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Synthesis of Substituted Pyrroles in the Glaser Reaction

S. A. Vizer,[1] K. B. Yerzhanov,[1] and V. M. Dembitsky[2]

[1]*Bekturov Institute of Chemical Sciences MES Kazakhstan, 106 Sh. Walikhanov Street, Almaty, 050010, Kazakhstan*

[2]*Department of Organic Chemistry, P.O. Box 39231, Hebrew University of Jerusalem, Jerusalem 91391, Israel*

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ABSTRACT: *The substituted pyrroles and dipyrroles along with diacetylenes and cumulenes have been synthesized in high yields using a new synthetic method under mild reaction conditions using the Glaser coupling reaction. Although diacetylenes are formed from 2-propargyl-1,3-dicarbonyl compounds having electron-donors substituents such as Ph or OEt, only polyfunctional substituted cumulenes are formed from those compounds under the modified conditions*. © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:66–73, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20184

INTRODUCTION

The reaction in which a compound containing an acetylenic hydrogen was coupled via oxidation of the Cu(I) acetylide, which was discovered by a German chemist Carl Glaser (1841–1935) in 1869 [1]. The Glaser coupling reaction is a synthesis of symmetric or cyclic bisacetylenes via a coupling reaction of terminal alkynes. More recently, a similar reaction was described by Eglinton [2a–d]. The Eglinton reaction is an oxidative coupling of terminal alkynes and allows the synthesis of symmetric or cyclic bisacetylenes via a reaction of the terminal alkyne with a stoichiometric Cu(II) salt in pyridine [2e]. The difference being the use of catalytic Cu(I), which is reoxidized in the catalytic cycle by oxygen in the reaction medium. The related Hay coupling reaction has several advantages as compared to the Glaser coupling, see also [3a–f]. The Cu-TMEDA complex used is soluble in a wide range of solvents, so that the reaction is more versatile [4]. The Glaser coupling reaction of terminal alkynes was also reported in the presence of $CuCl_2$ without organic solvents and bases under near-critical water [5]. A microwave-enhanced, solvent-free Glaser coupling reaction in the presence of $CuCl_2$ affords good yield of diacetylenes [6]. A detailed mechanism for the Hay modification of the Glaser oxidative coupling of terminal acetylenes was formulated on the basis of DFT calculations [7].

The Glaser coupling reaction was extended to different organic compounds and used not only for synthesis of acetylenes with conjugated system of triple bonds, but as the most important method for the synthesis of natural products such as amino acids, ether lipids, polyenes, vitamins, and sugars [8a–h]. The Glaser–Eglinton–Hay coupling reaction has been used to synthesize a number of fungal antibiotics [8i].

The Glaser coupling reaction along with Eglinton, Straus, and Cadiot–Chodkiewicz and other coupling reactions have been partly observed in the preparation of polyacetylenes and synthesis of heterocyclic compounds from/via acetylenes [9].

Here, we report a novel method for the synthesis of the substituted pyrroles and dipyrroles, along

Correspondence to: V. M. Dembitsky; e-mail: dvalery@cc.huji.ac.il.

with diacetylenes and cumulenes using the Glaser coupling reaction.

