SYNTHESES STARTING FROM 2,6-DIALKYLPHENYLHYDRAZINES

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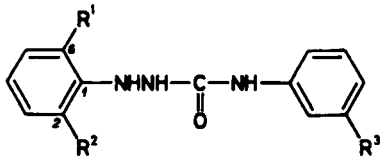
1,4-Disubstituted semicarbazides *I*, dithiocarbazates *II*, *III* and diesters of N-(2,6-dialkylphenylamino)-imidodithiocarbonic acid *IV*, *V* were prepared from 2,6-dialkylphenylhydrazines. The products were tested for pesticide activity.

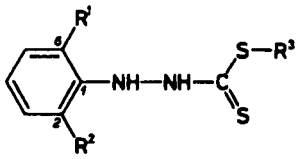
Utilization of 2,6-dialkylphenylhydrazines[1,2] especially 2,6-dimethylphenylhydrazine for the synthesis of fungicidally active compounds was several times patented in the last decade[3-10]. Hungarian authors[11,12] synthesized thiazolines with hypnotic activity and derivatives of 5-pyrazolecarboxylic acid effective as sedatives, hypnotics and muscle relaxants from 2,6-dimethylphenylhydrazine. Japanese authors[13] used this chemical for a synthesis of 3-amino-1,3-thiazolidinediones.

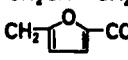
2,6-Dialkylphenylhydrazines were employed for preparation of substituted 1,2,4-triazole derivatives[14], indolylformazanes, indolylazetidinones and tetrazolium salts[15]. Also new rearrangements of 2,6-dialkylphenylhydrazone were published[10,16-18] and action of mild oxidation reagents on 2,6-dimethylphenylhydrazine and its condensation products was investigated[19-21].

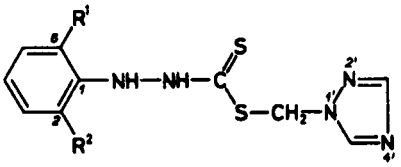
Our previous paper[22] concerned reactions of 2,6-dialkylphenylhydrazines with 2,3-dichloro- and 2,3-dibromo-4-oxo-2-butenoic acids, chloro-, bromo- and dichloromaleinic anhydride and N-(1,2,2,2-tetrachloroethyl)formamide. This paper presents reactions of 2,6-dialkylphenylhydrazines with phenyl and 3-chlorophenyl isocyanates leading to 1-(2,6-dialkylphenyl)-4-phenylsemicarbazides *Ia – Ic* and 1-(2,6-dialkylphenyl)-4-(3-chlorophenyl)semicarbazides *Id – If*. The reaction was carried out at 15 °C in ether with good yields (Table I). 2,6-Dialkylphenylhydrazines were further reacted with carbon disulfide in the presence of concentrated ammonium hydroxide to yield ammonium 2,6-dialkylcarbodithionate, which, on treatment with benzyl chloride in situ afforded dithiocarbazates *IIa – IIc*, with allyl chloride compounds *IId – IIf*, with methyl 5-chloromethyl-2-furancarboxylate compound *IIg* and with 1-chloromethyl-1,2,4-triazole compounds *IIIa – IIIc*. Some selected dithiocarbazates (*IIa*, *IIc*, *IId*, *IIg*) were used for preparation of diesters of N-(2,6-dialkylphenylamino)imidodithionic acid *IV*, *V*. Structure of compounds prepared was corroborated by the ^{1}H NMR spectra (Tables II – IV).



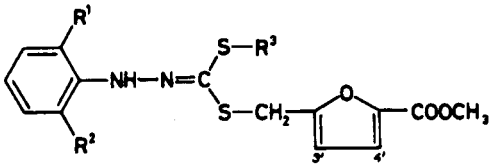
I	R^1	R^2	R^3
a	CH_3	CH_3	H
b	CH_3	C_2H_5	H
c	C_2H_5	C_2H_5	H
d	CH_3	CH_3	Cl
e	CH_3	C_2H_5	Cl
f	C_2H_5	C_2H_5	Cl



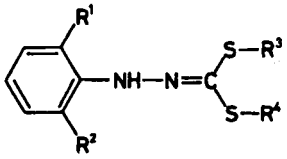
II	R^1	R^2	R^3
a	CH_3	CH_3	$CH_2C_6H_5$
b	CH_3	C_2H_5	$CH_2C_6H_5$
c	C_2H_5	C_2H_5	$CH_2C_6H_5$
d	CH_3	CH_3	$CH_2CH{=}CH_2$
e	CH_3	C_2H_5	$CH_2CH{=}CH_2$
f	C_2H_5	C_2H_5	$CH_2CH{=}CH_2$
g	CH_3	C_2H_5	



