12.6); 3.12 (d, 6 H, 2 Me, *J* = 5.0)

(*to be continued*)

Table 2 (*continued*)

Compound	δ, *J*/Hz									
	H(1)	H(2)	H(3)	H(4)	ArC(5)H	ArC(5)H	NC(6)H	NC(7)H	NC(8)H	Other signals
6d*	6.59—6.60 (m)	6.94 (dd, *J* = 8.0, 7.6)	6.59—6.60 (m)	7.00 (d, *J* = 6.1)	3.41 (d, *J* = 17.3)	2.71 (d, *J* = 17.3)	3.51—3.65 (m, 2 H)			1.35—1.70 (m, 6 H, 6 CH); 1.85—2.01 (m, 1 H, CH); 2.95—3.10 (m, 2 H, CH); 3.13, 3.16 (both s, 2 H each, Me)
6e*	6.48 (d, *J* = 8.3)	7.00 (dd, *J* = 8.3, 7.9)	6.53 (dd, *J* = 7.3, 7.9)	6.92 (d, *J* = 7.3)	3.38 (d, *J* = 10.0)	3.20 (d, *J* = 10.0)	3.68 (dd, *J* = 6.4, 2.7)	3.41—3.55 (m)		1.41—1.58 (m, 1 H, CH); 1.85—2.11 (m, 3 H, 3 CH); 3.08 (s, 3 H, Me); 3.15—3.20 (m, 1 H, CH); 3.24 (s, 3 H, Me)
7a*	6.91 (d, *J* = 8.0)	6.71 (dd, *J* = 8.0, 7.2)	7.02—7.09 (m, 2 H)		3.45 (d, *J* = 16.9)	3.36 (d, *J* = 16.9)	3.96 (dd, *J* = 11.2, 2.7)	3.09 (ddd, 1 H, CH, *J* = 11.2, 9.8, 3.7); 3.59 (d, 1 H, CH, *J* = 9.7); 3.64 (d, 1 H, CH, *J* = 11.1); 3.74—3.80 (m, 1 H, CH); 3.83—3.90 (m, 2 H, 2 CH); 7.30—7.35 (m, 2 H, Ph); 7.37—7.53 (m, 8 H, Ph);		
7b**	6.99—7.08 (m)	6.68 (ddd, *J* = 7.3, 7.1, 0.7)	6.99—7.08 (m)	6.91 (d, *J* = 8.0)	3.42 (d, *J* = 14.9)	3.30 (d, *J* = 14.9)	3.94 (dm, *J* = 11.6)	3.76 (dd, *J* = 10.1, 3.1)	3.1—3.31 (m)	2.08—2.22 (m, 2 H, CH); 2.28 (s, 3 H, Me); 2.72 (dm, 1 H, CH, *J* = 9.6); 2.81 (dm, 1 H, CH, *J* = 8.6); 7.27—7.32 (m, 2 H, ArH); 7.34—7.53 (m, 8 H, ArH)
7c*	6.85 (d, *J* = 8.2)	7.00 (ddd, *J* = 8.2, 6.5, 1.5)	6.63 (dd, *J* = 7.4, 6.5)	7.07 (dd, *J* = 7.4, 1.5)	3.46 (d, *J* = 17.2)	3.02 (d, *J* = 17.2)	4.26 (d, *J* = 10.8)	4.00 (d, *J* = 12.7)	3.21 (ddd, *J* = 11.8, 11.2, 0.9)	1.13—1.48 (m, 4 H, CH); 1.71—1.99 (m, 2 H, CH_2); 7.23—7.54 (m, 10 H, 2 Ph)
7d*	7.03 (d, *J* = 7.3)	6.48—6.63 (m, 2 H)		6.94 (dd, *J* = 7.5, 1.22)	3.60 (d, *J* = 17.7)	3.00 (d, *J* = 17.7)	4.22—4.41 (m)	3.79—4.00 (m)	1.35—2.20 (m, 8 H, 8 CH); 3.30—3.50 (m, 1 H, CH); 7.12—7.58 (m, 10 H, 2 Ph)	
7e*	6.44 (d, *J* = 8.2)	6.91—7.06 (m)	6.52 (dd, *J* = 7.3, 6.7)	6.91—7.06 (m)	3.56 (d, *J* = 16.7)	3.33 (d, *J* = 16.7)	3.73—3.85 (m)	3.20—3.30 (m)	2.90—3.00 (m)	1.98—2.20 (m, 3 H, 3 CH); 2.23—2.50 (m, 1 H, CH); 7.12—7.24 (m, 2 H, ArH); 7.28—7.55 (m, 8 H, ArH)

* In DMSO-d_6.
** In $CDCl_3$.