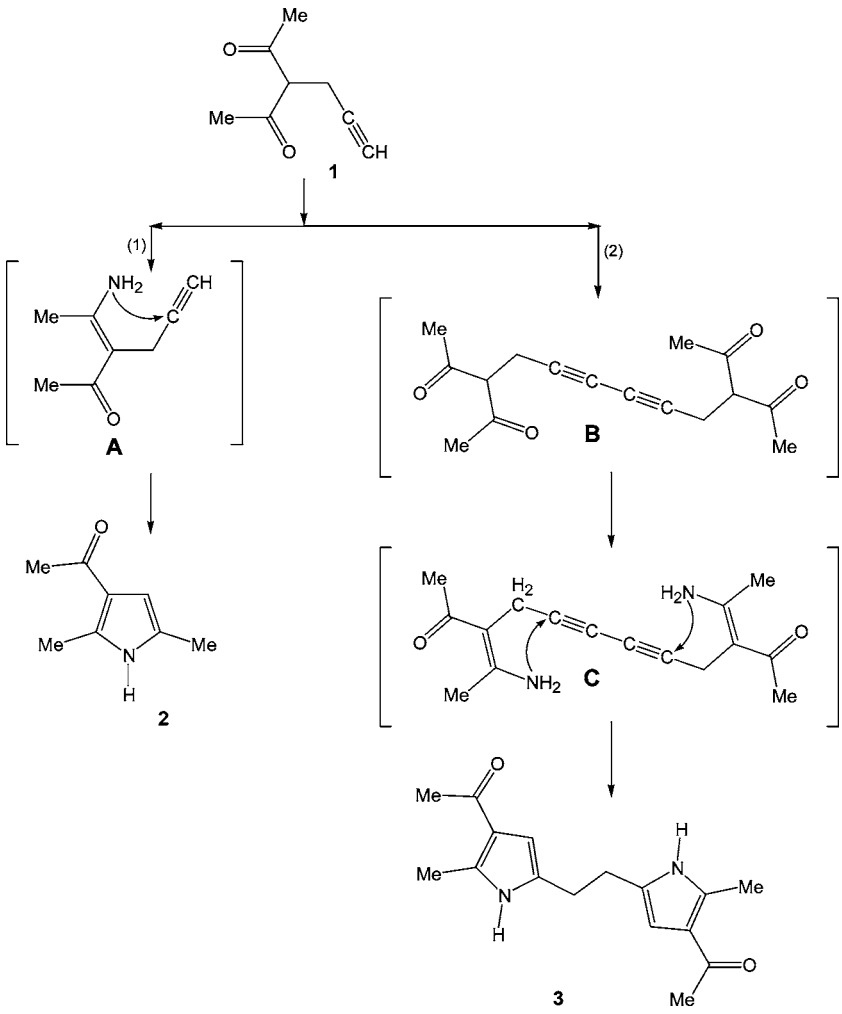
RESULTS AND DISCUSSION

For the first time an unusual behavior of 3-acetylhex-5-yn-2-one **1** in the Glaser reaction was established by us [10]. The oxidative dimerization reaction of this β-diketone **1** in water–ethanol solution of ammonium chloride, when cuprous chloride is used as a catalyst and oxygen as an oxidant at 50–60°C, leads to the formation of two products: 2,5-dimethyl-3-acetylpyrrole **2** and the corresponding compound dipyrrole **3**. The chromatographic control of the diketone **1** reaction showed the simultaneous formation of **2** and **3**. Two competitive paths in this process are (1) the formation of acetylenic amine **A** that leads to pyrrole **2**; (2) oxidative coupling leads to diacetylenic tetraketone **B**, that is its dienamine **C** is transformed to dipyrrole **3** (Scheme 1).

Pyrrole **2** and dipyrrole **3** have been isolated by column chromatography on SiO_2. It has to be stored at the reduced temperature in an inert atmosphere because they are quickly oxidized and polymerized at room temperature.

The data of elemental analysis (Table 1), IR, NMR ^1H, ^{13}C spectra, and mass spectra gave composition and structure of **2** and **3**. IR spectra of pyrrole **2** and dipyrrole **3** show intensive bands characteristic for valency oscillations of pyrroles ring and a band characteristic for amide's system O=C–C=C–N (Table 2). The signal of acetylenic proton disappears in ^1H-NMR spectrum of **2** (Table 3), and three methyl group signals appear at 2.1–2.5 ppm. At 6.1–6.2 ppm, a broad singlet characteristic for one proton of pyrrol's ring is observed. The proton of N–H group gives a broad singlet at 8.35 ppm.

^{13}C NMR spectra given in Table 4 confirm the structure of 2,5-dimethyl-3-acetylpyrrole **2**. We attributed signals of all carbon atoms by analysis of its



SCHEME 1

TABLE 1 Physical and Chemical Characteristics and Analytical Data for Synthesized Compounds

	Molecular Formula	Found, Calculated (%) C	H	N	R_f[a]	mp (°C), (solvent) or bp/Hg mm	Yield (%)
2	$C_8H_{11}NO$	70.01, 70.04	8.54, 8.08	–	0.5	81–82 (Hexan)	49
3	$C_{16}H_{20}N_2O_2$	70.00, 70.59	7.68, 7.34	–	0.2	98–99 (Hexan)	65
6	$C_{13}H_{12}O_2$	78.00, 77.98	6.23, 6.04	–	0.7	121–123/1(n_D^{28} 1.5456)	55
8	$C_{26}H_{22}O_4$	77.34, 78.37	6.16, 5.75	–	0.5	–	51
9	$C_{18}H_{22}O_6$	64.13, 64.66	6.00, 6.63	–	0.6	–	50
10	$C_{22}H_{29}NO_6$	65.31, 65.49	7.73, 7.24	3.10, 3.47	0.7	–	20
11	$C_{20}H_{24}O_8$	60.93, 61.22	6.62, 6.16	–	0.5	–	36
12	$C_{22}H_{28}O_{10}$	59.50, 58.40	6.46, 6.24	–	0.5	–	42

[a]Silufol, bzn: ac = 5 : 1.

