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Note

Syntheses of new Coumarinic Benzothiazepines, Benzodiazepines, and Benzopyranodiazepines

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Derivatives of 3-cinnamoyl-4-hydroxycoumarin were condensed with 2-aminothiophenol, *o*-phenylenediamine, and 3,4-diaminocoumarin to obtain (4'-hydroxycoumarin-3'-yl)-benzothiazepine, -benzodiazepine and -benzopyranodiazepine derivatives, respectively.

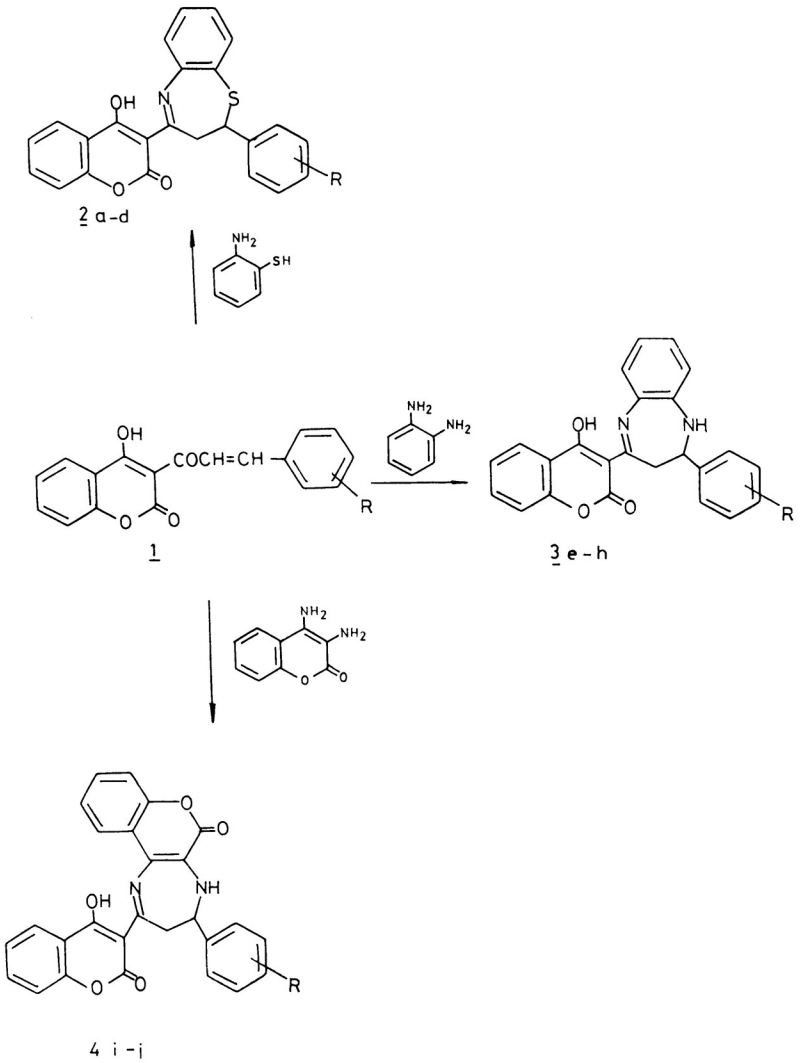
It is well known that α,β-unsaturated aromatic ketones (chalkones) undergo acid or base catalyzed condensation reactions with 1,2-diamines, to yield dihydrodiazepinic products.[1,3] In view of the broad spectrum of physiologic activities of benzodiazepines and benzothiazepines,[4,5] as well as of coumarin[6] itself and its derivatives, new derivatives of 1,5-benzothiazepine- (*2*), 1,5-benzodiazepine- (*3*), and benzopyrano-1,5-diazepine-substituted (*4*) 4-hydroxycoumarin (all in position 3) were synthesized.

Derivatives of 3-cinnamoyl-4-hydroxycoumarin (*1*) were condensed with 2-aminothiophenol in toluene to give 2-aryl-4-(4'-hydroxycoumarin-3'-yl)-2,3-dihydro-benzo[f] [1,5] thiazepines *2*. Yields, *mp*'s, IR and MS spectra, and elemental analyses of these compounds are summarized in Table I. Their magnetic resonance spectra could not be recorded because of their too low solubility in the sandard deuterated solvents at room temperature and their tendency to rearrange in attempts to achieve dissolution by heating.

In absolute ethanol, in the presence of triethylamine, derivatives of 3-cinnamoyl-4-hydroxycoumarin (*1*) and *o*-phenylenediamine gave the 2-aryl-4-(4'-hydroxycoumarin-3-yl)-5H-2,3-dihydro-benzo[f] [1,5] diazepines *3* (Table II). Under the same conditions, compounds *1* were condensed with 3,4-diaminocoumarin to give 2-aryl-4-(4'-hydroxycoumarin-3'-yl)-5H-2,3-dihydro-1*H*-benzopyrano[f] [1,5] diazepines *4* (Table III).