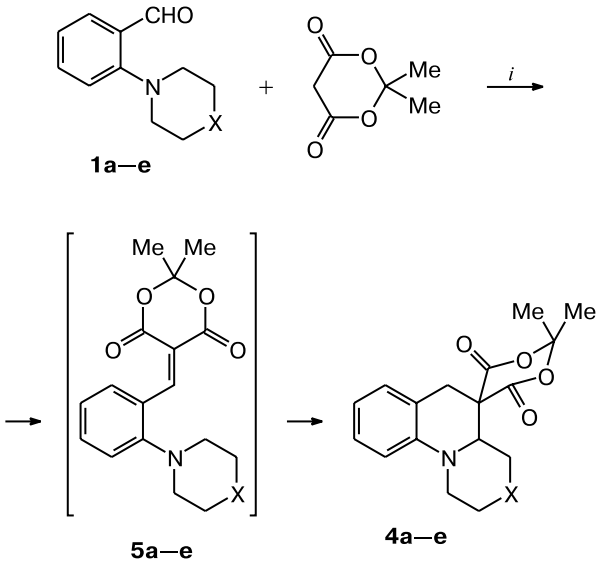


condensation product **2**. For example, the molecular ion of compound **2d** was observed as a doublet with 299 $[M + 2]^+$ and 297 $[M]^+$, peaks; the ratio between the [M] and [M + 2] peaks was 100 : 2.66. The NMR spectral patterns appeared to be much more complicated than those expected for compounds **3**, but they correspond to structure **2** (Tables 2 and 3).

Therefore, as distinct from the reactions of benzaldehydes **1** with acyclic derivatives of malonic acid, intermediates **3a—e** were not isolated but underwent cyclization to form spiro derivatives of [1,2-*a*]quinoline-2′-cyclohexane-1′,3′-dione **2a—e**.

The reactions of 2-dialkylaminobenzaldehydes **1a—e** with 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) proceeded analogously. It was demonstrated that the reactions were completed in 10 h to give spiro-fused [1,2-*a*]quinolines **4a—e**, whereas vinyl derivatives **5** were also not isolated (Scheme 3). The structures of compounds **4a—e** were confirmed by NMR, IR, and mass spectra as well as by the results of elemental analysis (see Tables 1—3).

Scheme 3



i. Toluene, Δ.

Spiro-fused quinolinepyrimidines **6a—e** and **7a—e** can be synthesized according to two procedures. One of them involves Knoevenagel condensation of 2-dialkylaminobenzaldehydes **1a—e** with malonic ester, cyclization of the resulting benzylidenemalonic esters **8** to fused quinolines **9**,[11,22] and condensation of the latter with disubstituted urea to give the target products. Another procedure involves the reaction of 2-dialkylaminobenzaldehydes **1a—e** with barbituric acids, where Knoevenagel condensation is accompanied by intramolecular cyclization of the intermediate vinyl derivatives (Scheme 4). Taking into account the results obtained in the earlier studies, it can be assumed that this reaction proceeds in one step to give spiro-fused quinolines **6a—e** and **7a—e**.

The synthesis of spiro derivatives of quinolines according to the first method involves difficulties associated, in particular, with the formation of by-products. In this connection, isolation of the pure target spiro-fused quinolines presents a problem. The total yield was 15% (for **7e**).

