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Dedicated to Full Member of the Russian Academy of Sciences
M.G. Voronkov on his 90th anniversary

Synthesis of α,ω-Bis(pyrazol-3-yl)alkanes: I. 1,4-Bis(1-methyl- and 1-benzyl-5-chloro-1*H*-pyrazol-3-yl)-butanes from 1,1,10,10-Tetrachlorodeca-1,9-diene-3,8-dione and 1,1-Dimethyl- or Benzylhydrazine

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Abstract—First representatives of bis-2-chloro- and 2,2-dichlorovinyl ketones, 1,10-dichlorodeca-1,9-diene-3,8-dione and 1,1,10,10-tetrachlorodeca-1,9-diene-3,8-dione, were synthesized by reaction of hexanedioyl dichloride with acetylene and 1,1-dichloroethene, respectively, in the presence of $AlCl_3$. 1,1,10,10-Tetrachlorodeca-1,9-diene-3,8-dione reacted with benzylhydrazine and 1,1-dimethylhydrazine to give 1,4-bis(1-benzyl-5-chloro-1*H*-pyrazol-3-yl)butane and 1,4-bis(5-chloro-1-methyl-1*H*-pyrazol-3-yl)butane, respectively.

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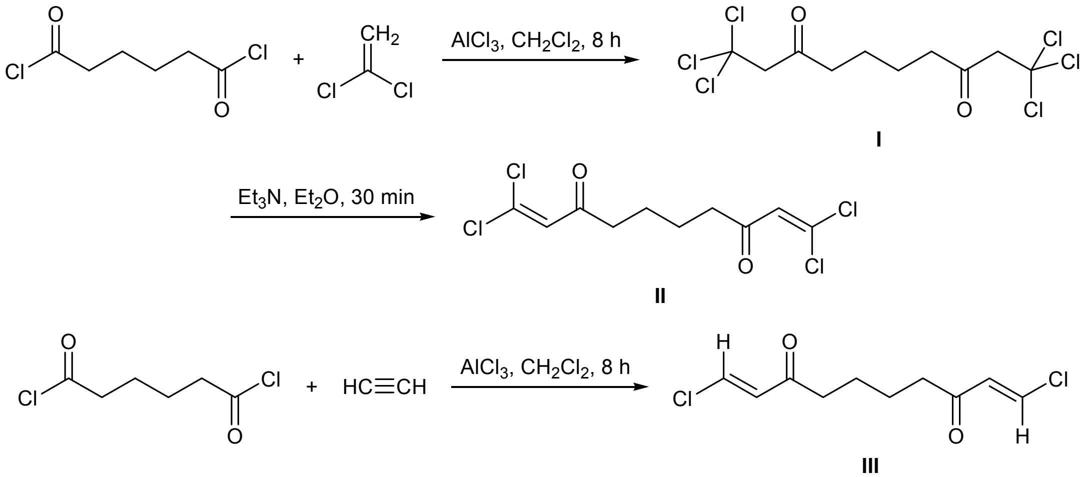
Organic compounds containing two and more pyrazole fragments attract considerable interest from both theoretical and practical viewpoints primarily due to the possibility of using them as ligands for the preparation of polynuclear complexes and coordination polymers possessing valuable properties [1–17]. Multitopic pyrazole-containing ligands are also used as sorbents and intermediate products for the synthesis of compounds exhibiting biological and catalytic activity, and they can be involved in self-assembly of supramolecular ensembles, etc. On the other hand, organic polypyrazole ligands were studied insufficiently because of their low accessibility; therefore, search for new synthetic approaches to such compounds remains an important problem [1–17].

The most widely known are ensembles in which pyrazole ring is linked through the pyrrole-type nitrogen atom [1–12]. 4,4′-Bis-pyrazole systems are fairly accessible; they are synthesized by reactions of polyelectrophiles with pyrazoles, aldehydes, and ketones [13–15]. A number of 3(5)-methyl(ethyl)-substituted bis-pyrazoles bridged at the 5,5′(3,3′)-positions by alkanediyl, 1,4-methylenephenyl, and 1,4′-diphenyleneoxy(disulfido) spacers were obtained by reaction of the corresponding bis-β-diketones with hydrazine hydrate [16, 17]. Thus chemoselective synthesis of 3,3′-bridged bis-pyrazoles attracts strong interest.