EXPERIMENTAL

All melting points are uncorrected. The ^{1}H-NMR spectra were recorded on a Perkin-Elmer R12A (60 MHz) spectrometer. Infrared spectra were recorded on a Perkin-Elmer M-337 spectrophotometer.



2-Aryl-4-(4'-hydroxycoumarin-3'-yl)-2,3-dihydro-benzo[f] [1,5] — thiazepines (new compounds 2a-d)

To an appropriately substituted 3-cinnamoyl-4-hydroxycoumarin (*1a-d;* 3 mmol) in dry toluene (80 cm^3) 2-aminothiophenol, (3.6 mmol) was added and the mixture refluxed for 3 hours with continuous water removal, then left to stand undisturbed. The solid product, precipitated overnight, was collected and crystallized from toluene (Table I).

2-Aryl-4-(4'-hydroxycoumarin-3'-yl)-5H-,2,3-dihydroxy-benzo[f] [1,5] diazepines (new compounds 3e-h; *see Table II)*

Equimolar amounts (1,7 mmol) of appropriate *1* derivative and *o*-phenylenediamine in absolute ethanol (50 cm^3 to which a few drops of triethylamine were

TABLE I

2-Aryl-4-(4'-hydroxycoumarin-3'-yl)-1,3-dihydrobenzo[f][1,5]thiazepines (2)

Product No.	R	Yield (%)	*m. p.* (C°) (Solvent)	Molecular Formula	$\bar{\nu}$ (cm^{-1}) (cm^{-1})	M. S. *m/e* (M^+)	*Analysis* Calc'd./Found C	H	N
2a	H	77	251—253 (toluene)	$C_{24}H_{17}NO_3S$ (399,39)	3020($CH_{arom.}$) 1700(CO) 1605($C=C_{arom.}$)	399	72.17 72.29	4.29 4.30	3.50 3.48
2b	4-Cl	64	245—247 (toluene)	$C_{24}H_{16}NO_3SCl$ (433,28)	3040($CH_{arom.}$) 1696(CO) 1608($C=C_{arom.}$)	433	66.52 66.55	3.72 3.69	3.23 3.14
2c	3-OH	62	255—257 (toluene)	$C_{24}H_{17}NO_4S$ (415,38)	3340(OH) 3010($CH_{arom.}$) 1700(CO) 1602($C=C_{arom.}$)	415	69.39 69.79	4.12 4.18	3.37 3.21
2d	4-$N(CH_3)_2$	60	246—249 (toluene)	$C_{26}H_{22}N_2O_3S$ (442,47)	3010($CH_{arom.}$) 2850(CH_3) 1695(CO) 1600($C=C_{arom.}$)	442	70.57 70.68	5.01 5.09	6.33 6.22

TABLE II

2-Aryl-4-(4'-hydroxycoumarin-3'-yl)-5H-2,3-dihydrobenzo[f] [1,5]diazepines 3

R	Product No.	Yield (%)	*m. p.* (C°) (Solvent)	Molecular Formula	IR (KBr) $\bar{\nu}$ (cm^{-1})	^{1}H-NMR(DMSO-d_6/TMS) δ (ppm)	M. S. *m/e* (M^+)	*Analysis* Calc'd./Found C	H	N
3e	H	60	218—220 (ethanol)	$C_{24}H_{18}N_2O_3$ (382.24)	3325(NH) 3030($CH_{arom.}$) 1685(CO) 1600($C=C_{arom.}$)	3.70(d,2H,CH_2); 5.10(t,1H,CH); 6.20(1H,NH); 7.10—8.15(m,13$H_{arom.}$)	382	75.41 75.38	4.74 4.81	7.32 7.20
3f	4-Cl	63	238—239 (ethanol)	$C_{24}H_{17}N_2O_3Cl$ (413.39)	3325(NH) 3030($CH_{roam.}$) 1685(CO) 1600($C=C_{arom.}$)	3.80(d,2H,CH_2); 5.20(t,1H,CH); 6.20(1H,NH); 7.00—8.10(m,12$H_{arom.}$)	413	69.73 69.43	4.14 4.14	6.77 6.66
3g	2-NO_2	74	208—210 (ethanol)	$C_{24}H_{17}N_3O_5$ (427.39)	3340(NH) 3040($CH_{arom.}$) 1630(CO) 1595($C=C_{aroin.}$) 1460(NO_2)	3.85(d,2H,CH_2); 5.45(t,1H,CH); 6.40(1H,NH); 7.10—8.30(m,12$H_{arom.}$)	427	67.44 67.72	4.01 4.09	9.83 9.67
3h	4-NO_2	75	235—236 (ethanol)	$C_{24}H_{17}N_3O_5$ (427.39)	3370(NH) 3040($CH_{arom.}$) 1685(CO) 1595($C=C_{arom.}$) 1460(NO_2)	4.00(d,2H,CH_2); 5.90(t,1H,CH); 6.30(1H,NH); 6.90—8.00(m,12$H_{arom.}$)	427	67.44 67.29	4.01 4.04	9.83 9.76