TABLE 2 IR Data for Synthesized Compounds, ν (cm^{-1})

2	1620 (N–C=C–C=O), 1360,1376,1448,1524,1552,1592 (Pyrrol), 3160 (N–H)
3	1620 (N–C=C–C=O), 1360,1376,1448,1524,1552,1592 (Pyrrol), 3160 (N–H)
6	1680, 1728 (C=O), 1544,1600 (Ph), 3312 (≡C–H)
8	1680, 1712 (C=O), 1448, 1596 (Ph), 688, 744 (C–H, Ph)
9	1744 (C=O), 2232 (C≡C), 1180 (C–O–C)
10	1670, 1740 (C=O), 2230 (C≡C), 1180 (C–O–C), 3450 (N–H)
11	1706, 1716 (C=O), 1648 (C=C, enol), 1232,1160 (C–O–C), 1950 (C=C=C=C)
12	1690, 1740 (C=O), 1264,1184, 1160 (C–O–C), 1950 (C=C=C=C)

TABLE 3 ^{1}H NMR Data for Synthesized Compounds, δ, (ppm) and J (Hz)

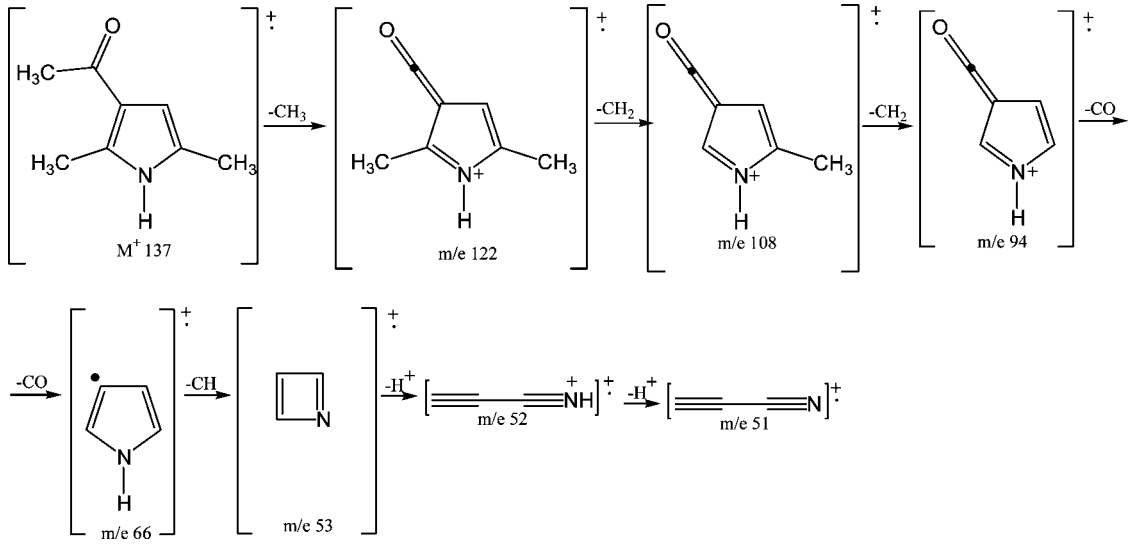
2	2.20 (3H, s, Pyr–$\underline{CH_3}$); 2.36 (3H, s, Pyr–$\underline{CH_3}$); 2.49 (3H, s, C(O)CH_3); 6.14 (1H, br s, Pyr–H); 8.35 (1H, br s, NH)
3	2.31 (6H, s, two Pyr–CH_3); 2.42 (6H, s, two C(O)CH_3); 3.69 (4H, s, –CH_2–CH_2–); 6.22 (2H, d, J = 2.7, two Pyr–$\underline{H}$); 9.40 (2H, brs, two NH)
4	1.99 (1H, t, J = 2.7, ≡C–H); 2.06 (3H, s, =-CH_3); 2.24 (3H, s, C(O)CH_3); 3.09 (2H, d, J = 2.7, ≡-CH_2-); 10.46 (2H, br s, NH_2)
5	1.94 (1H, t, J = 3.0, ≡C–H); 2.02 (3H, s, =-CH_3); 2.42 (2H, td, J^d = 7.8, J^t = 2.4, ≡-CH_2–); 6.14 (1H, m, =-H); 9.70 (2H, brs, NH_2)
6	2.00 (1H, t, J = 2.9, ≡C–H); 2,17 (2.25H, s, keto form); 2.40 (0.75H, s, enol form); 2.76 (0.75H, qd, J = 6.9, J = 3.0, J= 17.1, –CH_2–C≡, keto form); 2.91 (0.75H, qd, J = 7.8, 2.4, 17.1, –CH_2–C≡, keto form); 3.11 (0.5H, d, J = 2.4, –CH_2–C≡, enol form); 4.72 (1H, t, J = 7.2); 7.46 – 8.01 (5H, m Ph); 16.17 (0.25H, s, OH, enol form)
8	2.15 (6H, s, two CH_3); 2.88 (4H, qd, J^d = 7.5, J^d = 6.9, J^q = 17.4, J^q = 50.1, two –CH_2–C≡); 4.66 (2H, t, J = 7.1); 7.49 (4H, t, J = 7.8, Ph); 7.61 (2H, tm, J = 7.5, Ph); 7.97 (4H, d, J = 7.5, Ph)
