Novel approach toward the preparation of 1,6-enynes — substrates for the intramolecular Pauson-Khand cyclization

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A novel approach to the synthesis of polysubstituted 1,6-enynes is elaborated based on the protocol of the three-component coupling of arenesulfenyl chlorides, dicobalthexacarbonyl complexes of conjugated enynes, and nucleophiles of the π-donor type and a possibility to employ the 1,6-enyne derivatives thus prepared as the substrates for the intramolecular Pauson—Khand cyclization is demonstrated.

Key words: 1,6-enynes, arenesulfenyl chloride, dicobalthexacarbonyl complexes of alkynes, the Pauson-Khand reaction, 2-(trimethylsilylmethyl)buta-1,3-diene, electrophilic addition, episulfonium ion.

The intramolecular Pauson-Khand (IMPK) cyclization (alkene—alkyne—carbonyl cycloaddition) is widely employed as a general and efficient method for the creation of five-membered ring within the polycyclic framework of target compounds.[1] This reaction implies the use of precursors bearing 1,6- or 1,7-enyne moieties and most often it is carried out through the initial formation of μ-alkyne dicobalthexacarbonyl (DCHC) complexes. Except for the simplest cases, the synthesis of the necessary precursors involves multistep reaction sequences (see Ref. 1 and references cited therein). Therefore, the elaboration of synthetic procedures applicable for the ready preparation of enynes with a variable structural pattern from the available starting materials represents an important problem.

Earlier,[2] we have suggested a novel pathway for the preparation of functionalized derivatives of μ-alkyne DCHC complexes with the help of a one-pot three-component coupling which was based upon the controlled sequence of Ad_E reactions through the following steps:

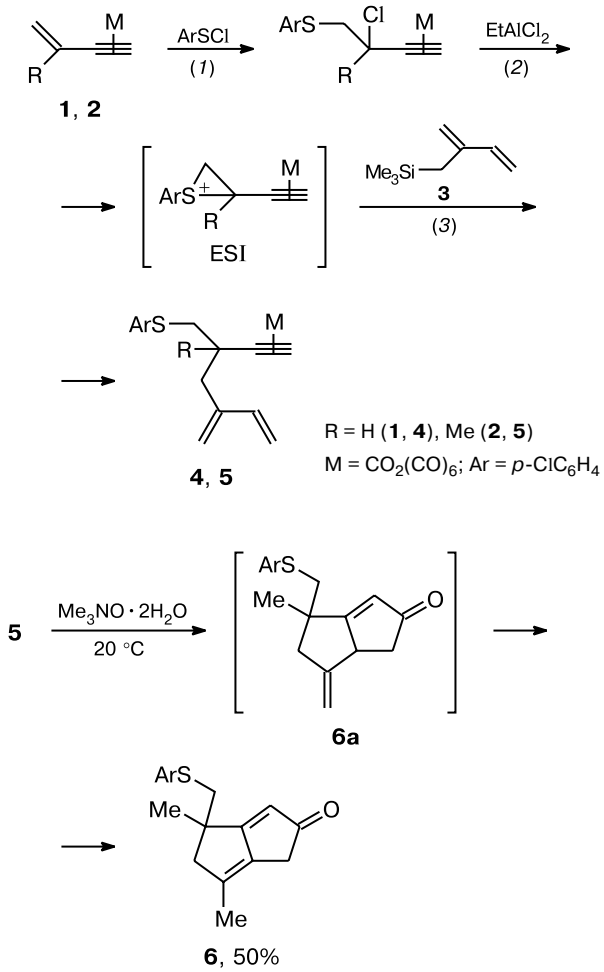
(*1*) the addition of arenesulfenyl chloride across the double bond of a DCHC complex of a conjugated enyne;

(*2*) transformation of the resulting adduct into the episulfonium ion (ESI)-like intermediate upon treatment with a Lewis acid;

(*3*) the reaction of this intermediate with carbon nucleophiles (Nu_C) such as allylsilanes or silyl enol ethers.

Here we present the results attesting to the utility of the aforementioned sequence for both the synthesis of the substrates directly amenable for the IMPK cyclization (option A, Scheme 1) and the preparation of precursors which could be easily transformed into the required 1,6-enyne derivatives (option B, Scheme 2).

Scheme 1



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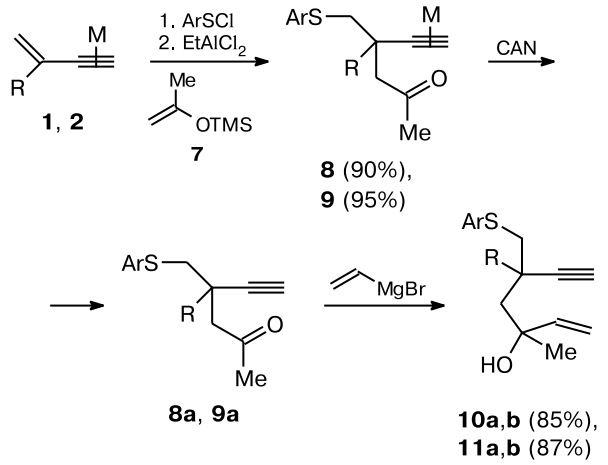
Scheme 2