TABLE III

2-Aril-4-(4'-hydroxycoumarin-3'-yl)-5H-2,3-dihydro-1H-benzopyran-2-on[f] [1,5] diazepines 3

Product No.	R	Yield (%)	*m. p.* (C°) (Solvent)	Molecular Formula	IR (KBr) $\bar{\nu}$ (cm^{-1})	^{1}H-NMR(DMSO-d_6/TMS) δ (ppm)	M. S. *m/e* (M^+)	*Analysis* Calc'd./Found C	H	N
4i	H	67	272—274 (ethanol)	$C_{27}H_{18}N_2O_5$ (450.37)	3330(NH) 3040($CH_{arom.}$) 1665(CO) 1600($C=C_{arom.}$)	3.00(d,2H,CH_2), 5.25(t,1H,CH) 7.30—8.20(m,1H, NH, 13$H_{arom.}$)	450	72.01 71.90	4.03 4.13	6.22 6.51
4j	4-NO_2	71	284—286 (DMSO)	$C_{27}H_{17}N_3O_7$ (495.35)	3340(NH) 3050($CH_{arom.}$) 1670(CO) 1600($C=C_{arom.}$) 1500(NO_2)	3.05(d,2H,CH_2); 5.30(t,1H,CH) 7.40—8.40(m,1H, NH, 12$H_{arom.}$)	495	69.10 68.77	3.46 3.67	8.48 8.21

added was refluxed for 3 hours, then left to cool. Yellow solids separated gradually. They were finally collected and crystallized from ethanol.

2-Aryl-4-(4'-hydroxycoumarin-3'-yl)-5H-2,3-dihydro-1H-benzopyrano[f] [1,5] diazepines (new compounds 4i-j; *see Table III)*

The procedure described in the preceding paragraph was used with an equimolar (1.7 mmol) mixture of phenyl and 4-nitrophenyl- and 3,4-diaminocoumarin, respectively, (the same solvent and catalyst).

Orange-yellow crudes separated. Compd. *4i* was crystallized from ethanol, compd. *4j* from DMSO.

REFERENCES

1. V. D. Orlov, H. Kiroga, and N. N. Kolos, *Khim. Geterotsikl. Soed.* **3** (1987) 363.
2. V. D. Orlov, N. N. Kolos, F. G. Yaremenko, and V. F. Lavrušin, *Khim. Geterotsikl. Soed.* **5** (1980) 697.
3. V. D. Orlov, I. Z. Papiašvili, and P. A. Grigorov, *Khim. Geterotsikl. Soed.* **5** (1983) 671.
4. D. P. Clifford, P. Jackson, and R. V. Edwards, *Jeffereyp. Pestic. Sci.* **7** (1976) 453; *Chem. Abstr.* **87** (1977) 146947.
5. C. Kaiser and V. L. Zilkle, *Medicinal Chemistry,* 3rd Edit., S. Burger (Ed.), Part II, J. Wiley, Interscience, New York, 1970, p. 1481.
6. L. W. Wattenberg, L. K. Lam, and A. V. Fladmoe, *Cancer Res.* **39** (1979) 1651.

SAŽETAK

Sinteza novih kumarinskih benztiazepina, benzdiazepina i benzpiranodiazepina

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Reakcijom derivata 3-cinamoil-4-hidroksikumarina (*1*) i 2-aminotiofenola u toluenu dobiveni su 2-aryl-4-(4'-hidroksikumarin-3'-il)-2,3-dihidrobenz [f] [1,5]tiazepini (*2*).

U apsolutnom alkoholu uz trietilamin 3-cinamoil-4-hidroksikumarini (*1*) s *o*-fenilendiaminom daju derivate 1,5-benzdiazepina supstituirane na 4-hidroksikumarinu u položaju 3 (*3*).

Reakcijom spojeva (*1*) s 3,4-diaminokumarinom dobiveni su 2-aril-4-(4'-hidroksikumarin-3'-il)-5H-2,3 dihidro-1*H*-benzpirano [f] ([1,5]diazepini (*4*).