9	1.28 (6H, t, J = 7.2, two $OCH_2\underline{CH_3}$); 2.28 (6H, s, two C(O)CH_3); 2.75 (4H, d, J = 6.9, two –CH_2- ≡); 3.66 (2H, t, J = 7.2, –$\underline{CH}$–CH_2); 4.21 (4H, d, J = 7.2, two $O\underline{CH_2}CH_3$)
10	1.25 (6H, t, J = 7.2, two $OCH_2\underline{CH_3}$); 2.05 (3H, s, CH_3); 2.29 (3H, s, CH_3); 2.75 (2H, d, J = 7.5, ≡-$\underline{CH_2}$–CH); 3.22 (2H, s, ≡-CH_2-=); 3.50 (2H, dd, J = 5.4, J = 5.7 Hz, N–$\underline{CH_2}$–CH_2–O); 3.66 (1H, t, J = 7.5, ≡-CH_2–$\underline{CH}$–); 3.77 (2H, t, J = 5.7, N–CH_2–$\underline{CH_2}$–O); 4.02 (1H, dd, J = 4.5, J = 2.1 Hz, CH_2–CH–O); 4.10 (2H, q, J = 7.3, O–$\underline{CH_2}CH_3$); 4.19 (1H, m, $\underline{CH_2}$–CH); 6.47 (1H, dd, J = 6.9, J = 14.4 Hz, O$\underline{CH}$=CH_2); 9.48 (1H, t, J = 5.4, NH)
11	2.03 (12H (0.25), s, CH_3 enol form); 2.18 (6H, s, OC(O)CH_3); 2.25 (12H (0.75), s, CH_3 keto form); 3.00 (4H (0.75) d, J= 7.5, CH_2 keto form); 3.40 (4H (0.25), s, CH_2 enol form); 4.17 (1H, t, J = 6.9, CH keto form); 16.81 (0.5 H, s, OH enol form)
12	1.26 (6H, t, J = 7.2, OCH_2CH_3); 2.18 (6H, s OC(O)CH_3, 2.34 (6H, s, OC(O)CH_3); 3.03 (4H, qd, J = 8.7, J = 18.3, J = 6.0 Hz, $\underline{CH_2}$–CH); 4.00 (2H, dd, J = 6.0, J = 8.4, $\underline{CH_2}$–CH); 4.18 (4H, q, J = 7.2, O–$\underline{CH_2}CH_3$)

monoresonance spectrum. Mass spectrum and the supposed scheme of disintegration at an electronic impact are given in Scheme 2. Earlier, pyrrole **2** has been synthesized by other methods [11a–d], and it has depressant effect on the central nervous system in mice and has side effects in man [11e].