We develop a novel approach to linearly bridged α,ω-bis(pyrazol-3-yl)alkanes via heterocyclization of difunctional halovinyl ketones. In the present communication we report on the synthesis of first representatives of difunctional 2,2-dichloro- and 2-chlorovinyl ketones, 1,1,10,10-tetrachlorodeca-1,9-diene-3,8-dione (**II**) and 1,10-dichlorodeca-1,9-diene-3,8-dione (**III**) by reactions of adipoyl chloride with 1,1-dichloroethene and acetylene, respectively, in the presence of aluminum chloride according to the procedure described in [18] (Scheme 1). The reactions were carried out in methylene chloride at –5 to 20°C (reaction time 8 h. Unlike known procedures for the synthesis of alkyl 2,2-dichlorovinyl ketones [18], dehydrochlorination of 1,1,1,10,10,10-hexachlorodecane-3,8-dione (**I**) was effected by treatment with triethylamine. The yields (unoptimized) of ketones **II** and **III** were 21 and 62%, respectively. Compounds **II** and **III** were isolated as crystalline substances with a specific odor; they were poorly soluble in hexane and readily soluble in other organic solvents.

Scheme 1.



We previously showed [19] that 2,2-dichlorovinyl alkyl (or aryl) ketones chemoselectively react with alkyl-, aryl-, and dialkylhydrazines to give the corresponding 1-substituted 5-chloropyrazoles. Reactions of 2-chlorovinyl alkyl ketones with dialkylhydrazines lead to 1,3-substituted pyrazoles, whereas alkylhydrazines give rise to mixtures of 1,3- and 1,5-dialkylpyrazoles [20]. We have found that bis(dichlorovinyl ketone) **II** reacts with benzylhydrazine and 1,1-dimethylhydrazine in a chemoselective fashion, yielding previously unknown bridged bis-pyrazoles, 1,4-bis(1-benzyl-5-chloro-1*H*-pyrazol-3-yl)butane (**IV**) and 1,4-bis(5-chloro-1-methyl-1*H*-pyrazol-3-yl)butane (**V**), respectively, in up to 83% yield (Scheme 2). Pyrazoles **IV** and **V** are oily substances with a specific odor; they are poorly soluble in hexane and readily soluble in other organic solvents. The structure of diketones **I**–**III** and bis-pyrazoles **IV** and **V** was confirmed by their ^{1}H and ^{13}C NMR spectra and elemental analyses.

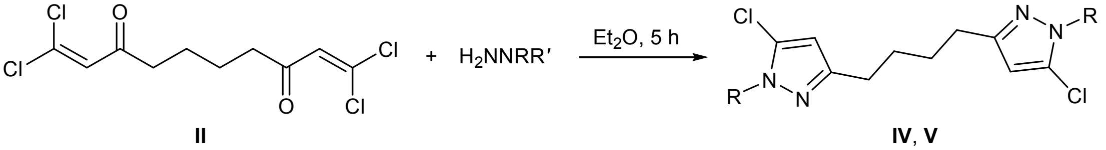
Thus we were the first to synthesize bis(chloro- and dichlorovinyl ketones) and demonstrate their potential for the synthesis of bis-pyrazole ensembles.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400.13 and 100.61 MHz, respectively, from solutions in $CDCl_3$ using hexamethyldisiloxane as internal reference. Adipoyl chloride was prepared by heating a mixture of adipic acid and 4 equiv of thionyl chloride under reflux over a period of 40 h; bp 95–97°C (4 mm).

1,1,1,10,10,10-Hexachlorodecane-3,8-dione (I) and 1,1,10,10-tetrachlorodeca-1,9-diene-3,8-dione (II). Adipoyl chloride, 9.15 g (0.05 mol), was dissolved in 100 ml of thionyl chloride, 13.33 g (0.1 mol) of aluminum chloride was added under vigorous stirring at room temperature, and the mixture was stirred for 15–20 min. The mixture was then cooled to –5 to 0°C, 5.82 g (0.06 mol) of 1,1-dichloroethene was added dropwise over a period of 10 min, and the mixture was stirred for 8 h, allowing it to gradually warm up to 20°C, and poured onto ice. The organic phase was separated, the aqueous phase was extracted with methylene chloride, and the extract was combined with the organic phase and dried over $MgSO_4$. The drying agent was filtered off, and the filtrate was evaporated. The residue was a mixture containing 78% of diketone **I** and 22% of diketone **II**. Recrystallization from hexane gave 4.12 g of mixture **I**/**II** with mp 36–50°C. ^{1}H NMR spectrum, δ, ppm: **I**: 1.63 m (4H, CH_2, $J = 6.8$ Hz), 2.26 m (4H, CH_2, $J = 6.8$ Hz), 3.79 s (4H, CH_2CCl_3); **II**: 1.62 m (4H, CH_2, $J = 6.9$ Hz), 2.30 m (4H, CH_2, $J = 6.9$ Hz), 6.67 s (2H, CH=). ^{13}C NMR

Scheme 2.



