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Tertiary Acetylenic Alcohols and Peroxides Derived from 4,4'-Bis(dimethylamino)benzophenone (Michler's Ketone)

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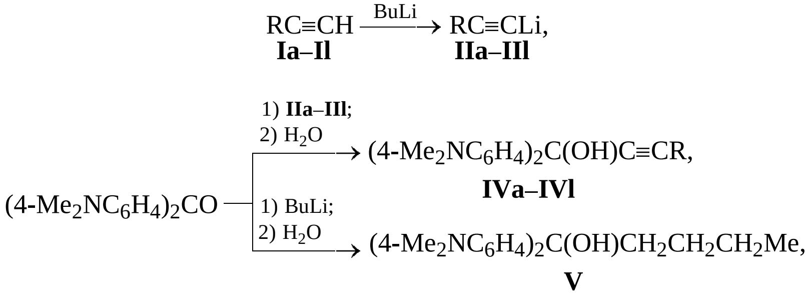
Abstract—Tertiary acetylenic alcohols were obtained by treatment of 4,4'-bis(dimethylamino)benzophenone with 1-alkynyl- and 2-phenylehynyl, as well as lithium *tert*-alkylperoxyacetylides.

Previously we reported on the synthesis of acetylenic nitrogen-containing peroxy alcohols by the action of lithium peroxyacetylides on aminobenzaldehydes, 2*e*-methyldecahydroquinolin-4-one, and γ-aminoketones [1–3]. Acetylenic alcohols with various functional groups, including nitrogen-containing, have been studied in terms of biological activity [4].

In the present work we describe the synthesis of tertiary acetylenic nitrogen-containing alcohols **IVa**–**IVl** from lithium acetylides **IIa**–**IIl** obtained by metalation of 1-alkynes **Ia**–**Il** with butyllithium, and 4,4'-bis(dimethylamino)benzophenone (Michler's ketone) (**III**). Alcohols **IVa**–**IVl** were isolated with preparative yields (69–86%). The O–O bond in compounds **IIf**–**IIl** does not prevent reaction and does not adversely affect the yields of the target products [1–3].

The reaction of Michler's ketone (**III**) with butyllithium gave alcohol **V** in 84% yield.



$$\underset{\mathbf{Ia–Il}}{RC{\equiv}CH} \xrightarrow{BuLi} \underset{\mathbf{IIa–IIl}}{RC{\equiv}CLi},$$

$$(4\text{-}Me_2NC_6H_4)_2CO \xrightarrow[2)\ H_2O]{1)\ \mathbf{IIa–IIl};} \underset{\mathbf{IVa–IVl}}{(4\text{-}Me_2NC_6H_4)_2C(OH)C{\equiv}CR},$$

$$(4\text{-}Me_2NC_6H_4)_2CO \xrightarrow[2)\ H_2O]{1)\ BuLi;} \underset{\mathbf{V}}{(4\text{-}Me_2NC_6H_4)_2C(OH)CH_2CH_2CH_2Me},$$

I, II, IV, R = H (**a**), $(CH_2)_3Me$ (**b**), $(SH_2)_{14}Me$ (**c**), $(CH_2)_{15}Me$ (**d**), Ph (**e**), CMe_2OOCMe_3 (**f**), CMe_2OOCMe_2Et (**g**), CMe_2OOCMe_2Pr (**h**), $CMe_2OOCMe_2(CH_2)_4Me$ (**i**), $CMe_2OOCMe_2C_6H_{11}$-*cyclo* (**j**), CMe_2OOCPh_3 (**k**), $CMe_2OOCMe_2C{\equiv}CCMe_2OOCMe_3$ (**l**).

Compound **IVa**–**IVl** and **V** are colorless crystals. They can be handled for a long time in sealed ampules in the dark but darken quickly on contact with air and light. The composition and structure of compounds **IVa**–**IVl** and **V** were proved by TLC, elemental analysis (Table 1), and ^1H NMR (Table 2), IR, and UV spectroscopy (Table 3).