In dipyrrole **3**, ^{1}H NMR spectrum (Table 3) appears as a singlet from two methylene groups at 3.69 ppm with intensity corresponding to four protons. Two singlets of methyl groups appear at 2.31 and 2.42 ppm. At 6.22 ppm a doublet appears with $^1J_{CH}$ = 2.7 Hz. Protons of N–H groups appear in the low

TABLE 4 ^{13}C NMR (monoresonance) Data for Synthesized Compounds, δ, ppm, J; Hz

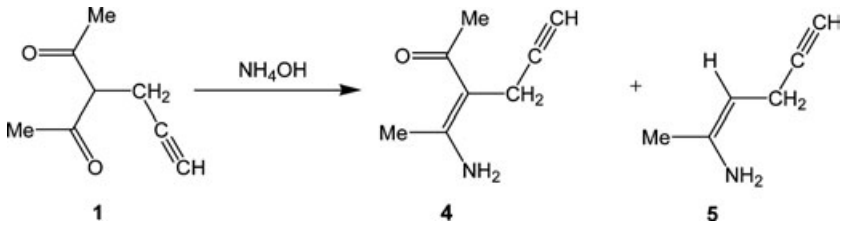
2	12.3 (q, $^1J_{CH} = 128.2$, CH_3—Pyr); 13.5 (q, $^1J_{CH} = 129.4$, CH_3—Pyr); 28.2 (q, $^1J_{CH} = 126.9$, CH_3—C(O)); 107.5 (d, $^1J_{CH} = 169.7$, C-3 Pyr); 120.5 (s, C-2 Pyr); 125.2 (s, C-4 Pyr); 133.7 (s, C-1 Pyr); 194.9 (s, C=O)
3	13.9 (q, $^1J_{CH} = 128.3$, CH_3Pyr); 28.3 (q, $^1J_{CH} = 127.0$, CH_3C(O)); 67.0 (t, $^1J_{CH} = 143.4$, Pyr CH_2CH_2 Pyr); 108.3 (d, $^1J_{CH} = 172.0$, C-3 Pyr); 120.7 (s, C-2 Pyr); 127.1 (s, C-4 Pyr); 135.5 (s, C-1 Pyr); 195.6 (s, C=O)
4	18.5 (t, $^1J_{CH} = 261.3$, =-CH_2-≡); 21.4 (q, $^1J_{CH} = 128.2$, CH_3-=); 28.0 (q, $^1J_{CH} = 127.0$, CH_3—C(O)); 67.8 (d, $^1J_{CH} = 247.8$, ≡C); 83.4 (dt, d $^2J_{CH} = 49.8$, —C≡); 100.3 (s, C=); 160.3 (s, NH_2—C=); 196.5 (s, O=C—)
6	18.0 (—CH_2— ≡); 28.2 ($\underline{C}H_3$—C(O)); 61.0 (C(O)$\underline{C}$HC(O)); 70.0 (≡CH); 80.5 (CH_2—$\underline{C}$≡); 128.6 (4CH, Ph); 133.6 (1CH, Ph); 136.0 (1C, Ph); 194.4 ($\underline{C}$(O)Ph); 201.3 ($\underline{C}$(O)Me)
8	19.1 (t, $^1J_{CH} = 140.4$, —CH_2-≡); 28.7 (q, $^1J_{CH} = 128.2$, CH_3—C(O)); 61.1 (d, $^1J_{CH} = 133.1$, CH); 67.3 (s, =(—C≡); 74.5 (t weak resolv., —C≡); 129.1 (d, $^1J_{CH} = 162.4$, C-3 Ph); 129.2 (d, $^1J_{CH} = 162.4$, C-4 Ph); 134.3 (d_m, d $^1J_{CH} = 161.2$, m weak resolv., C-4 Ph); 135.9 (t weak resolv., C-1 Ph); 194.4 (s, C(O)-Ph); 201.6 (s, C(O)—CH_3)
9	14.0 (q, $^1J_{CH} = 127.0$, $\underline{CH_3}$—CH_2O); 18.0 (dt, t $^1J_{CH} = 136.7$, d, $^2J_{CH} = 3.6$, ≡-$\underline{CH_2}$—CH); 29.5 (q, $^1J_{CH} = 128.2$, CH_3—C(O)); 57.8 (d, $^1J_{CH} = 134.3$, CH); 61.9 (t, $^1J_{CH} = 149.0$, ≡-CH_2); 66.6 (s, ≡C—C≡); 74.0 (t, $^2J_{CH} = 9.8$, ≡$\underline{C}$—CH_2); 167.8 (s, C(O)O); 200.7 (s, $\underline{C}$C(O)CH_3)
10	14.5 (q, $^1J_{CH} = 127.0$, $\underline{CH_3}$—CH_2O); 15.3 (q, $^1J_{CH} = 128.1$, CH_3-=); 17.6 (t, $^1J_{CH} = 132.4$, ≡-CH_2-=); 18.1 (t, $^1J_{CH} = 135.5$, —CH_2); 29.6 (q, $^1J_{CH} = 128.2$, CH_3—C(O)); 42.4 (q, $^1J_{CH} = 136.1$, N—CH_2); 57.9 (d, $^1J_{CH} = 127.0$, C(O)$\underline{CH}$C(O)); 59.1 (t, $^1J_{CH} = 150.2$, O$\underline{C}H_2$—CH_3); 61.9 (s, ≡$\underline{C}$—C≡); 63.9 (s, ≡C—C≡); 66.8 (t, $^1J_{CH} = 144.0$, O$\underline{C}H_2$—CH_2N); 72.8 (t, weak resolv., CH_2—$\underline{C}$≡); 78.4 (t, weak resolv., CH_2—$\underline{C}$≡); 86.9 (td, t $^1J_{CH} = 162.4$, d, $^2J_{CH} = 8.5$, ≡-$\underline{C}H_2$—CH); 87.8 (s, $\underline{C}$=C—N); 151.4 (d, $^1J_{CH} = 183.1$, =CH—O); 160.8 (s, N—$\underline{C}$=C—C(O)); 167.8 (s, O—$\underline{C}$(O)—C=C—N); 169.7 (s, $\underline{C}$(O)—O); 200.9 (s, $\underline{C}$(O)—CH_3)
11	23.0 (q, $^1J_{CH} = 128.2$, $\underline{CH_3}$—C(O)=, enol); 29.7 (q, $^1J_{CH} = 127.5$, $\underline{CH_3}$C(O)O); 29.9 (q, $^1J_{CH} = 128.2$, $\underline{CH_3}$C(O), keto-form); 41.7 (t, $^1J_{CH} = 128.2$, —$\underline{CH_2}$CH, keto-form); 42.1 (t, $^1J_{CH} = 125.2$, —$\underline{CH_2}$—C=, enol); 62.2 (d, $^1J_{CH} = 131.9$, CH, keto-form); 122.5 (s, =C—O); 192.3 (s, $\underline{C}$(O)O); 203.7 (s, C=O, keto-form); 205.6 (s, =C=)
12	14.0 (q, $^1J_{CH} = 127.0$, $\underline{CH_3}$—CH_2O); 29.6 (q, $^1J_{CH} = 128.2$, $\underline{CH_3}$—C(O)O); 30.0 (q, $^1J_{CH} = 128.2$, $\underline{CH_3}$C(O)C); 41.5 (t, $^1J_{CH} = 128.2$, CH_2—C=); 53.7 (d, $^1J_{CH} = 131.8$, $\underline{CH}$—CH_2); 61.7 (t, $^1J_{CH} = 147.7$, O$\underline{C}H_2$—CH_3); 125.0 (s, =C—O); 168.7 (s, $\underline{C}$(O)O); 202.3 (s, $\underline{C}$(O)CH_3); 205.7 (s, =C=)