R = H, R′ = $PhCH_2$; R = R′ = Me; **IV**, R = $PhCH_2$; **V**, R = Me.

spectrum, δ_C, ppm: **I**: 22.7 (CH_2), 43.8 (CH_2), 63.8 (CH_2), 92.8 (CCl_3), 200.7 (CO); **II**: 19.6 (CH_2), 22.7 (CH_2), 43.6 (CH_2), 126.3 (=CH), 134.5 (CCl_2), 195.0 (CO).

1,1,10,10-Tetrachlorodeca-1,9-diene-3,8-dione (II). A solution of 4.12 g of diketone mixture **I**/**II** in 50 ml of diethyl ether was cooled to –5 to 0°C, an equimolar amount of triethylamine was added, and the mixture was stirred for 10 min and treated with water. The organic phase was separated, dried over $MgSO_4$, filtered, and evaporated, and the residue was recrystallized from hexane. Yield 3.16 g (21%, calculated on the initial adipoyl chloride), mp 76–78°C. Found, %: C 39.71; H 3.52; Cl 46.05. $C_{10}H_{10}Cl_4O_2$. Calculated, %: C 39.51; H 3.32; Cl 46.65.

1,10-Dichlorodeca-1,9-diene-3,8-dione (III). Acetylene was bubbled over a period of 2 h through a solution of 9.15 g (0.05 mol) of adipoyl chloride in 100 ml of methylene chloride under vigorous stirring at room temperature. The mixture was cooled to 0°C, 13.33 g (0.1 mol) of aluminum chloride was added, and the mixture was stirred for 8 h, allowing it to slowly warm up to 20°C, and poured onto ice. The organic phase was separated, the aqueous phase was extracted with methylene chloride, the extract was combined with the organic phase, dried over $MgSO_4$, filtered, and evaporated, and the residue was recrystallized from petroleum ether. Yield 7.29 g (62%), *E*/*Z*-isomer ratio ~99:1, mp 63–66°C. ^1H NMR spectrum, δ, ppm: *E* isomer: 1.63 m (4H, CH_2, $J = 6.8$ Hz), 2.54 m (4H, CH_2, $J = 6.8$ Hz), 6.50 d (2H, CH=, $J = 13.6$ Hz), 7.28 d (2H, CHCl, $J = 13.6$ Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.8 (CH_2), 41.2 (CH_2), 132.4 (=CH), 136.9 (=CHCl), 196.9 (CO). Found, %: C 50.71; H 5.52; Cl 30.05. $C_{10}H_{12}Cl_2O_2$. Calculated, %: C 51.09; H 5.14; Cl 30.16.

3,3′-(Butane-1,4-diyl)bis(1-benzyl-5-chloro-1*H*-pyrazole) (IV). Diketone **II**, 1.52 g (0.005 mol), was dissolved in 50 ml of diethyl ether, and 1.22 g (0.01 mol) of benzylhydrazine and 1.01 g of triethylamine were added dropwise. When the exothermic reaction was over, the mixture was stirred for 5 h and poured into water. The organic phase was separated, the aqueous phase was extracted with diethyl ether, and the extract was combined with the organic phase, dried over $MgSO_4$, filtered, and evaporated. Yield 1.83 g (83%), oily substance. ^1H NMR spectrum, δ, ppm: 1.62 m (4H, CH_2, $J = 6.8$ Hz), 2.55 m (4H, CH_2, $J = 6.8$ Hz), 5.19 s (4H, $\mathbf{CH_2}Ph$), 5.96 s (2H, 4-H), 7.19 m (10H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (CH_2), 28.8 (CH_2), 52.3 (NCH_2), 103.5 (C^4), 126.9 (C^o), 127.6 (C^5), 128.4 (C^p), 128.7 (C^m), 136.2 (C^i), 153.1 (C^3). Found, %: C 66.22; H 5.78; Cl 5.64; N 12.36. $C_{24}H_{24}Cl_2N_4$. Calculated, %: C 65.61; H 5.51; Cl 16.14; N 12.75.

3,3′-(Butane-1,4-diyl)bis(5-chloro-1-methyl-1*H*-pyrazole) (V) was synthesized in a similar way from 1.52 g (0.005 mol) of diketone **II** and 1.2 g (0.02 mol) of 1,1-dimethylhydrazine. Yield 1.27 g (80%), oily substance. ^1H NMR spectrum, δ, ppm: 1.65 m (4H, CH_2, $J = 6.8$ Hz), 2.55 m (4H, CH_2, $J = 6.8$ Hz), 3.73 s (6H, NCH_3), 5.95 s (2H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (CH_2), 28.9 (CH_2), 35.7 (NCH_3), 103.0 (C^4), 126.9 (C^5), 152.6 (C^3). Found, %: C 50.29; H 5.68; Cl 24.99; N 19.01. $C_{12}H_{16}Cl_2N_4$. Calculated, %: C 50.19; H 5.62; Cl 24.69; N 19.51.

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