It was found by thermal analysis [5] that peroxy alcohols **IVf**–**IVl** are rather fairly stable thermally. Alkylperoxy alcohols **IVf**–**IVi** begin to decompose at appreciable rate and a well-defined exothermic effect at 118–128°C, cycloalkylperoxy alcohol **IVj**, at 116°C, whereas bis(alkylperoxy) alcohols, at 130°C. The weight losses in the first stage (up to 185–225°C) are 17–30 (**IVf**–**IVj**) and 40% (**IVl**). The weight loss for arylalkylperoxy alcohol **IVk** up to 145°C is no more than 4%, which is associated with the formation of nonvolatile decomposition products.

EXPERIMENTAL

The IR spectra were measured on a Specord IR-75 instrument in KBr pellets. The ^1H NMR spectra were

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Table 1. Properties of compounds **IVa–IVl** and **V**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calculated
IVa	86	141–142	77.84	7.71	9.40	$C_{19}H_{22}N_2O$	77.52	7.53	9.52	290.1	294.4
IVb	78	44–45	79.16	8.81	8.06	$C_{23}H_{30}N_2O$	78.82	8.63	7.99	341.2	350.5
IVc	71	54–55	81.22	10.50	5.21	$C_{34}H_{52}N_2O$	80.90	10.38	5.55	493.0	504.8
IVd	80	55–56	81.31	10.48	5.53	$C_{35}H_{54}N_2O$	81.03	10.49	5.40	506.3	518.8
IVe	83	166–167	81.17	7.27	7.56	$C_{25}H_{26}N_2O$	81.05	7.07	7.56	359.8	370.5
IVf	73	101–102	73.91	8.70	6.51	$C_{26}H_{36}N_2O_3$	73.55	8.55	6.60	416.3	424.6
IVg	72	76–77	74.15	8.99	6.07	$C_{27}H_{38}N_2O_3$	73.94	8.73	6.39	425.1	438.6
IVh	81	63–64	74.73	9.11	5.95	$C_{28}H_{40}N_2O_3$	74.30	8.91	6.19	440.7	452.6
IVi	78	71–72	75.21	9.07	5.49	$C_{30}H_{44}N_2O_3$	74.96	9.23	5.83	468.4	480.7
IVj	81	87–88	75.53	9.06	5.91	$C_{31}H_{44}N_2O_3$	75.57	9.00	5.69	479.5	492.7
IVk	74	158–159	81.02	7.12	4.11	$C_{41}H_{42}N_2O_3$	80.62	6.93	4.59	583.6	610.8
IVl	69	76–77	72.72	8.45	5.41	$C_{34}H_{48}N_2O_5$	72.31	8.57	4.96	543.8	564.8
V	84	111–112	77.16	9.27	8.74	$C_{21}H_{30}N_2O$	77.26	9.26	8.58	320.7	326.5

