4-(5-PHENYL-1,3,4-OXADIAZOL-2-YL)BIPHENYL-4'-CARBOXYLIC ACID: ITS FUNCTIONAL DERIVATIVES AND THEIR HETEROCYCLIZATION INTO 1,3-THIAZINE-6-THIONES

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Received February 13, 1990
Accepted May 12, 1990

The title carboxylic acid *II* prepared by hypobromide oxidation of 4'-acetyl derivative *I* was converted into its functional derivatives *III*—*IX* by standard preparative procedures. The C-acylation of 1,1-dichloroethene with acyl chloride *III* gave dichloroethenyl ketone *X* affording 2,4-disubstitued 1,3-thiazine-6-thiones *XIa*—*XIe* and *XII* by cyclocondensations with appropriate thioamides. The reactivity of heterocycles *XIb*, *XIc* was checked by their conversion into the expected products *XIII*—*XV*. IR and NMR spectroscopic patterns of the new prepared compounds are discussed.

The regioselective electrophilic 4''-substitution of a well known organic luminophore 2-(biphenyl-4'-yl)-5-phenyl-1,3,4-oxadiazole (PBD)[1] offers novel routes to various related compounds of interesting optical properties. One of the synthetic exploitations might start from the easily accessible[2] methyl ketone *I* via the corresponding 4'-carboxylic acid *II* to its functional derivatives. In this connection especially 2,2-dichloroethenyl ketone *X* seems to be of interest as a potential precursor for 1,3-thiazine-6-thione ring closure[3-7].

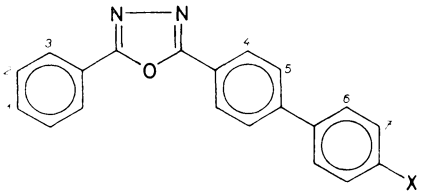
The starting 4'-carboxylic acid *II* was really prepared in excellent yield by oxidation of the methyl ketone *I* with sodium hypobromide–sodium hydroxide mixture and easily transformed to corresponding methyl ester *IV*. The acyl chloride *III* was obtained from the acid *II* by reaction with thionyl chloride at elevated temperature and was used as a key intermediate for other chemical transformations. Thus the corresponding amides *V*—*VII* were isolated in satisfactory yields after treatment of *III* with aqueous ammonia, aniline or 4-aminobiphenyl, respectively. The 4'-carboxamide *V* was also converted nto 4'-nitrile *VIII* or 4'-thioamide *IX* on heating with thionyl chloride or phosphorus pentasulfide, respectively.

The above mentioned preparative experiments show that the acid *II* behaves quite ordinary in attempts to be transformed into typical functional derivatives. Therefore

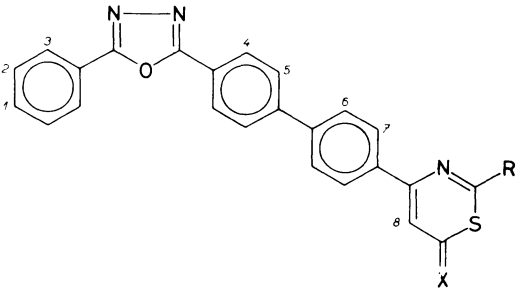
it may be expected that the large 4-(5-phenyl-1,3,4-oxadiazol-2-yl)-biphenyl-4'-yl group responsible for electronic absorption and emission phenomena of appropriate derivatives will be capable of incorporation into certain heterocyclic skeletons just via the above described derivatives. To verify this assumption we have tried to use various known heterocyclization procedures to connect the luminophoric PBD fragment with other heterocyclic parts within a given molecule. In this paper we report a 1,3-thiazine ring connection using the cyclocondensation of 2,2-dichloroethenyl ketones with thioamides[3-7] having so been far applied only to phenyl substituents.

The necessary 2,2-dichloroethenyl ketone *X* was prepared by aluminium trichloride catalyzed C-acylation[8] of 1,1-dichloroethene with acyl chloride *III* in 70% yield. The cyclocondensations of the dichloro derivative *X* with ethanethioamide, S-methyldithiocarbamate, benzenethioamide, thiourea as well as N,N-dimethylthiourea proceeded at elevated temperature in a dioxane–methanol–acetic acid mixture to give the expected 2,4-disubstituted 1,3-thiazine-6-thiones in good yields (Table I).