R = H (**1**, **8**, **8a**, **10a**,**b**), Me (**2**, **9**, **9a**, **11a**,**b**)
CAN = $Ce(NH_4)_2(NO_3)_6$
M = $Co_2(CO)_6$; Ar = *p*-ClC_6H_4

DCHC complexes of vinylacetylene **1** and isopropenylacetylene **2** were chosen as the model substrates. *p*-Chlorobenzenesulfenyl chloride was used as a starting electrophile in the step (*1*), while $EtAlCl_2$ served as a Lewis acid in the step (*2*).*

Option A (see Scheme 1) is based on the use of 2-(trimethylsilylmethyl)buta-1,3-diene **3**, which can be easily prepared from isoprene,[3] as the final Nu_C bearing an additional vinyl group. It was shown that the presence of the conjugated diene moiety in the silane **3** does not affect essentially the efficiency of the reaction of this C-nucleophile with an ESI, prepared as described earlier[2] and the respective three-component coupling products **4** or **5** were prepared in high yields.

Ample literature data on the synthetic application of the IMPK cycloaddition[1] do not contain any reference to its applicability for the 1,6-enynes that contain alkene fragment as the part of the conjugated diene system. We have found that this type of compounds can serve as the suitable substrates for this reaction and the adduct **5** readily underwent the conversion into the respective bicyclo[3.3.0]octadienone **6** under the standard cyclization conditions.[4] The structure of the latter was unambigiously proved by ^1H and ^{13}C NMR data. Obviously, the formation of this compound proceeds through an initial formation of an adduct **6a** followed by the *exo-endo* double bond shift to give the fully conjugated dienone system of the product **6**.

Option B takes advantage of an easy preparation of the DCHC complexes of 5-oxoalkynes as a result of the earlier described three-component coupling with the use of silyl enol ethers as the C-nucleophiles.[2] It was anticipated that these adducts could be further transformed into the required 1,6-enynes by the Grignard addition of vinylmagnesium bromide. To check the viability of this approach we have chosen DCHC complexes of oxoalkynes **8** and **9** prepared by the reaction of the coresponding ESI intermediates with 2-trimethylsilyloxypropene (**7**) (see Scheme 2). Thanks to the optimization of the reaction conditions, we succeeded in preparation of the adducts **8** and **9** in virtually quantitative yields (in the previous study,[2] the yields of this type of adducts were typically within 30—40% range).

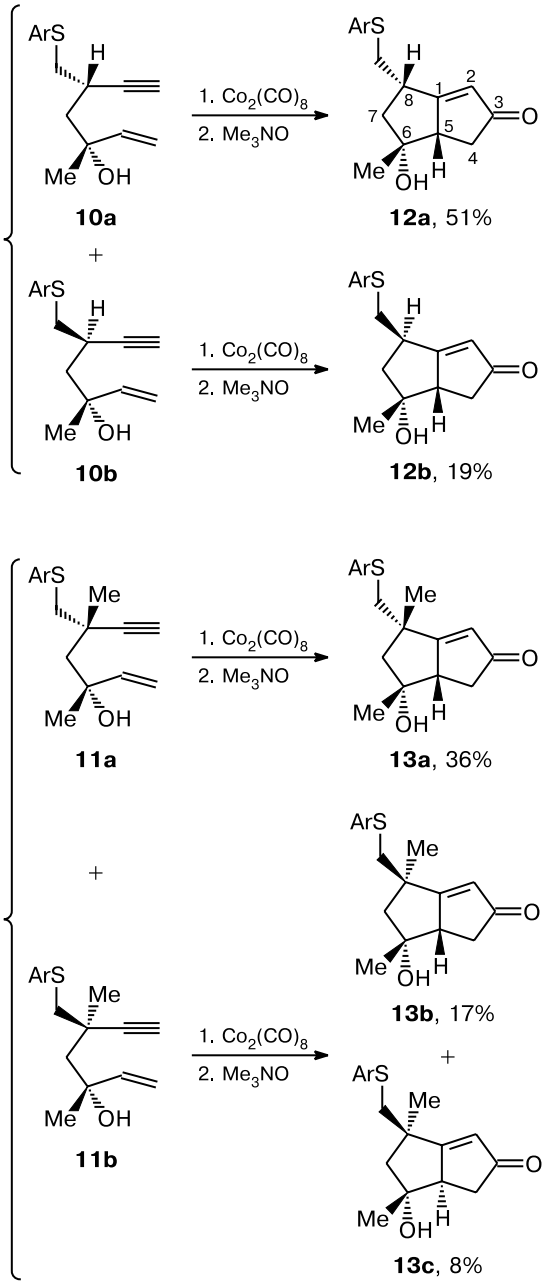
The attempts to carry out the Grignard reaction of vinylmagnesium bromide directly with DCHC complexes **8** and **9** turned out to be rather unsuccessful, since no reaction was observed at low temperature (−30 °C), while an intense decomposition of the starting materials occured at higher temperature (0 °C) and the target products were formed in only trace amounts (TLC data). At the same time, we faced no problems when performing the reaction of vinylmagnesium bromide with the decomplexed adducts **8a** and **9a** to give good yields of the respective 1,6-enynes **10a,b** and **11a,b** as mixtures of diastereomers, their ratio having been established from ^1H NMR data.