SCHEME 2 Mass spectrum fragmentation of pyrrole **2**, m/z (int, %): 138 ([$M^+ + 1$] 4), 137 (M +50), 123 (9), 122 (100), 108 (2), 94 (13), 93 (7), 67 (13), 66 (3), 65 (4), 60 (7), 53 (8), 52 (7), 51, (7).

field at 9.4 ppm as a broad singlet with intensity in two protons. Identification of **3** is confirmed by ^{13}C NMR spectrum, as shown in Table 4. As against spectrum of pyrrole **2,** only one signal of methyl group at 12.3 ppm disappears and the novel signal looks like a triplet in monoresonance spectrum when double intensity appears at 67.0 ppm from two methylene groups.

On modification of reaction's conditions, namely by replacing ammonium chloride by ammonia, only



1 4 5

SCHEME 3

a mixture of enamines **4** and **5** in 4:1 ratio arises 50–60°C. Enamine **5** arises from diketone **1** or enamine **4** as a result of deacetylation (Scheme 3). The data of ^{1}H and ^{13}C NMR spectra of **4** and **5** are given in Tables 3 and 4, respectively.

Pyrrole **2** is also not formed in the reaction of **1** with ammonium chloride in water–ethanol solution by $CuCl_2$ catalysis or without catalysis.