The success in the heterocyclizations stimulated a final attempt to join the two bulky four-ring residues within one molecule via the 1,3-thiazine-6-thione bridge. The dichloroderivative *X* was therefore allowed to react with thioamide *IX* under the heterocyclization conditions. The expected nine-ring product *XII* was isolated from the resulting reaction mixture in 30% yield. This findings show the versatility of the 1,3-thiazine-6-thione synthesis in the field of large oligophenylene heterocycles.



I, X = $COCH_3$
II, X = COOH
III, X = COCl
IV, X = COOMe
V, X = $CONH_2$
VI, X = CONHPh
VII, X = $CONHC_6H_4Ph$
VIII, X = CN
IX, X = $CSNH_2$
X, X = $COCH{=}CCl_2$



XIa, R = Me ; X = S
XIb, R = SMe ; X = S
XIc, R = Ph ; X = S
XId, R = NH_2 ; X = S
XIe, R = NMe_2 ; X = S
XIII, R = Ph ; X = O

To check the chemical behaviour of the both heterocyclic ring systems in molecules of the synthesized compounds their selective transformations were attempted. Such

TABLE I

Characteristic parameters for the compounds *XIa*—*XIe*

Compound	Reaction time, h	M.p. °C	Yield %	Solvent	$\tilde{\nu}$(CS) cm^{-1}
XIa	8	245—246	80	toluene	1 278
XIb	20	207—208	76	dioxane	1 277
XIc	12	276—277	85	toluene	1 275
XId	8	294—296	67	DMF	1 270
XIe	10	283—284	90	chlorobenzene	1 269

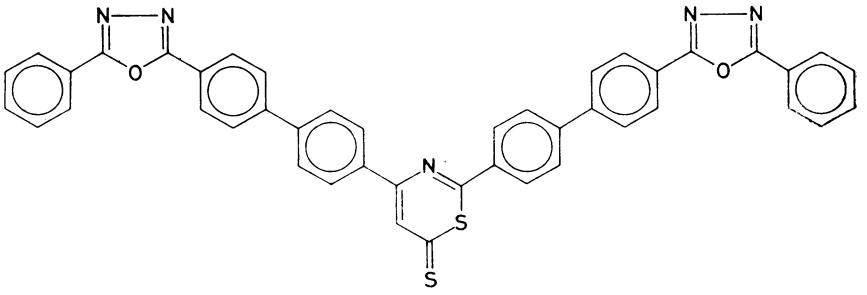
TABLE II

^{1}H NMR spectra (δ, ppm; J, Hz) of the compounds *II*—*X*

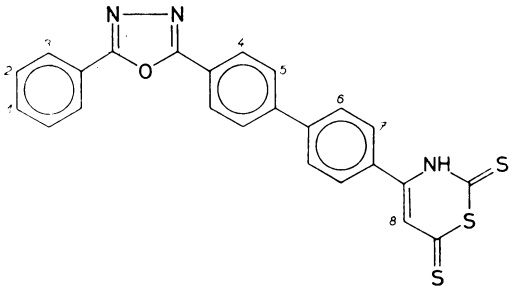
Compd.	H-1, 2	H-3	H-4	H-5	H-6	H-7
II	7·70 m	8·24 dd	8·34 d J = 8·4	8·09 d J = 8·4	8·00 d J = 8·4	8·18 d J = 8·3
III	7·70 m	8·23 dd	8·32 d J = 7·2	8·07 d J = 7·2	7·98 d J = 7·3	8·18 d J = 7·7
IV[a]	7·55 m	8·15 m	8·23 d J = 8·24	7·79 d J = 8·23	7·72 d J = 8·19	8·15 m
V	7·67 m	8·20 dd	8·29 d J = 8·3	8·02 d J = 8·5	7·89 d J = 8·3	8·12 d J = 8·2
VI[b]	7·66 m	8·19 dd	8·29 d J = 8·4	8·03 d J = 8·4	7·94 d J = 8·4	8·19 d
VII[c]	7·61 m	8·16 dd	8·27 d J = 7·75	7·89 d J = 7·70	7·98 d J = 8·04	8·04 d J = 8·04
VIII	7·56 m	8·17 dd	8·26 d J = 8·4	7·76 m	7·76 m	7·76 m
IX[d]	7·69 m	8·22 dd	8·31 d J = 8·4	8·06 d J = 8·4	7·90 d J = 8·4	8·19 d J = 8·4
X[e]	7·55 m	8·15 dd	8·23 d J = 8·52	7·79 d J = 8·50	7·76 d J = 8·46	8·03 d J = 8·52