The separation of diastereomers failed. Our efforts to separate the DCHC complexes prepared from enynes **10a**,**b** were also of no avail. Therefore, further transformations were performed with the mixtures of diastereomers **10a**,**b** and **11a**,**b**. The reactions of these adducts with $Co_2(CO)_8$ resulted in the formation of the respective DCHC complexes. The latter were not isolated but used directly as the substrates for the IMPK reaction under the conventional conditions of the oxidative initiation under the action of Me_3NO.[4]

It was found that the cyclization of the mixture **10a**,**b** produced a mixture of only two (out of four possible) diastereomers **12a,b** in the ratio 2.5 : 1, which roughly corresponded to that of the diastereomers in the starting material (Scheme 3). Individual products **12a** and **12b** were isolated by preparative TLC and their structures were unambiguosly established by ^1H and ^{13}C NMR data including measurements of NOE in the rotating coordinate system (ROESY). Thus the the ROESY spectrum of compound **12a** exhibited intense cross-peaks between the protons at C(5) and C(8) as well as between the Me group at C(6) and the proton at C(8). This pattern attests to the proximity of these protons and hence should be taken as evidence of their *cis*-arrangement. In a similar way, the *cis*-configuration of the protons at C(5), the Me-group at C(6), and the $ArSCH_2$ substituent in the isomer **12b** was established.

* We have found that these reagents enable couplings under milder conditions and in higher yields as compared to previously employed[2] *p*-methylbenzenesulfenyl chloride and $TiCl_4$, respectively.

Scheme 3



Since the cycloadducts **12a** and **12b** differ only in the configuration of the $ArSCH_2$ substituents at C(8), one may assume that the IMPK cyclization of both diastereomers **10a** and **10b** proceeded with high diastereoselectivity (TLC data of the crude reaction mixture indicated also the possible presence of other diastereomers in trace amounts (<3—5%)).

A rather different diastereoselectivity pattern was observed for the cyclization of the mixture **11a**,**b**, which furnished a mixture of three isomers **13a**,**b**,**c** in a ratio 4 : 2 : 1. The components of this mixture were separated by preparative TLC and their structures and stereochemistry were established using ^1H and ^{13}C NMR spectroscopy (including ROESY). In this case, the IMPK reaction of **11a** proceeded with a nearly complete diastereoselectivity to give adduct **13a**, while the conversion of **11b** into the mixture **13b,c** exhibited a rather modest diastereoselectivity (see Scheme 3).

It is well known that the steric course of the IMPK reaction may vary depending on the nature and position of the substituents in the starting compound.[5] The results of the present study are far from being sufficient to deduce any general conclusions regarding the nature of the factors which might have been responsible for the observed stereochemical pattern. This is especially true, since the data on the steric course of the similar transformations published earlier refers largely to a simpler cases of the formation of bicyclic compounds bearing only two chiral centers. Our current studies are aimed at both the broadening of the scope of the preparative utility of the elaborated approach and a more detailed investigation of the steric course of the IMPK reaction for polysubstituted substrates.

Experimental

All experiments were carried out under dry argon using anhydrous solvents purified following the standard methods.[6] TLC analysis was carried out on plates with silica gel (Merck, SiO_2, 60 mesh ASTM) or with alumina (POLYGRAM ALOX N/UV_{254}, Al_2O_3, 0.2 mm). Column chromatography was performed on Merck silica gel (220—240 mesh ASTM) or on neutral alumina. Due to the thermal lability of DCHC complexes of alkynes, the removal of solvents was carried out using a rotary evaporator with the water bath at temperature below 30 °C.

Commercial reagents: $EtAlCl_2$ (Aldrich, 1 *M* solution in hexane), $Co_2(CO)_8$ (Merck, 97%) vinylmagnesium bromide (Aldrich, 1 *M* solution in THF) were employed.

Vinylacetylene was prepared from 2-methylhex-5-en-3-yn-2-ol in accordance with the known method[7] and used as a 1 *M* solution in CH_2Cl_2; *p*-ClC_6H_4SCl was prepared as described previously[8]; DCHC complex of 2-methylbut-1-en-3-yne (**2**) was prepared following the standard procedure[9]; the known procedure[10] was modified for the preparation of the DCHC complex of but-1-en-3-yne (**1**) (see below); the preparation of 2-(trimethylsilylmethyl)buta-1,3-diene (**3**) was carried out using the modified method[3] (see below); 2-trimethylsilyloxypropene (**7**) was prepared using the described method.[11]

The ^1H and ^{13}C NMR spectra were recorded on Bruker WM-250, Bruker AC-200, Bruker AM-300, and Bruker DRX-500 instruments. The chemical shifts (δ) are given in ppm, spin-spin coupling constants (*J*) in Hertz.