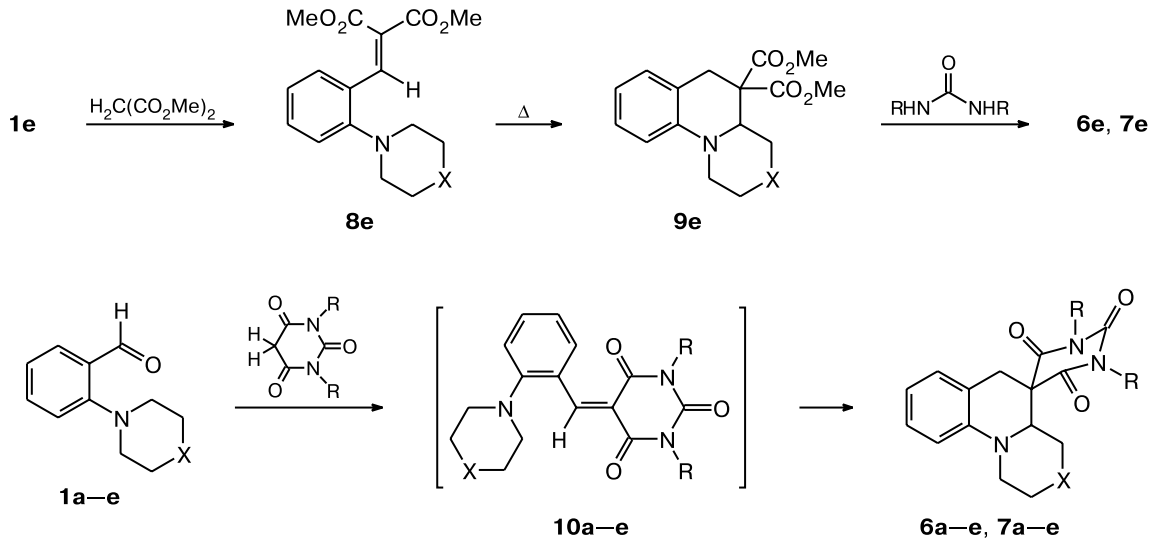
Table 3. ^{13}C NMR spectra ($CDCl_3$) of fused quinolines **2d**, **4a**, **6d**, and **7d**

Atom	δ*			
	2d**	**4a**	**6d**	**7d**
C(1)	110.8	112.6	113.4	112.5
C(1a)	141.4	144.1	144.5	143.1
C(2)	126.5	127.6	126.6	128.2
C(3)	117.1	119.0	117.4	117.9
C(4)	129.1	128.7	128.2	129.3
C(4a)	119.8	119.2	120.4	119.7
ArC(5)	23.6	27.85	26.0	26.0
NC(6)	64.2	67.3	67.2	67.1
NC(7)	50.5	48.5	50.5	51.0
C(9)	27.0	59.4	29.6	28.8
C(10)	29.9	46.4	30.1	30.2
C(1′)	205.2	168.7	170.1	169.4
C(2′)	70.0	67.3	53.2	54.7
C(3′)	203.8	164.8	168.7	168.3
C(5′)	10.6	66.7	151.2	151.2

* Other signals: **2d:** 25.4, 25.7 (C(X)); 37.8 (C(4′)); 38.1 (C(6′)); **4a:** 30.2, 34.6 (Me); **6d:** 27.2 (C(X)); 28.9 (Me); 29.5 (C(X)); **7d:** 26.68, 28.11 (C(X)); 126.79, 128.26, 128.75, 128.97, 129.17, 129.41, 129.48, 134.43 (Ph).

** In DMSO-d_6.

Scheme 4



R = Ph (**6**), Me (**7**)

The second method is preparatively more convenient because it involves one step. We demonstrated that the reactions of 2-dialkylaminobenzaldehydes **1a—e** with dimethyl- and diphenylbarbituric acids afforded spiro compounds **6a—e** and **7a—e**. Their structures were confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy, mass spectrometry, and elemental analysis (see Tables 1—3). It should be noted that cyclization gave spiro-fused quinolines **6** and **7** in good yields on refluxing in toluene for 3 h. An increase in the reaction time led to a decrease in the yield and resinification of the products. In this approach, the total yield of the target products **6a—e** and **7a—e** varied from 26 to 70%.

To summarize, we developed a one-step method for the synthesis of new heterocyclic systems, *viz.*, spiro derivatives of pyrrolo[1,2-*a*]quinoline, benzo[*c*]quinolizine, [1,4]oxazino[1,2-*a*]quinoline, and azepino[1,2-*a*]quinoline.