For numbering see formulae in text. [a] 3·96 s (CH_3). [b] 10·14 s (NH); 7·91 d, J = 8·0 (*ortho*); 7·37 t, J = 8·0 (*meta*); 7·12 t, J = 7·6 (*para*). [c] 7·80 d, J = 7·04 (*ortho*); 7·65 m (others). [d] 9·65 s, 9·86 s (NH_2). [e] 7·30 s (CH).

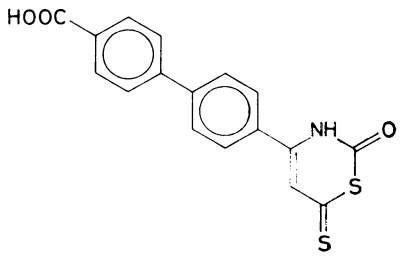
transformations of 1,3-thiazine-6-thione ring were accomplished by the reaction of 2-phenyl derivative *XIc* with mercury(II) acetate[3] yielding 2-phenyl-1,3-thiazine--6-one *XIII* as well as the conversion of 2-methylthio derivative *XIb* into the corresponding 2,6-dithione *XIV* with hydrogensulfide–triethyl amine[5]. The hydrolytic 1,3,4-oxadiazole ring cleavage[9] accompanied with a partial transformation of 2--methylthio function into 2-carbonyl group was observed after heating compound *XIb* with hydrochloric acid[6]. The new carboxylic acid *XV* was isolated from the resuting reaction mixture in 55% yield.



XII



XIV



XV

The molecular structures of investigated compounds *II*–*XV* were confirmed on the basis of their high-resolution ^{1}H NMR spectra. Except of the unresolved 1,2--proton absorptions of 5-phenyl groups in 4'-carboxylic derivatives *II*–*X*, all other signals could be assigned to corresponding protons at the 400 MHz measurement conditions (Table II). As expected, additional singlet signals $\delta = 7{\cdot}00$ to $\delta = 7{\cdot}85$ assigned to H-8 of the 1,3-thiazine-6-thione rings were detected in the spectra of all sulfur-containing heterocycles *XI*–*XV* (Table III). Elemental analysis of all new compounds are listed in Table IV.

EXPERIMENTAL

Melting points were determined on a Boetius block and are uncorrected. Infrared spectra ($\tilde{\nu}$ in

cm^{-1}) were measured in KBr on a Perkin–Elmer 325 spectrophotometer, ^1H NMR spectra were measured on a Bruker AM 400 (400 MHz) instrument using heptadeuteriodimethylformamide as solvent and tetramethylsilane as internal standard. Samples for elemental analyses were dried over phosphorus pentoxide. The purity of the compounds and the course of the reaction were followed by means of TLC on Silufol or Alufol foils (Kavalier Votice).

2-(4′-Carboxybiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*II*)

Solution of 15 g ketone *I* in dioxane was added dropwise to a freshly prepared solution of sodium hypobromide (28·5 g bromine, 21·3 g sodium hydroxide, 500 ml water) during 0·5 h at temperature 30–40°C. After stirring for 5 h the reaction mixture was treated with a solution of sodium sulfite and then acidified with conc. hydrochloric acid. After cooling, the precipitate formed, was collected by suction, washed with water, and dried at 80°C to yield 14·85 g (98%) of product. Recrystallization from dioxane gave compound *II*, m.p. above 310°C. IR spectrum: 3 420 (OH), 1 675 (C=O).