Oxidative decomplexation (general procedure). A solution of 1 mmol of a DCHC complex in a minimal amount of acetone was added to a solution of $Ce(NH_4)_2(NO_3)_6$ (CAN) (2.74 g, 5 mmol) in acetone (10 mL) with stirring at −40——50 °C. The cooling was removed, ether (50 mL) was added and the solution

was washed with water (2×100 mL). The organic phase was dried with $CaCl_2$. Additional purification (if any needed) was carried out using chromatography on silica gel. The yields of the products were 90—95%.

DCHC complex of but-3-en-1-yne (1). Vinylacetylene (104 mg, 2 mmol) was dissolved in ether (20 ml), $Co_2(CO)_8$ (342 mg, 1 mmol) was added to the solution, and the mixture was stirred until the evolution of CO ceased (40 min). The reaction mixture was filtered through a thin layer of silica gel using ether as the eluent. After evaporation of the solvent, the residue was dissolved in hexane and again filtered through silica gel using hexane as the eluent. Removal of the solvent furnished compound **1** (308 mg, 91%) as a dark brownish oil (R_f 0.7, SiO_2, hexane).

2-(Trimethylsilylmethyl)buta-1,3-diene (3). Solutions of 2,2,6,6-tetramethylpyperidine (TMP) (7.19 g, 51 mmol) in dry THF (5 mL) and Bu^tOK (6.71 g, 55 mmol) in dry THF (25 mL) were placed into the three-necked flask and cooled down to −100 °C. Then a 1.64 *M* solution of BuLi in hexane (30.5 mL, 50 mmol) was added with stirring over 5 min keeping the temperature within the interval −100—−90 °C. The temperature of the reaction mixture was gradually increased to −70 °C in 20 min. The formation of a precipitate which hindered the stirring was observed. A solution of isoprene (1.70 g, 25 mmol) in dry THF (5 ml) was added in one batch and the dark red solution formed was kept at −70 °C for an additional 15 min. After that the reaction mixture was cannulated slowly to a solution of Me_3SiCl (5.45 g, 50 mmol) in dry THF (50 mL) keeping the temperature below −90 °C. The reaction mixture was warmed up to −20 °C, quenched with water (100 mL), acidified with 0.1 *M* H_2SO_4 to pH 4, and extracted with ether (3×50 mL). The combined organic extracts were dried with Na_2SO_4. The solvent was removed and the residue was distilled *in vacuo* to give **3** (1.44 g, 41%), b.p. 60 °C (30 Torr). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 0.05 (s, 9 H, $SiMe_3$), 1.72 (s, 2 H, CH_2), 4.80 (s, 1 H, H(1)), 4.90 (s, 1 H, H(1), 5.13 (d, 1 H, H(4), ^3J = 17.4 Hz), 5.06 (d, 1 H, H(4), ^3J = 10.6 Hz), 6.39 (dd, 1 H, H(3), $^3J_1$ = 17.4 Hz, $^3J_2$ = 10.6 Hz).

DCHC complex of 5-(4-chlorophenylthiomethyl)-3-methylidenehept-1-en-6-yne (4). A 1 *M* solution of *p*-ClC_6H_4SCl (1 mL, 1 mmol) in CH_2Cl_2 was added to a solution of the DCHC complex of vinylacetylene **1** (338 mg, 1 mmol) in CH_2Cl_2 (7 mL) at −70 °C. After 10 min, a 1 *M* solution of $EtAlCl_2$ in hexane (1 mL, 1 mmol) was added and after 5 min diene **3** (210 mg, 1.5 mmol) was added. The reaction mixture was kept at −30 °C for 1 day and then quenched with a mixture of saturated aq. $NaHCO_3$ and ether. After additional extraction with ether, the combined extract was dried with $MgSO_4$ and filtered through a thin layer of silica gel (eluent, ether). The residue after removal of the solvent was purified by chromatography on silica gel to give adduct **4** (440 mg, 80%) as a dark brownish oil (R_f 0.61, SiO_2, ethyl acetate—hexane, 1 : 10). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.55 (dd, 1 H, H(4), ^3J = 5.5, ^2J = 14.0 Hz), 2.68 (dd, 1 H, H(4), ^3J = 7.3 Hz, ^2J = 14.0 Hz), 2.95 (m, 1 H, H(5)), 3.18 (m, 2 H, SCH_2), 5.07 and 5.20 (both s, 1 H each, CH_2=), 5.09 (d, 1 H, H(1), ^3J = 11.0 Hz), 5.21 (d, 1 H, H(1), ^3J = 17.6 Hz), 6.23 (dd, 1 H, H(2), $^3J_1$ = 11.0 Hz, $^3J_2$ = 17.6 Hz), 7.25 (s, 4 H, Ar). Found (%): C, 68.63; H, 5.82; Cl, 13.32; S, 12.05. $C_{15}H_{15}ClS$. Calculated (%): C, 68.55; H, 5.75; Cl, 13.49; S, 12.21.