Table 2. ^{1}H NMR spectra of compounds **III, IVa–IVl**, and **V**

Comp. no.	^{1}H NMR spectrum, δ, ppm
III	3.04 s (12H, Me_2N), 6.56–7.88 m (8H, $2C_6H_4$)
IVa	2.67 s (1H, OH), 2.78 s (1H, C≡CH), 2.91 s (12H, $2Me_2N$), 6.55–7.55 m (8H, $2C_6H_4$)
IVb	0.95 t (3H, Me), 1.12–2.15 m [4H, $(CH_2)_2$], 2.22 t (2H, $CH_2C≡C$), 2.50 s (1H, OH), 2.92 s (12H, Me_2N), 6.53–7.53 m (8H, $2C_6H_4$)
IVc	0.89 t (3H, Me), 1.10–1.70 m [26H, $(CH_2)_{13}$], 2.28 t (2H, $CH_2C≡C$), 2.54 s (1H, OH), 2.90 s (12H, Me_2N), 6.48–7.48 m (8H, $2C_6H_4$)
IVd	0.88 t (3H, Me), 1.10–1.70 m [28H, $(CH_2)_{14}$], 2.32 t (2H, $CH_2C≡C$), 2.58 s (1H, OH), 2.91 s (12H, Me_2N), 6.55–7.50 m (8H, $2C_6H_4$)
IVe	2.78 s (1H, OH), 2.92 s (12H, $2Me_2N$), 6.57–6.80 m, 7.17–7.65 m (13H, $2C_6H_4$ i Ph)
IVf	1.23 s (9H, Me_3COO), 1.50 s (6H, Me_2C), 2.69 s (1H, OH), 2.90 s (12H, Me_2N), 6.50–7.55 m (8H, $2C_6H_4$)
IVg	0.87 t (3H, Me), 1.18 s (6H, Me_2COO), 1.51 q (2H, CH_2), 1.52 s (6H, Me_2C), 2.61 s (1H, OH), 2.90 s (12H, Me_2N), 6.55–7.55 m (8H, $2C_6H_4$)
IVh	0.88 t (3H, Me), 1.20 s (6H, Me_2COO), 1.50 s (6H, Me_2C), 1.40–1.55 m [4H, $(CH_2)_2$], 2.68 s (1H, OH), 2.89 s (12H, Me_2N), 6.48–7.48 m (8H, $2C_6H_4$)
IVi	0.87 t (3H, Me), 1.20 s (6H, Me_2COO), 1.22–1.70 m [8H, $(CH_2)_4$], 1.52 s (6H, Me_2C), 2.64 s (1H, OH), 2.90 s (12H, Me_2N), 6.50–7.50 m (8H, $2C_6H_4$)
IVj	1.00–1.90 m [11H, C_6H_{11}], 1.15 s (6H, Me_2COO), 1.51 s (6H, Me_2C), 2.60 s (1H, OH), 2.90 s (12H, Me_2N), 6.55–7.50 m (8H, $2C_6H_4$)
IVk	1.32 s (6H, Me_2C), 2.41 s (1H, OH), 2.89 s (12H, Me_2N), 6.45–7.50 m (23H, $2C_6H_4$ i CPh_3)
IVl	1.24 s (9H, Me_3COO), 1.42 s, 1.48 s, 1.56 s (18H, $3Me_2C$), 2.62 s (1H, OH), 2.91 s (12H, Me_2N), 6.50–7.50 m (8H, $2C_6H_4$)
V	0.87 t (3H, Me), 1.18–1.45 m [4H, $(CH_2)_2$], 1.95 s (1H, OH), 2.18 t [2H, $C\underline{H}_2C(OH)$], 2.90 s (12H, Me_2N), 6.55–7.30 m (8H, $2C_6H_4$)