2-(4′-Chlorocarbonylbiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*III*)

Acid *II* was refluxed in 100 ml thionyl chloride for 9 h with exclusion of moisture. The unreacted thionyl chloride was then distilled off, and the solid residue was recrystallized from benzene to give 13·15 g (84%) compound *III*, m.p. 201–203°C. IR spectrum: 1 772, 1 730 (C=O).

TABLE III

^1H NMR spectra (δ, ppm; J, Hz) of the compounds *XIa*–*XIe*, *XIII* and *XIV*

Compd.	H-1, 2	H-3	H-4	H-5	H-6	H-7	H-8
XIa[a]	7·65 m	8·20 dd	8·29 d J = 8·39	8·07 d J = 8·35	8·00 d J = 8·23	8·35 d J = 8·36	7·72 s
XIb[b]	7·66 m	8·20 dd	8·31 d J = 8·61	8·07 d	8·07 d	8·19 d J = 8·60	7·85 s
XIc[c]	7·68 m	8·21 dd	8·31 d J = 8·42	8·06 d J = 8·41	8·10 d J = 8·37	8·51 d J = 8·34	7·83 s
XId	7·66 m	8·21 dd	8·27 d J = 8·49	7·97 d J = 8·48	8·06 d J = 8·40	8·30 d J = 8·39	7·44 s
XIe[d]	7·66 m	8·21 dd	8·30 d J = 8·56	8·07 d J = 8·51	7·98 d J = 8·56	8·33 d J = 8·54	7·46 s
XIII[e]	7·68 m	8·21 dd	8·31 d J = 8·13	8·09 d J = 8·07	8·04 d J = 8·29	8·45 d J = 8·46	7·00 s
XIV	7·67 m	8·21 dd	8·31 d J = 8·53	8·08 m	8·00 d J = 8·32	8·08 m	7·17 s

[a] 2·74 s (CH_3). [b] 2·94 s (CH_3). [c] 8·27 d, J = 7·25 (*ortho*); 7·68 m (*meta*, *para*). [d] 3·42 s (CH_3). [e] 8·25 d, J = 7·34 (*ortho*); 7·68 m (*meta*, *para*).

TABLE IV

Elemental analyses of compounds *II*—*XV*

Compound	Formula (M.w.)	Calculated/Found				
		% C	% H	% Cl	% S	% N
II	$C_{21}H_{14}N_2O_3$	73·67	4·13	—	—	8·18
	(342·4)	73·79	4·30	—	—	8·19
III	$C_{21}H_{13}ClN_2O_2$	69·80	3·64	9·82	—	7·76
	(360·8)	69·99	3·74	9·84	—	7·65
IV	$C_{22}H_{16}N_2O_3$	74·16	4·49	—	—	7·87
	(356·3)	73·69	4·52	—	—	7·92
V	$C_{21}H_{15}N_3O_2$	73·88	4·44	—	—	12·31
	(341·4)	73·66	4·37	—	—	12·18
VI	$C_{27}H_{19}N_3O_2$	77·70	4·56	—	—	10·07
	(417·4)	77·53	4·77	—	—	10·14
VII	$C_{33}H_{22}N_2O_2$	82·81	4·60	—	—	5·86
	(478·5)	82·44	4·87	—	—	5·67
VIII	$C_{21}H_{13}N_3O$	77·97	4·02	—	—	12·99
	(323·3)	77·77	4·20	—	—	12·74
IX	$C_{21}H_{15}N_3OS$	70·59	4·20	—	8·96	11·77
	(357·3)	70·73	4·08	—	8·88	11·68
X	$C_{23}H_{14}Cl_2N_2O_2$	65·56	3·32	16·86	—	6·65
	(421·2)	64·99	3·31	16·56	—	6·32
XIa	$C_{25}H_{17}N_3OS_2$	68·34	3·87	—	14·57	9·57
	(439·5)	68·19	4·14	—	14·26	9·00
XIb	$C_{25}H_{17}N_3OS_3$	63·69	3·61	—	20·38	8·92
	(471·6)	64·03	3·75	—	19·58	8·42
XIc	$C_{30}H_{19}N_3OS_2$	71·86	3·79	—	12·77	8·33
	(501·5)	72·05	3·92	—	12·20	8·19
XId	$C_{24}H_{16}N_4OS_2$	65·45	3·64	—	14·54	12·73
	(440·5)	65·42	3·90	—	14·45	12·60
XIe	$C_{26}H_{20}N_4OS_2$	66·67	4·27	—	13·67	11·97
	(468·5)	66·27	4·46	—	13·70	12·10
XII	$C_{44}H_{27}N_5O_2S_2$	73·23	3·74	—	8·88	9·71
	(721·7)	72·73	3·97	—	8·56	9·31
XXIII	$C_{30}H_{19}N_3O_2S$	74·23	3·92	—	6·60	8·66
	(485·4)	74·14	4·17	—	6·19	7·99
XIV	$C_{24}H_{15}N_3OS_3$	63·02	3·28	—	21·06	9·19
	(457·5)	62·78	3·46	—	20·86	9·27
XV	$C_{17}H_{11}NO_3S_2$	59·82	3·32	—	18·77	4·11
	(341·4)	59·88	3·46	—	18·27	3·90