DCHC complex of 5-(4-chlorophenylthiomethyl)-5-methyl-3-methylidenehept-1-en-6-yne (5). Following the procedure described above, the DCHC complex of isopropenylacetylene **2** (352 mg, 1 mmol) was converted into complex **5** (462 mg, 82%), dark brownish oil (R_f 0.61, SiO_2, ethyl acetate—hexane, 1 : 10). ^{1}H NMR (250 MHz, $CDCl_3$), δ: 1.39 (s, 3 H, CH_3), 2.54 and 2.77 (both s, 1 H each, H(4), ^2J = 13.5 Hz), 3.09 (s, 2 H, SCH_2), 5.13 (d, 1 H, H(1), ^3J = 11.0 Hz), 5.20 and 5.32 (both s, 1 H each, CH_2=), 5.35 (d, 1 H, H(7), ^3J = 19.0 Hz), 6.34 (s, 1 H, H(7)), 6.46 (dd, 1 H, H(2), $^3J_1$ = 11.0 Hz, $^3J_2$ = 19.0 Hz), 7.20 and 7.25 (both d, 2 H each, Ar, ^3J = 8.8 Hz). Found (%): C, 69.52; H, 6.23; Cl, 12.52; S, 11.35. $C_{16}H_{17}ClS$. Calculated (%): C, 69.42; H, 6.19; Cl, 12.81; S, 11.58.

8-(4-Chlorophenylthiomethyl)-6,8-dimethylbicyclo[3.3.0]octa-1,5-dien-3-one (6). Trimethylamine N-oxide dihydrate (333 mg, 3 mmol) was added to the solution of complex **5** (282 mg, 0.5 mmol) in a CH_2Cl_2—THF mixture (8 mL, 1 : 1). The mixture was kept at 20 °C overnight and then filtered through a thin layer of SiO_2 (eluent, ether). After removal of the solvent, the residue was purified by chromatography on SiO_2 (eluent, ethyl acetate—hexane, 1 : 3) to give cycloadduct **6** (76 mg, 50%) as a yellow oil (R_f 0.31, SiO_2, ethyl acetate—hexane, 1 : 3). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.33 (s, 3 H, CH_3 at C(8), 1.87 (s, 3 H, CH_3 at C(6)), 2.52 and 2.84 (both s, 1 H each, H(7), ^2J = 8.1 Hz), 2.79 (s, 2 H, H(4)), 3.10 (s, 2 H, SCH_2), 5.72 (s, 1 H, H(2)), 7.21 (s, 4 H, Ar). ^{13}C NMR (300 MHz, $CDCl_3$), δ: 15.5, 25.7, 35.3, 44.2, 44.9, 53.8, 119.0, 128.9, 130.9, 132.2, 135.2, 138.0, 141.6, 192.2, 207.2. Found (%): C, 66.12; H, 5.23; Cl, 11.99; S, 10.87. $C_{16}H_{15}ClOS$. Calculated (%): C, 66.08; H, 5.20; Cl, 12.19; S, 11.03.

DCHC complex of 4-(4-chlorophenylthiomethyl)hex-5-yn-2-one (8). A 1 *M* solution of *p*-ClC_6H_4SCl (1 mL, 1 mmol) in CH_2Cl_2 was added to a solution of the DCHC complex of vinylacetylene **1** (338 mg, 1 mmol) in CH_2Cl_2 (7 mL) at −70 °C. After 10 min, a 1 *M* solution of $EtAlCl_2$ in hexane (1 mL, 1 mmol) was added followed by addition, after 5 min, of 2-trimethylsilyloxypropene (**7**) (195 mg, 1.5 mmol). The reaction mixture was kept at −30 °C for 1 day and then quenched with a mixture of saturated aqueous $NaHCO_3$ and ether and additionally extracted with ether. The combined extract was dried with $MgSO_4$ and filtered through a thin layer of silica gel (eluent, ether). The residue after removal of ether was purified by chromatography on silica gel to give the adduct **8** (486 mg, 90%) as a dark brownish oil (R_f 0.30, SiO_2, ethyl acetate—hexane, 1 : 10). ^{1}H NMR (200 MHz, $CDCl_3$), δ: 2.17 (s, 1 H, H(6)), 2.20 (s, 3 H, CH_3), 2.79 (dd, 1 H, H(3), ^2J = 17.3 Hz, ^3J = 6.6 Hz), 2.88 (dd, 1 H, H(3), ^2J = 17.3 Hz, ^3J = 5.4 Hz), 3.12 (m, 3 H, H(4) and SCH_2), 7.31 and 7.37 (both d, 2 H each, Ar, ^3J = 8.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$), δ: 27.9, 31.2, 39.4, 47.8, 71.7, 85.5, 130.1, 132.3, 133.6, 134.9, 206.5. Found (%): C, 61.87; H, 5.26; Cl, 13.68; S, 12.26. $C_{13}H_{13}ClOS$. Calculated (%): C, 61.77; H, 5.18; Cl, 14.03; S, 12.69.