Table 3. IR and UV spectra of compounds **III, IVa**–**IVl**, and **V**

Comp. no.	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm ($\varepsilon \times 10^{-3}$)
III	3090, 3040 (CH_{Ar}); 2980, 2895, 2820 (CH_{Alk}); 1595 (C=O); 1560, 1525 (Ar); 825, 815, 760, 745 (CH_{Ar})	208 (19), 247 (11), 368 (25)
IVa	3270 (≡C–H); 3205 (OH); 3100, 3075, 3030 (CH_{Ar}); 2995, 2960, 2910, 2880, 2855, 2810, 2800 (CH_{Ar}); 2100 (C≡C); 1605, 1560, 1510 (Ar); 1055 (C–OH); 825, 815 (CH_{Ar})	211 (15), 263 (11), 309 (10), 396 (15), 620 (15), 690 (22)
IVb	3290 (OH); 3090, 3070, 3035 (CH_{Ar}); 2965, 2935, 2800 (CH_{Alk}); 2225 (C≡C); 1610, 1510 (Ar); 1445 (CH_2); 1025 (C–OH); 830, 810 (CH_{Ar})	208 (19), 258 (12), 390 (9), 420 (15), 620 (14), 680 (70)
IVc	3245 (OH); 3095, 3975, 3040 (CH_{Ar}); 2955, 2920, 2850, 2800 (CH_{Alk}); 2225 (C≡C); 1615, 1560, 1525, 1515 (Ar); 1470 (CH_2); 1025 (C–OH); 840, 820, 805 (CH_Ar)	210 (18), 258 (12), 315 (25), 420 (16), 445 (27), 655 (92)
IVd	3260 (OH); 3090, 3075, 3040, 3005 (CH_{Ar}); 2980, 2955, 2945, 2850, 2805 (CH_{Alk}); 2225 (C≡C); 1610, 1570, 1525, 1505 (Ar); 1025 (C–OH); 840, 820, 805 (CH_{Ar})	208 (22), 258 (12), 328 (30), 420 (18), 440 (30), 650 (100)
IVe	3100, 3080, 3030 (CH_{Ar}); 2980, 2960, 2880, 2840, 2790 (CH_{Alk}); 1605, 1590, 1520, 1505 (Ar); 1050 (C–OH); 840, 820, 805, 790, 755, 690 (CH_{Ar})	208 (16), 250 (12), 312 (15), 485 (38), 675 (100)
IVf	3240 (OH); 3090, 3070, 3035 (CH_{Ar}); 2975, 2925, 2875, 2850, 2795 (CH_{Alk}); 1605, 1505 (Ar); 1020 (C–OH); 870 (O–O); 830, 810, 775, 745 (CH_{Ar})	209 (16), 258 (9), 367 (9), 418 (10), 444 (10), 670 (60)
IVg	3250 (OH); 3095, 3075, 3040 (CH_{Ar}); 2975, 2930, 2880, 2845, 2800 (CH_{Alk}); 1605, 1520, 1505 (Ar); 1470 (CH_2); 1020 (C–OH); 860 (O–O); 835, 805, 780, 750 (CH_{Ar})	208 (15), 255 (10), 370 (9), 400 (9), 442 (9), 620 (20), 670 (58)
IVh	3425 (OH); 3100, 3080, 3040 (CH_{Ar}); 2985, 2960, 2935, 2890, 2870, 2805 (CH_{Alk}); 1605, 1505 (Ar); 1470 (CH_2); 1020 (C–OH); 870 (O–O); 825, 820, 810, 745 (CH_{Ar})	208 (15), 255 (9), 370 (9), 400 (8), 441 (8), 620 (18), 670 (61)
IVi	3400 (OH); 3095, 3075, 3040 (CH_{Ar}); 2980, 2955, 2940, 2890, 2855, 2805 (CH_{Alk}); 2225 (C≡C); 1610, 1565, 1510 (Ar); 1470 (CH_2); 1020 (C–OH); 870 (O–O); 825, 810 (CH_{Ar})	211 (14), 258 (8), 310 (7), 400 (8), 440 (8), 610 (15), 650 (58)
IVj	3400 (OH); 3090, 3080, 3040 (CH_{Ar}); 2955, 2930, 2850, 2805 (CH_{Alk}); 1610, 1565, 1515 (Ar); 1475 (CH_2); 1020 (C–OH); 870 (O–O); 820 (CH_{Ar})	211 (15), 258 (7), 312 (16), 420 (9), 440 (15), 650 (90)
IVk	3400, 3120 (OH); 3090, 3055, 3040, 3025 (CH_{Ar}); 2980, 2905, 2875, 2845, 2805, 2795 (CH_{Alk}); 2230 (C≡C); 1610, 1565, 1510, 1495 (Ar); 1025 (C–OH); 880 (O–O); 840, 820, 775, 770, 750, 700 (CH_{Ar})	211 (35), 258 (8), 315 (12), 425 (7), 440 (14), 670 (65)
IVl	3420, 3220 (OH); 3100, 3075, 3030 (CH_{Ar}); 2985, 2940, 2885, 2845, 2800 (CH_{Alk}); 2230 (C≡C); 1610, 1565, 1520, 1510 (Ar); 1025 (C–OH); 880 (O–O); 840, 825, 810 (CH_{Ar})	211 (20), 258 (12), 315 (10), 420 (12), 444 (22), 680 (90)
V	3280 (OH); 3100, 3080, 3040, 3015 (CH_{Ar}); 2960, 2940, 2880, 2850, 2800 (CH_{Alk}); 1620, 1520 (Ar); 1475 (CH_2); 840, 820, 805, 775 (CH_{Ar})	210 (16), 265 (11), 300 (8), 605 (16)