The presence of active carbonyl groups in the molecule of **1** results in a reaction with ammonium chloride that also gives a complex with cuprous chloride. The intramolecular addition of amine group to a carbon–carbon triple bond in **4** occurred by cuprous chloride catalysis leading to cyclization and then isomerization to **2** (Scheme 4).

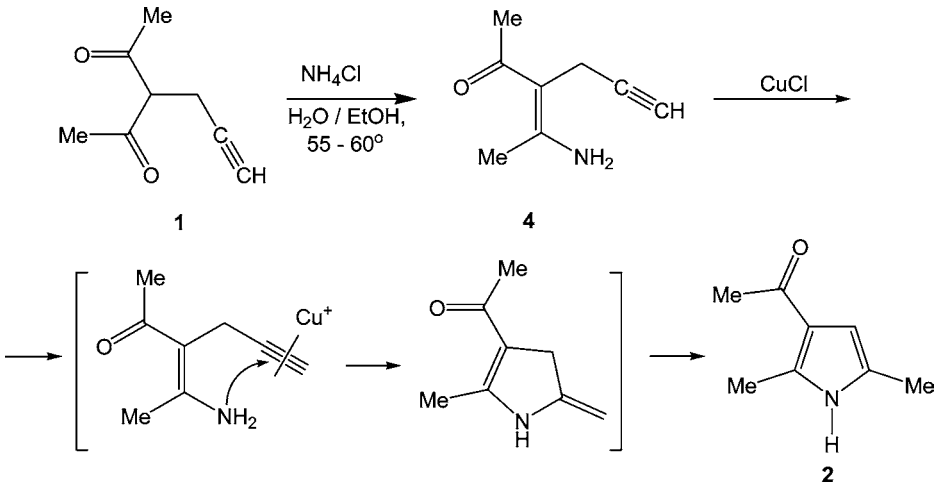
We determined that a variation in CuCl and NH_4Cl concentration influences the yield of **2**. Maximum yield 49% was obtained by using three times excess of cuprous chloride and ten times excess of ammonium chloride and oxygen as the oxidant. Without continuous bubbling by air, the yield of **2** rather decreases. Replacing cuprous chloride by palladium chloride reduces pyrrole **2** yield to 19% and rises dipyrrole **3**'s yield up to 65% with simultaneous increase of reaction time to 24 h (Table 5).

TABLE 5 The Influence of Reagents and Catalyst Concentrations on the Yields of **2** and **3**

Mole of Reagents					
Cat.	*NH_4Cl*	*Oxidant*	*Catalyst*	**2** *(%)*	**3** *(%)*
1	1	Air	Cu_2Cl_2	22	12
1	5	Air	Cu_2Cl_2	43	18
3	10	O_2	Cu_2Cl_2	49	25
3	10	Air	Cu_2Cl_2	46	20
3	10	Air	$PdCl_2$	19	65

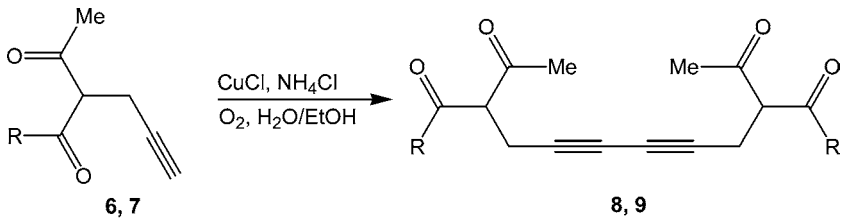
3-Benzoylhex-5-yn-2-one **6** and 2-acetylpent-4-ynic acid ethyl ester **7**, in the above conditions of the Glaser reaction, gave only diacetylenic compounds **8** and **9**, respectively with 50% yield (Scheme 5).

The specific triplet signal of acetylenic proton at 2 ppm disappears from ^{1}H NMR spectra of tetraketone **8** and diketodiester **9** (Table 3). The signals of nine types of carbon atoms for **9** and ten types for **8** are in their ^{13}C NMR spectra. The chemical shifts of most of the carbon atoms are practically unchanged as against spectra of **6, 7**. Only resonance signals of the triple bond move 3–6 ppm to the high field (Table 4), and their form in monoresonance spectra