DCHC complex of 4-methyl-4-(4-chlorophenylthiomethyl)hex-5-yn-2-one (9). Following the same procedure, the DCHC complex of isopropenylacetylene **2** (352 mg, 1 mmol) was converted into adduct **9** (527 mg, 95%), dark brownish oil (R_f 0.32, SiO_2, ethyl acetate—hexane, 1 : 10). ^{1}H NMR for **9a** (500 MHz, $CDCl_3$), δ: 1.39 (s, 3 H, CH_3 at C(4)), 2.14 (s, 3 H, CH_3CO), 2.22 (s, 1 H, H(6)), 2.68 and 2.79 (both s, 1 H each, H(3), ^2J = 16.0 Hz), 3.29 (d, 2 H, SCH_2, ^2J = 12.0 Hz), 7.23

and 7.33 (both d, 2 H each, Ar, ^3J = 8.8 Hz). Found (%): C, 63.28; H, 5.85; Cl, 12.80; S, 11.73. $C_{14}H_{15}ClOS$. Calculated (%): C, 63.03; H, 5.67; Cl, 13.29; S, 12.02.

5-(4-Chlorophenylthiomethyl)-3-methylhept-1-en-6-yn-3-ol (10a,b). A 1 *M* solution of vinylmagnesium bromide in THF (2 mL, 2 mmol) was added to a solution of ketone **8a** (126 mg, 0.5 mmol) in THF (6 mL) at −60 °C. The reaction mixture was kept for 1 day at −30 °C, quenched with saturated aqueous NH_4Cl and extracted with ether. After drying with $MgSO_4$, the ethereal extract was filtered through a thin layer of silica gel (eluent, ether). Removal of the solvent followed by chromatography of the residue on Al_2O_3 (eluent, ethyl acetate—hexane, 1 : 10) furnished product **10a,b** (119 mg, 85%, **10a** : **10b** = 2.5 : 1) as a yellowish oil (R_f 0.27, Al_2O_3, ethyl acetate—hexane, 1 : 10). Found (%): C, 64.42; H, 6.31; Cl, 12.14; S, 11.16. $C_{15}H_{17}ClOS$. Calculated (%): C, 64.16; H, 6.10; Cl, 12.62; S, 11.42. DCHC complex of **10a**. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.31 (s, 3 H, CH_3), 1.91 (d, 1H, H(4), ^3J = 2.6 Hz), 1.96 (d, 1 H, H(4), ^3J = 5.2 Hz), 2.98 (dd, 1 H, (SCH_2), ^2J = 12.5 Hz, ^3J = 7.3 Hz), 3.12 (m, 1 H, H(5)), 3.31 (dd, 1 H, (SCH_2), ^2J = 12.5 Hz, ^3J = 5.7 Hz), 5.01 (d, 1 H, H(1), ^3J = 10 Hz), 5.21 (d, 1 H, H(1), ^3J = 17.2 Hz), 7.23 and 7.30 (both d, 2 H each, Ar, ^3J = 8.5 Hz). ^{13}C NMR (300 MHz, $CDCl_3$), δ: 28.7, 37.5, 42.2, 48.2, 76.2, 102.3, 112.0, 129.0, 131.0, 132.3, 134.5, 145.0, 198.8. DCHC complex of **10b**. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.34 (s, 3 H, CH_3), 1.85 (d, 1 H, H(4), ^3J = 3.3 Hz), 2.02 (d, 1 H, H(4), ^3J = 4.6 Hz), 2.86 (dd, 1 H, (SCH_2), ^2J = 13.0 Hz, ^3J = 8.8 Hz), 3.12 (m, 1 H, H(5)), 3.56 (dd, 1 H, (SCH_2), ^2J = 13.0 Hz, ^3J = 4.8 Hz), 5.06 (d, 1 H, H(1), ^3J = 11.0 Hz), 5.17 (d, 1 H, H(1), ^3J = 16.5 Hz), 7.23 and 7.30 (both d, 2 H each, Ar, ^3J = 8.5 Hz). ^{13}C NMR (300 MHz, $CDCl_3$), δ: 30.4, 38.1, 42.2, 48.7, 73.1, 102.3, 112.9, 129.0, 131.0, 132.3, 134.5, 143.7, 198.8.

3-(4-Chlorophenylmethyl)-3,5-dimethylhept-1-en-6-yn-3-ol (11a,b). In a similar way, adduct **9a** (133 mg, 0.5 mmol) was converted into compound **11a,b** (128 mg, 87%, **11a** : **11b** = 1.3 : 1 as a yellowish oil (R_f 0.30, ethyl acetate—hexane, 1 : 10). Found (%): C, 65.40; H, 6.68; Cl, 11.63; S, 10.60. $C_{16}H_{19}ClOS$. Calculated (%): C, 65.18; H, 6.50; Cl, 12.02; S, 10.88. Compound **11a**. ^{1}H NMR (250 MHz, $CDCl_3$), δ: 1.30 (s, 3 H, CH_3 at C(5)), 1.40 (s, 3 H, CH_3 at C(3)), 1.78 and 2.05 (both d, 1 H each, H(4), ^2J = 14.4 Hz), 3.22 and 3.30 (both d, 2 H each, SCH_2, ^2J = 13.3 Hz), 5.07 (d, 1 H, H(1), ^3J = 5.2 Hz), 5.34 (br.s, 1 H, H(1)), 6.00 (m, 1 H, H(2)), 7.28 (d, 4 H, Ar, ^3J = 8.5 Hz). Compound **11b**. ^{1}H NMR (250 MHz, $CDCl_3$), δ: 1.33 (s, 3 H, CH_3 at C(3), 1.35 (s, 3 H, CH_3 at C(5)), 1.86 and 2.01 (both d, 1 H each, H(4), ^2J = 15.1 Hz), 3.10 and 3.16 (both d, 2 H each, SCH_2, ^2J = 13.1 Hz), 5.03 (d, 1 H, H(1), ^3J = 4.6 Hz), 5.27 (br.s, 1 H, H(1), 6.00 (m, 1 H, H(2)), 7.28 (d, 4 H, Ar, ^3J = 8.5 Hz).