III	R^1	R^2
a	CH_3	CH_3
b	CH_3	C_2H_5
c	C_2H_5	C_2H_5



IV	R^1	R^2	R^3
a	CH_3	CH_3	$CH_2C_6H_5$
b	C_2H_5	C_2H_5	$CH_2C_6H_5$
c	CH_3	CH_3	$CH_2CH{=}CH_2$
d	CH_3	C_2H_5	$CH_2CH{=}CH_2$
e	C_2H_5	C_2H_5	$CH_2CH{=}CH_2$
f	CH_3	C_2H_5	$CH_2C_6H_4$-4-NO_2



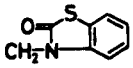
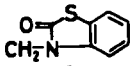
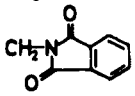
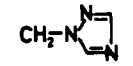
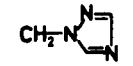
V	R^1	R^2	R^3	R^4
a	CH_3	CH_3	$CH_2C_6H_5$	
b	CH_3	CH_3	$CH_2CH{=}CH_2$	
c	CH_3	CH_3	$CH_2C_6H_5$	
d	CH_3	CH_3	$CH_2C_6H_5$	
e	C_2H_5	C_2H_5	$CH_2C_6H_5$	

TABLE I
Characteristic data for compounds *Ia – Ie*

Compound	Formula (M. w.)	M. p., °C (Yield, %)	Calculated/Found			
			% C	% H	% N	% S[a]
Ia	$C_{15}H_{17}N_3O$	135 – 140	70.57	6.71	16.46	–
	(255.3)	(91)	70.42	6.70	16.26	
Ib	$C_{16}H_{19}N_3O$	110 – 113	71.35	7.11	15.40	–
	(269.3)	(87)	71.43	7.01	15.20	
Ic	$C_{17}H_{21}N_3O$	152 – 155	72.05	7.47	14.85	–
	(283.4)	(77)	72.36	7.34	14.65	
Id	$C_{15}H_{16}ClN_3O$	180 – 184	62.18	5.57	14.50	12.23
	(289.8)	(84)	61.96	5.62	14.58	12.36
Ie	$C_{16}H_{18}ClN_3O$	125 – 128	63.26	5.97	13.83	11.67
	(303.8)	(63)	63.06	5.87	13.63	11.57
If	$C_{17}H_{20}ClN_3O$	121 – 125	64.25	6.34	13.22	11.15
	(317.8)	(75)	64.05	6.32	13.46	11.32
IIa	$C_{16}H_{18}N_2S_2$	131 – 133	63.53	6.00	9.26	21.20
	(302.5)	(87)	63.65	5.95	9.22	20.95
IIb	$C_{17}H_{20}N_2S_2$	137 – 139	64.51	6.37	8.85	20.26
	(316.5)	(86)	64.25	5.96	8.37	20.06
IIc	$C_{18}H_{22}N_2S_2$	127 – 129	65.42	6.71	8.46	19.40
	(330.5)	(89)	65.18	6.62	8.28	19.65
IId	$C_{12}H_{16}N_2S_2$	130 – 133	57.10	6.39	11.10	25.41
	(252.4)	(84)	56.98	6.10	10.76	25.06
IIe	$C_{13}H_{18}N_2S_2$	104 – 106	58.59	6.81	10.51	24.06
	(266.5)	(83)	58.39	6.62	10.68	24.28
IIf	$C_{14}H_{20}N_2S_2$	115 – 116	59.96	7.19	9.99	22.86
	(280.5)	(82)	59.74	7.10	9.84	22.66
IIg	$C_{17}H_{20}N_2O_3S_2$	113 – 117	56.02	5.53	7.68	17.59
	(364.5)	(90)	56.05	5.91	7.91	17.46
IIIa	$C_{12}H_{15}N_5S_2$	128 – 133	49.12	5.16	23.87	21.85
	(293.4)	(54)	48.96	4.92	23.95	21.91
IIIb	$C_{13}H_{17}N_5S_2$	124 – 129	50.79	5.51	22.78	20.86
	(307.4)	(49)	50.56	5.54	22.59	20.92
IIIc	$C_{14}H_{19}N_5S_2$	124 – 127	52.31	5.95	21.78	19.95
	(321.5)	(53)	52.42	5.85	21.86	19.76