Table 4. Physicochemical characteristics of *o*-dialkylaminobenzaldehydes **1a—e**

Compound*	Yield (%)	Found / Calculated N (%)	Molecular formula	IR, (KBr), ν/cm^{-1} C=O	MS, *m/z* (I_{rel} (%))
1a	87	7.50 / 7.32	$C_{11}H_{13}NO_2$	1745, 1720	191 (94)
1b	88	13.20 / 13.72	$C_{12}H_{16}N_2O$	1690	204 (79)
1c	87	7.62 / 7.40	$C_{12}H_{15}NO$	1680	189 (100)
1d	82	6.56 / 6.89	$C_{13}H_{17}NO$	1675	203 (100)
1e	95	7.50 / 7.99	$C_{11}H_{13}NO$	1680	175 (96)

* Oil.

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-250 spectrometer (250 MHz for ^{1}H) and a Bruker DRX-400 instrument (400 MHz for ^{1}H and 100 MHz for ^{13}C) in DMSO-d_6 and $CDCl_3$ with Me_4Si as the internal standard. The IR spectra were measured on a UR-20 spectrometer in KBr pellets. The mass spectra were obtained on a MAT11 instrument (EI, 70 eV). The course of the reactions and purity of the compounds synthesized was monitored by TLC on DC-Plastikfolien Kieselgel 60 F 254 plates using the 15 : 1 dichloromethane—hexane system. The melting points are uncorrected. Compounds **1a**,[14] **1b**,[15] **1c,e**, **8e**, and **9e** [16] were synthesized according to known procedures. The physicochemical characteristics and spectroscopic data for the compounds synthesized are given in Tables 1—5.

Synthesis of *o*-dialkylamino-substituted benzaldehydes 1a—e (general procedure). Dialkylamine (9.88 mmol) and potassium carbonate (1.38 g, 9.88 mmol) were added to a solution of 2-fluorobenzaldehyde (1.0 mL, 9.49 mmol) in DMF (8.0 mL). The reaction mixture was refluxed on a glycerol bath at 150 °C for 20 h. The completion of the reaction was judged from the TLC data. Then the reaction mixture was cooled to ~20 °C, water (75 mL) was added, and the product was extracted with ethyl acetate (3×60 mL). The combined organic extract was washed with a solution of ammonium chloride. The organic layer was dried with Na_2SO_4 and the solvent was removed *in vacuo*.

Synthesis of spiro derivatives of fused quinolines (general procedure). Cyclic CH-active compounds (2.3 mmol) were added to a solution of 2-dialkylaminobenzaldehyde **1a—e** (2.3 mmol)

Table 5. ^{1}H NMR spectra (DMSO-d_6) of *o*-dialkylaminobenzaldehydes **1a—e**

Compound	δ (*J*/Hz)					
	CHO	ArH				Dialkylamino group
1a	10.22 (s)	7.06 (d, *J* = 7.4)	7.01 (dd, *J* = 8.2, 8.0)	6.85 (d, *J* = 8.0)	6.66 (dd, *J* = 7.4, 8.2)	2.50—2.57, 3.00—3.11 (both m, 4 H each, $N(CH_2)$ + $O(CH_2)$)
1b	10.20 (s)	7.64—7.65 (m)	7.50—7.51 (m)	7.13 (d, *J* = 7.7)	7.09 (dd, *J* = 10.3, 7.6)	2.27 (s, 3 H, CH_3); 2.50—2.61, 3.00—3.10 (both m, 4 H each, 4 CH_2)
1c	10.19 (s)	7.66 (dd, *J* = 6.1, 1.5)	7.54—7.55 (m)	7.00—7.15 (m, 2 H)		1.30—1.81 (m, 6 H, 3 CH_2); 2.87—3.05 (m, 4 H, 2 CH_2)
1d	10.10 (s)	7.60 (d, *J* = 7.4)	7.45 (dd, *J* = 8.1, 7.5)	7.15 (d, *J* = 8.2)	6.90 (dd, *J* = 7.8, 7.2)	2.60, 2.76 (both s, 6 H each, 6 CH_2)
1e	10.02 (s)	7.65 (dd, *J* = 7.2, 6.4)	7.65 (dd, *J* = 8.0, 7.3)	6.65—6.90 (m, 2 H)		2.76 (s, 4 H, 2 CH_2); 2.89 (s, 4 H, 2 NCH_2)

in toluene (20 mL). The reaction mixture was refluxed for 3 h. The completion of the reaction was determined by TLC. Then the reaction mixture was cooled to ~20 °C and concentrated *in vacuo*. The residue was triturated with ethanol.

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