8-(4-Chlorophenylthiomethyl)-6-hydroxy-6-methyl-bicyclo[3.3.0]oct-1-en-3-one (12a,b). Dicobalt octacarbonyl (188 mg, 0.55 mmol) was added to a solution of a mixture of diastereomers **10a,b** (140 mg, 0.5 mmol) in THF (6 mL). The mixture was stirred at 20 °C until the evolution of CO ceased (40 min) and the solution of trimethylamine N-oxide dihydrate (333 mg, 3 mmol) in CH_2Cl_2 (6 mL) was added. After standing overnight at 20 °C, the reaction mixture was filtered through a thin layer of silica gel (eluent, ether). The solvent was removed and the residue was chromatographed on silica gel (eluent, ethyl acetate — hexane, 1 : 1) to give **12a** (78.5 mg, 51%) and **12b** (29.3 mg, 19%) (both yellowish oils). Found (for a mixture **12a,b**) (%): C, 62.50; H,5.73; Cl, 11.01; S, 9.94. $C_{16}H_{17}ClOS$. Calculated (%): C, 62.23; H, 5.55; Cl, 11.48; S, 10.38. Compound **12a** (5S*,6*R**,8*S**-isomer). R_f 0.28 (ethyl acetate—hexane, 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.33 (s, 3 H, CH_3 at C(6)), 1.98 (d, 1 H, H(7), ^2J = 15.0 Hz), 2.35 (m, 3 H, 2H(4) and H(7)), 2.87 (br.s, 1 H, H(5)), 2.99 (dd, 1 H, SCH_2, ^2J = 12.4 Hz, ^3J = 8.1 Hz), 3.07 (m, 1 H, (H)), 3.18 (dd, 1 H, SCH_2, ^2J = 12.4 Hz, ^3J = 5.6 Hz), 6.01 (s, 1 H, H(2)), 7.20 and 7.23 (both d, 2 H each, Ar, ^3J = 8.8 Hz). ^{13}C NMR (500 MHz, $CDCl_3$), δ: 26.3, 35.4, 37.8, 38.9, 47.2, 56.8, 76.0, 125.6, 129.2, 131.3, 132.7, 134.0, 190.1, 210.6. Compound **12b** (5S*,6*R**,8*R**-isomer). R_f 0.36 (ethyl acetate—hexane, 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.43 (s, 3 H, CH_3 at C(6)), 1.95 (dd, 1 H, H(7), ^2J = 14.0 Hz, ^3J = 8.2 Hz), 2.36 (m, 3 H, 2 H(4) and H(7)), 2.99 (m, 1 H, H(5)), 3.07 (dd, 1 H, SCH_2, ^2J = 12.8 Hz, ^3J = 7.0 Hz), 3.12 (dd, 1 H, SCH_2, ^2J = 12.8 Hz, ^3J = 7.8 Hz), 3.22 (m, 1 H, H(8)), 6.02 (s, 1 H, H(2)), 7.28 and 7.30 (both d, 2 H each, Ar, ^3J = 8.1 Hz). ^{13}C NMR (500 MHz, $CDCl_3$), δ: 26.0, 35.8, 37.5, 38.5, 48.6, 55.4, 76.1, 127.5, 129.2, 131.3, 132.8, 133.8, 188.6, 210.5.