2-(4′-Methoxycarbonylbiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*IV*)

Methanol (2 ml, 0·05 mol) was added to a solution of 1 g acyl chloride *III* (2·8 mmol) in 100 ml methylen chloride. After reflux for 1 h the solvent was removed, and the residue recrystallized from toluene to yield 0·9 g (90%) product *IV*, m.p. 190–101°C. IR spectrum: 1 718 (C=O).

2-(4′-Carbamoylbiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*V*)

Acyl chloride *III* (5 g, 13·8 mmol) was dissolved in hot dioxane and 7 ml 25% ammonium hydroxide was added during 10 min. Reaction mixture was then stirred at 20°C for 2·5 h and let to stand for 12 h. After pouring into water the separated solid was collected by suction and dried to yield 4·43 g product. Recrystallization from dioxane gave crystals with m.p. 283·5–285°C. IR spectrum: 3 380, 3 180 (NH); 1 647 (C=O).

2-(4′-Phenylcarbamoylbiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*VI*)

Aniline (5 ml, 0·055 mol) was added to a solution of chloride *III* (1 g, 2·8 mmol) in 200 ml dioxane at 60°C. After 2 h stirring and cooling, the solid was separated by filtration, and recrystallized from dioxane to yield 1·0 g (77%) product *VI*, m.p. 252°C. IR spectrum: 3 330 (NH); 1 665 (C=O).

2-(4′-(Biphenyl-4-ylcarbamoyl)biphenyl-4-yl-5-phenyl-1,3,4-oxadiazole (*VII*)

Solution of chloride *III* (1·00 g, 2·8 mmol) in 120 ml dioxane was added dropwise during 30 min to the solution of 4-aminobiphenyl (0·5 g, 3 mmol) and 2 ml pyridine in 20 ml dioxane at 60°C. After 2 h stirring and cooling of the reaction mixture the separated solid was isolated by suction. Recrystallization from dioxane gave 0·7 g (67%) product *VII*, m.p. 300–302°C. IR spectrum: 3 290 (NH); 1 660 (C=O).

2-(4′-Cyanobiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*VIII*)

Mixture of amide *V* (0·8 g, 2·3 mmol) and 30 ml thionyl chloride was refluxed 20 h. Excess of thionyl chloride was then distilled off, the solid residue washed with 20 ml light petroleum and recrystallized from toluene to yield 0·5 g (60%) product *VIII*, m.p. 186–187°C. IR spectrum: 2 225 (CN).

2-(4′-Thiocarbamoylbiphenyl-4-yl)-5-phenyl-1,3,4-oxadiazole (*IX*)

Phosphorus pentasulfide (2·0 g, 4·5 mmol) was added to the boiling suspension of amide *V* (1·0 g, 3 mmol) in 200 ml toluene. After 3 h refluxing reaction mixture was cooled to 70°C, 150 ml chloroform was added and hot solution was filtered. Solvent was then removed and oily residue let to crystallize for 2 days. Separated solid was collected by filtration and recrystallized from dioxane to give 0·5 g (48%) thioamide *IX*, m.p. 272–274°C. IR spectrum: 3 290, 3 150 (NH); 1 076 (C=S).