TABLE I
(*Continued*)

Compound	Formula (M. w.)	M. p., °C (Yield, %)	Calculated/Found			
			% C	% H	% N	% S[a]
IVa	$C_{23}H_{24}N_2O_3S_2$	34 – 35	62.70	5.49	6.36	14.55
	(440.6)	(67)	62.60	5.42	6.42	14.67
IVb	$C_{25}H_{28}N_2O_3S_2$	28 – 29	64.07	6.02	5.98	13.68
	(468.6)	(81)	63.92	5.92	5.78	13.70
IVc	$C_{19}H_{22}N_2O_3S_2$	31 – 32	58.44	5.68	7.17	16.42
	(390.5)	(65)	58.36	5.48	7.10	16.36
IVd	$C_{20}H_{24}N_2O_3S_2$	30 – 31	59.38	5.98	6.92	15.85
	(404.5)	(54)	59.46	5.81	6.71	15.76
IVe	$C_{21}H_{26}N_2O_3S_2$	27 – 28	60.26	6.26	6.69	15.32
	(418.6)	(62)	60.06	6.32	6.75	15.16
IVf	$C_{24}H_{25}N_2O_5S_2$	48 – 49	57.70	5.04	8.41	12.83
	(499.6)	(73)	57.66	5.37	8.38	12.76
Va	$C_{24}H_{23}N_3OS_3$	102 – 104	61.90	4.98	9.02	20.66
	(465.6)	(85)	61.72	4.68	9.05	20.56
Vb	$C_{20}H_{21}N_3OS_3$	63 – 64	57.78	5.09	10.11	22.91
	(415.6)	(85)	57.62	4.98	10.70	22.52
Vc	$C_{25}H_{23}N_3O_2S_3$	54 – 58	65.05	5.02	9.10	13.89
	(461.6)	(82)	64.92	5.00	9.16	13.63
Vd	$C_{19}H_{21}N_5S_2$	121 – 123	59.50	5.51	18.26	16.72
	(383.52)	(73)	59.63	5.28	18.16	16.61
Ve	$C_{21}H_{25}N_5S_2$	77 – 80	61.24	6.18	17.07	15.57
	(411.9)	(67)	61.36	6.26	17.16	15.36

[a] % of Cl.

These compounds were supposed to be potential pesticides, but none of them, tested for fungicide[23] and herbicide[24] activities by standard methods, showed effects comparable with those of the standards used.

EXPERIMENTAL

The ^1H NMR spectra of deuteriochloroform solutions containing tetramethylsilane as an internal reference were measured with a Bruker AM-300 apparatus operating at 300 MHz.

2,6-Dialkylphenylhydrazinium chlorides were synthesized according to refs[9,10]; the corresponding hydrazines were liberated with sodium hydroxide.

1-(2,6-Dimethylphenyl)-4-phenylsemicarbazide (*Ia*)

Phenyl isocyanate (1.1 g, 10 mmol) in ether (15 ml) was added to a stirred solution of 2,6-dimethylphenylhydrazine (1.64 g, 10 mmol) in ether (20 ml) at 15 °C. Stirring was continued at room temperature for additional 2 h. The precipitate was filtered off and washed with ether. Yield 2.1 g (77.6%).

This procedure was also applied for preparation of 1-(2-ethyl-6-methylphenyl)-4-phenylsemicarbazide (*Ib*), 1-(2-diethylphenyl)-4-phenylcarbazide (*Ic*) and 1-(2,6-dialkylphenyl)-4-(3-chlorophenyl)semicarbazides *Id* – *If*, when starting from 2,6-dialkylphenylhydrazines and 3-chlorophenyl isocyanate.

Characteristic data for compounds *Ia* – *If* are listed in Table I.

Benzyl-3-(2,6-dimethylphenyl)dithiocarbazate (*IIa*)

Concentrated ammonium hydroxide (2.3 ml) and dropwise carbon disulfide (2 g, 20 mmol) were added to a stirred solution of 2,6-dimethylphenylhydrazine (3 g, 20 mmol) in ethanol (20 ml) at 5 – 10 °C. The mixture was stirred at 25 – 30 °C for 1 h; then, benzyl bromide (3.42 g, 20 mmol) was poured in and stirring was continued at 25 – 30 °C for 24 h. Afterwards, water (40 ml) was added, the mixture was cooled to 5 °C, the product was filtered off, washed with water to a neutral reaction and dried at 25 – 30 °C.