8-(4-Chlorophenylthiomethyl)6-hydroxy-6,8-dimethylbicyclo[3.3.0]oct-1-en-3-on (13a—c). In a similar way, a mixture of diastereomers **11a,b** (147 mg, 0.5 mmol) was converted into cycloadducts **13a** (58 mg, 36%), **13b** (28 mg, 17%), and **13c** (13 mg, 8%) as yellowish oils. Found for a mixture **13a—c** (%): C, 63.45; H, 6.08; Cl, 10.67; S, 9.58. $C_{17}H_{19}ClOS$. Calculated (%): C, 63.24; H, 5.93; Cl, 10.98; S, 9.93. Compound **13a** (5*S**,6*R**,8*S**-isomer). R_f 0.37 (ethyl acetate—hexane, 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.28 (s, 3 H, CH_3 at C(8)), 1.30 (s, 3 H, CH_3 at C(6)), 1.94 and 2.24 (both d, 1 H each, H(7), ^2J = 14.4 Hz), 2.27 (dd, 1 H, H(4), ^2J = 17.8 Hz, ^3J = 6.3 Hz), 2.37 (dd, 1 H, H(4), ^2J = 17.8 Hz, ^3J = 3.2 Hz), 3.00 (m, 1 H, H(5)), 3.10 and 3.24 (both d, 1 H each, SCH_2, ^2J = 12.6 Hz), 5.84 (s, 1 H, H(2)), 7.16 and 7.22 (both d, 2 H each, Ar, ^3J = 8.6 Hz). ^{13}C NMR (500 MHz, $CDCl_3$), δ: 26.3, 27.5, 35.6, 43.7, 45.1, 54.6, 55.2 75.8, 124.3, 129.1, 130.9, 132.3, 135.3, 193.7, 210.7. Compound **13b** (5*S**, 6*R**,8*R**-isomer). R_f 0.29 (ethyl acetate—hexane, 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.32 (s, 3 H, CH_3 at C(6)), 1.35 (s, 3 H, CH_3 at C(8)), 1.90 and 2.20 (both d, 1 H each, H(7), ^2J = 14.1 Hz), 2.28 (dd, H(4), ^2J = 17.9 Hz, ^3J = 5.9 Hz), 2.33 (dd, 1 H, H(4), ^2J = 17.9 Hz, ^3J = 3.4 Hz), 3.01 (m, 1 H, H(5)), 3.02 and 3.07 (both d, 1 H each, SCH_2, ^2J = 12.3 Hz), 5.84 (s, 1 H, H(2)), 7.16 and 7.19 (both d, 2 H each, Ar, ^3J = 8.7 Hz). ^{13}C NMR (500 MHz, $CDCl_3$), δ: 26.6, 27.0, 35.9, 43.5, 46.3, 55.2, 56.1, 76.1, 125.7, 129.1, 130.9, 132.3, 135.3, 194.1, 210.6. Compound **13c** (5*R**,6*R**,8*R**-isomer). R_f 0.24 (ethyl acetate—hexane, 1 : 1). ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.06 (s, 3H, CH_3 at C(6)), 1.40 (s, 3 H, CH_3 at C(8)), 2.08 and 2.20 (both d, 1 H each, H(7), ^2J = 13.9 Hz), 2.23 (dd, 1 H, H(4), ^2J = 18.4 Hz, ^3J = 2.9 Hz), 2.41 (dd, 1 H, H(4), ^2J = 18.4 Hz, ^3J = 6.6 Hz), 2.98 and 3.09 (both d, 1 H each, SCH_2, ^2J = 12.3 Hz), 3.41 (m, 1 H, H(5)), 5.88 (s, 1 H, H(2)), 7.19 and 7.22 (both d, 2 H each, Ar, ^3J = 8.7 Hz). ^{13}C NMR (500 MHz, $CDCl_3$), δ: 24.1, 28.1, 36.5, 43.0, 45.1, 54.9, 55.1, 76.4, 123.8, 129.2, 131.0, 132.5, 135.3, 192.2, 209.8.

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References

1. N. E. Shore, *Org. Reac.*, 1991, **40**, 2; O. Geis and H.-G. Schmalz, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 911; K. M. Brummond and J. L. Kent, *Tetrahedron*, 2000, **56**, 3263.
2. M. I. Lazareva, S.-T. Nguyen, M.-C. Nguyen, H. Emiru, N. A. McGrath, R. Caple, and W. A. Smit, *Mendeleev Commun.*, 2001, 224.
3. P. A. A. Klusener, H. H. Hommes, H. D. Verkruijsse, and L. Brandsma, *J. Chem. Soc.*, *Chem. Commun.*, 1985, 1677.
4. S. Shambayati, W. E. Crowe, and S. L. Schreiber, *Tetrahedron Lett.*, 1990, **37**, 5289.
5. J. Castro, A. Moyano, M. A. Pericas, and A. Riera, *Tetrahedron*, 1995, **51**, 6541.
6. L. F. Tietze and T. Eicher, *Reaktionen und Synthesen im organisch-chemischen Praktikum und Forschungslaboratorium*, Georg Thieme Verlag, Stuttgart—New York, 1991.
7. D. V. Sokolov, G. S. Litvinenko, and Zh. I. Isin, *Izv. Akad. Nauk Kaz. SSR*, *Ser. Khim.* [*Bulletin of Academy of Sciences of Kazakhstan Republic*], 1959, **2**, 68 (in Russian).
8. M. I. Lazareva, Y. K. Kryschenko, R. Caple, V. G. Young Jr., and W. A. Smit, *Mendeleev Commun.*, 1999, 24.
9. A. L. Veretenov, Ph. D. (Chem.) Thesis, Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow, 1989 (in Russian).
10. A. A. Shchegolev, W. A. Smit, G. S. Mikaelyan, A. S. Gybin, Yu. B. Kal´yan, M. Z. Krimer, and R. Caple, *Izv. Akad. Nauk SSSR*, *Ser. Khim.*, 1984, 2571 [*Bull. Acad. Sci. USSR*, *Div. Chem. Sci.*, 1984, **33**, 2355 (Engl. Transl.)].
11. P. Cazeau, F. Duboudin, F. Moulines, O. Babot, and J. Dunogues, *Tetrahedron*, 1987, **43**, 2075.

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