obtained on a Tesla BS-567A instrument in $CDCl_3$, internal reference TMS. The UV and visible specta were taken on a Specord UV-Vis instrument in 1×10^{-4} M solutions in methanol. Freshly prepared solutions were used. Thermal analysis was performed on a Paulik–Paulik–Erdey derivatograph in argon, heating rate 7 deg/min. Sample 100 mg, DTA 1/10, DTG 1/10. Purity control was performed by TLC on Silufol plates, eluent hexane–diethyl ether (3:1), developer *N*,*N*-dimethyl-*p*-phenylenediamine dihydrochloride. The analysis of peroxides **IVf**–**IVl** for active oxygen by iodometry with conc. HCl [6] gave overestimated results, apparently, because of the presence of a C≡C bond. The molecular weights were determined by cryoscopy in benzene.

Peroxy alkynes **If**–**Il** and bytillithium were synthesized by the procedures in [7, 8].

1,1-Di[4,4'-bis(dimethylamino)phenyl]-2-propyn-1-ol (IVa). Michler's ketone (**III**), 0.02 mol, was added in one portion to a solution of 0.03 mol of lithium acetylide HC≡CLi (**IIa**) [obtained by adding dropwise over the course of 0.5 h at –70°C a hexane solution of butyllithium (0.03 mol) to 100 ml of absolute THF through which we barboted acetylene **Ia**. The reaction mixture was stirred for 4 h at 20–23°C and left to stand for 18 h. The lithium alcoholate that formed was treated with 300 ml of water, alcohol **VIa** was extracted with ether, and the extract was dried with $CaCl_2$. The solvent was removed, and the reaction product was recrystallized from hexane.

4,4'-Bis(dimethylaminophenyl)alkynyl(arylalkynyl)methanols IVb–IVl. A hexane solution of 0.011 mol of butyllithium was added under argon over the course of 0.5 h to a cooled (–40 to –20°C) and vigorously stirred solution of 0.013 mol of 1-alkyne **Ib**–**Il** in 20 ml of absolute THF. The mixture was stirred for 1 h, and, after addition of 0.01 mol of Michler's ketone (**III**), heated to 0–5°C 0.02 over the course of 1–2 h, stirred for an additional 3–4 h, left to stand for 18 h at 20–23°C, and treated with 300 ml of water. Alcohols **VIb**–**VIl** were extracted with ether, the extracts were dried with $CaCl_2$, the solvent was removed, and the reaction products were recrystallized from hexane.

1,1-Di[4,4'-bis(dimethylamino)phenyl]-1-pentanol (V). A hexane solution of 0.013 mol of butyllithium was added under argon over the course of 0.5 h to a cooled (0–5°C) and vigorously stirred solution of 0.011 mol of Michler's ketone (**III**) in 50 ml of absolute THF. The mixture was stirred of 1 h, heated to 20–23°C over the course of 1–2 h, stirred for an additional 3–4 h, left to stand for 18 h at 20–23°C, and treated with 300 ml of water. Alcohol **V** was extracted with ether, the extract was dried with $CaCl_2$, the solvent was removed, and the reaction product was recrystallized from hexane.

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