Benzyl 3-(2-ethyl-6-methylphenyl)dithiocarbazate (*IIb*) and benzyl 1-(2,6-dialkylphenyl)dithiocarbazate (*IIc*) were prepared from 2,6-dialkylphenylhydrazines and benzyl bromide, allyl 3-(2,6-dialkylphenyl)dithiocarbazates *IId* – *IIf* from allyl bromide and 5-methoxycarbonyl-2-furfuryl-3-(2-ethyl-6-methyl)dithiocarbazate (*IIg*) from methyl 5-chloromethyl-2-furancarboxylate.

1,2,4-Triazol-1-ylmethyl-3-(2,6-dialkylphenyl)dithiocarbazates *IIIa* – *IIIc* were prepared from 1-chloromethyl-1,2,4-triazole in an analogous way.

Characteristic data for compounds *IIa* – *IIg* and *IIIa* – *IIIc* are presented in Table I.

TABLE II
^{1}H NMR data (δ, ppm) of compounds *Ia* – *If*

Compound	H_{arom}[a]	NH	R^1	R^2
Ia	7.48 d, 7.30 t, 7.06 d	8.20 bs, 6.45 bs	2.34 s	2.34 s
Ib	7.44 d, 7.30 t, 7.06 d	8.23 bs, 6.42 bs	2.34 s	2.70 q 1.25 t
Ic	7.50 d, 7.30 t, 7.06 d	8.28 bs, 6.45 bs	2.71 q 1.26 t	2.71 q 1.26 t
Id	7.62 t, 7.30 d, 7.20 t	8.28 bs, 6.52 bs	2.34 s	2.34 s
Ie	7.62 t, 7.30 d, 7.20 t	8.30 bs, 6.53 bs	2.35 s	2.71 q 1.26 t
If	7.62 t, 7.30 d, 7.20 t	8.30 bs, 6.55 bs	2.70 q 1.26 t	2.70 q 1.26 t

[a] For *Ia* – *If*: 6.90 – 7.10 m (H-3, H-4, H-5).

N-(2,6-Dimethylphenylamino)-S-benzyl-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVa*)

Benzyl 3-(2,6-dimethylphenyl)dithiocarbazate (3.0 g, 10 mmol) was dropped into methanolic potassium hydroxide (0.6 g, 25 ml) with stirring at 15 °C, till a homogeneous solution is formed. Methyl 5-chlo-

TABLE III
^{1}H NMR data (δ, ppm; *J*, Hz) of compounds *IIa* – *IIg*

Compound	R^1	R^2	NH	R^3			
				CH_2	H-A	H-B	H-C
IIa[a]	2.30 s	2.30 s	8.36; 5.88 bs	4.55 s	–	–	–
IIb[a]	2.34 s	2.66 q 1.22 t	8.23; 5.90 bs	4.57 s	–	–	–
IIc[a]	2.61 q 1.15 t	2.61 q 1.15 t	8.20; 5.78 bs	4.50 s	–	–	–
IId[b]	2.31 s	2.31 s	8.53; 5.89 bs	3.96 d	5.32 d	5.17 d	5.91 m
IIe[b]	2.21 s	2.56 q 1.13 t	8.22; 5.82 bs	3.85 d	5.22 d	5.07 d	5.82 m
IIf[b]	2.61 q 1.16 t	2.61 q 1.16 t	8.13; 5.85 bs	3.91 d	5.27 d	5.11 d	5.85 m
IIg[c]	2.31 s	2.62 q 1.21 t	8.37; 5.87 bs	4.64 s	–	–	–

[a] For *IIa* – *IIc*: 6.90 – 7.05 m (H-3, H-4, H-5), 7.00 – 7.40 m (C_6H_5); [b] for *IId* – *IIf*: R^3 = CH_2–CH_C= $C(H_A)$–H_B, *J*(H-A, H-C) = 16.9, *J*(H-B, H-C) = 9.7, *J*(H-A, H-B) ~ 1, *J*(CH_2, H-C) = 6.6; [c] furan protons: 7.10 d (H-4'), 6.50 d (H-3'), *J*(H-3', H-4') = 3.6.

TABLE IV
^{1}H NMR data (δ, ppm; *J*, Hz) of compounds *IIIa* – *IIIc*

Compound	H_{arom}[a]	R^1	R^2	CH_2	H-3'	H-5'	NH
IIIa	7.00 bs	2.25 s	2.25 s	6.08 s	7.77 s	8.51 s	9.46 bs 6.00 bs
IIIb	7.05 bs	2.26 s	2.61 q 1.18 t	6.10 s	7.85 s	8.56 s	9.21 bs 6.02 bs
IIIc	7.09 bs	2.59 q 1.15 t	2.59 q 1.15 t	6.06 s	7.61 s	8.39 s	10.00 bs 6.00 bs

[a] Protons H-3, H-4, H-5.