1,1-Dichloro-3-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)biphenyl-4′-yl)-prop-1-en-3-one (*X*)

Solution of acyl chloride *III* (6 g, 17 mmol) in 300 ml methylene chloride was added to the suspension of aluminum trichloride (4·5 g, 34 mmol) in 30 ml methylene chloride, and 1,1-dichloroethene (13·3 ml, 0·166 mol) was added dropwise within 20 min at gently reflux. After 15-min

boiling the reaction mixture was poured onto 150 g ice. Aqueous layer was extracted three times with 40 ml methylene chloride, combined organic layers were washed with water, dried with $CaCl_2$ and evaporated. Recrystallization of residue from toluene (charcoal) gave 5·0 g (70%) of compound *X*, m.p. 212—213°C. IR spectrum: 1 690 (C=O).

2-Substituted-4-(5-phenyl-1,3,4-oDadiazol-2-yl)biphenyl-4′-yl)--1,3-thiazin-6-thiones (*XIa—XIe*)

Dichloroethenyl ketone *X* (1·0 g, 2·37 mmol) was dissolved in 25 ml hot dioxane, and mixture of 20 ml ethanol and 4 ml glacial acetic acid was added. Then the corresponding thioamide (11·8 mmol) was added and reaction mixture was stirred under reflux until all the ketone *X* had reacted (TLC). Separated solid thiones *XI* was collected by filtration and recrystallized from suitable solvent (see Table I).

2,4-Bis(4-(5-phenyl-1,3,4-oxadiazol-2-yl)biphenyl-4′-yl)-1,3-thiazine-6-thione (*XII*)

Mixture of dichloroethenyl ketone *X* (0·24 g, 0·57 mmol) and thioamide *IX* (0·4 g, 1·12 mmol) in 20 ml dioxane, 15 ml methanol and 3 ml glacial acetic acid was stirred under reflux for 100 h. Separated solid was collected and recrystallized from DMF followed by crystallization from DMSO to yield 0·12 g of thione *XII* (30%), m.p. 300—302°C. IR spectrum: 1 270 (CS).

2-Phenyl-4-(4-(5-phenyl-1,3,4-oxadiazol-2-yl)biphenyl-4′-yl)-1,3-thiazine-6-one (*XIII*)

Solution of mercury(II) acetate (3·2 g, 0·01 mol) in 25 ml glacial acetic acid was added dropwise to the boiling solution of compound *XIc* (0·5 g, 1 mmol) in 100 ml dichloromethane. After 3 h reflux reaction mixture was filtered, filtrate washed with 150 ml water, 40 ml 15% $NaHCO_3$ solution, and again three times with 40 ml water. Thereafter the solution was dried with $CaCl_2$, and solvent was removed under reduced pressure to give 0·35 g (72%) of compound *XIII*, m.p. 272—273°C (dioxane). IR spectrum: 1 650 (C=O).

4-(4-(5-Phenyl-1,3,4-oxadiazol-2-yl)biphenyl-4′-yl)-1,3-thiazine-2,6-dithione (*XIV*)

Triethylamine (0·15 ml, 1 mmol) was added to a solution of compound *XIb* (0·5 g, 1 mmol) in 150 ml dioxane, and dry H_2S was bubbled through reaction mixture under stirring for 8 h. Solution was then concentrated to crystallization, separated solid washed with 20 ml ether and recrystallized from dioxane to yield 0·3 g (62%) compound *XIV*, m.p. 267—269°C. IR spectrum: 1 265 (CS).

4-(2-Oxo-1,3-thiazine-6-thion-4-yl)biphenyl-4′-yl carboxylic acid (*XV*)

Mixture of compound *XIb* (0·5 g, 1 mmol), 200 ml dioxane and 30 ml conc. hydrochloric acid was stirred under reflux for 20 h. Reaction mixture was concentrated to half a volume, separated solid collected by suction and recrystallized from dioxane to yield 0·2 g of product *XV* (55%), m.p. 328—329°C. IR spectrum: 1 680 (C=O); 1 275 (CS).

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Translated by the author (P.L.).