TABLE V
^{1}H NMR data (δ, ppm; *J*, Hz) of compounds *IVa – IVf*

Compound[a]	H-3′	H-4′	CH_2	OCH_3	R^3				R^1	R^2
					CH_2	H-A	H-B	H-C		
IVa[b]	6.16 d	7.01 d	4.18 s	3.84 s	4.14 s	–	–	–	2.20 s	2.20 s
IVb[b]	6.10 d	7.14 d	4.12 s	3.76 s	4.03 s	–	–	–	2.45 q 1.05 t	2.45 q 1.05 t
IVc[c]	6.36 d	7.06 d	4.25 s	3.84 s	3.57 dt	5.11 d	5.06 d	5.89 m	2.25 s	2.25 s
IVd[c]	6.09 d	6.93 d	4.09 s	3.79 s	3.51 dt	5.12 d	5.00 d	5.75 m	2.20 s	2.57 q 1.11 t
IVe[c]	6.30 d	7.00 d	4.18 s	3.78 s	3.48 dt	5.08 d	5.00 d	5.78 m	2.51 q 1.10 t	2.51 q 1.10 t
IVf[b]	6.10 d	7.00 d	4.22 s	3.86 s	4.14 s	–	–	–	2.15 s	2.49 q 1.11 t

[a] For *IVa – IVe*: 6.80 – 7.00 m (H-3, H-4, H-5); [b] for *IVa*, *IVb*: 7.20 – 7.30 m (C_6H_5), for *IVf*: 8.13 (H-B), 7.45 (H-A); [c] $J(CH_2, H\text{-}C)$ = 6.6, *J*(H-A, H-C) = 16.9, *J*(H-B, H-C) = 10.2, *J*(H-A, H-B) = 1.0.

TABLE VI
^{1}H NMR data (δ, ppm; *J*, Hz) of compounds *Va – Ve*

Compound	H_{arom}[a]	R^1	R^2	R^3		CH_2N	Other signals	
				CH_2	C_6H_5			
Va	6.70 – 6.90 m	2.02 s	2.02 s	4.05 s	[b]	5.32 s	7.05 – 7.35	H_{arom}
Vb	6.70 – 6.90 m	2.05 s	2.05 s	3.50 d	[c]	5.35 s	7.05 – 7.35	H_{arom}
Vc	6.90 – 7.05 m	2.18 s	2.18 s	4.13 s	[b]	4.88 s	7.05 – 7.35	H_{arom}
Vd[d]	6.75 – 6.95 m	2.08 s	2.08 s	4.06 s	7.16 bs	5.48 s	7.85 H-5′ 7.70 H-3′	
Ve[d]	6.96 bs	2.41 q 1.05 t	2.41 q 1.05 t	4.05 s	7.18 bs	5.50 s	7.86 H-5′ 7.72 H-3′	

[a] Protons H-3, H-4, H-5; [b] in multiplet H_{arom} of substituent R^4; [c] protons for CH_2–CH=CH_2: 5.11 (H-A), 5.01 (H-B), 5.81 (H-C), *J*(A,C) = 16.9, *J*(B,C) = 10.2, *J*(A,B) ~ 1.0, $J(CH_2, H\text{-}C)$ = 6.6; [d] protons of 1,2,4-triazole: H-3′, H-5′.

romethyl-2-furancarboxylate (1.7 g, 10 mmol) was added and stirred at 25 °C for 3 h. The mixture was poured into ice water (100 ml), the precipitate was filtered and crystallized from ethanol.

This procedure was applied for preparation of N-(2,6-diethylphenylamino)-S-benzyl-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVb*), N-(2,6-dimethylphenylamino)-S-allyl-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVc*), N-(2-ethyl-6-methylphenylamino)-S-allyl-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVd*), N-(2,6-diethylphenylamino)-S-allyl-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVe*), and N-(2-ethyl-6-methylphenylamino)-S-(4-nitrobenzyl)-S-(5-methoxycarbonyl-2-furfuryl)imidodithiocarbonate (*IVf*).

Compounds *Va* – *Ve* were obtained by applying the procedure for preparation of *IVa*. Characteristic data for compounds *IVa* – *IVf* and *Va* – *Ve* are listed in Table I.

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