1 4 2

SCHEME 4



6, 8 R = -C_6H_5; **7, 9** R = -O-CH_2-CH_3

SCHEME 5

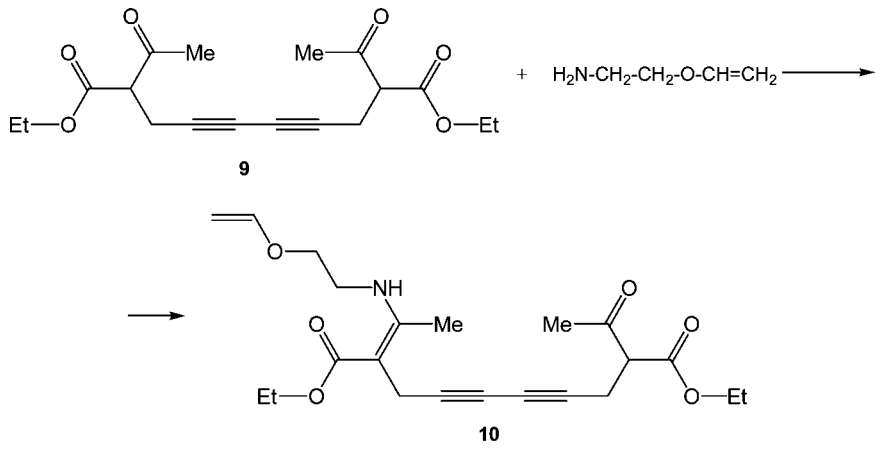
is changed. The signals from two external acetylene atoms of diacetylenic system look like triplets, but not as a doublet of triplets as in the spectra of **6** and **7**. The signals from two internal acetylene atoms look like singlet, but not like doublets as it was in the initial compounds. Attempts to obtain benzoyl or ethoxycarbonyl containing pyrroles like pyrrole **2** failed. Apparently this caused by the electronic influence of substituents R.

Diacethylenic group keeps the reaction of diacetylenic compounds **8, 9** with primary amines. We realized that the reaction of diethyl diester of **9** with vinyl ether of monoethanol amine by refluxing in absolute benzene gives only monoenamine **10** in 20% yield in the presence of molecular sieves of 4 Å and in twofold amine excess for 6 h (Scheme 6).

In the IR spectrum of **10**, bands of conjugated N—C=C—C=O system (1670 cm^{-1}), acetylene bond (2230 cm^{-1}), and N—H group (3450 cm^{-1}) were found. The ^1H NMR spectrum showed that the intensity of methyne proton's triplet at 3.66 ppm is reduced by twofold as a result of one amine molecule addition. Intensity of methylene doublet at 2.75 ppm also is reduced by twofold against **9**, but the novel singlet at 3.22 ppm appears with intensity corresponding to two protons. The formation of monoenamine also proves the appearance of signals in the spectrum corresponding to one vinyl ether of monoethanol amine substituents (Table 3). The ^{13}C NMR spectrum also confirmed the structure of **10** (Table 4). The signals of 20 carbon atoms are present in the spectrum. The novel signals of enamine group and vinyloxy ethyl substituent also appear.

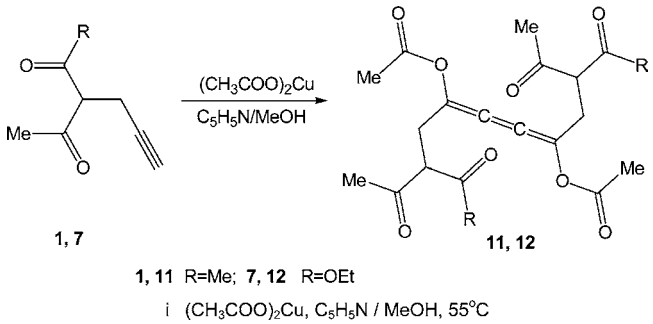
We have found for the first time that oxidative condensation of **1** and **7** at 55°C in pyridine–methanol solution and with the use of cupric acetate as an oxidant and a catalyst led to the formation of cumulenes **11** and **12** in accordance with TLC controlling for the course of reaction. The cumulenes **11** and **12** were isolated from the reaction mixture by column chromatography on SiO_2 with 36–42% yield (Scheme 7).

In IR-spectra of cumulens **11** and **12** the broad band of valets vibration of C=O bonds having two for **11** and three for **12** local maximums is observed in usual area. The series of intensive absorbtion bonds



i: reflux 6h in abs bzn, m.s. 4Å

SCHEME 6



SCHEME 7

in the 1160–1260 sm^{-1} area are connected with vibrations of polar bonds C—O—C, cumulenes group gave the absorbtion bands at the 1950 sm^{-1} (Table 1).

In the ^1H NMR spectra (Table 3), the signal of acetylenic proton disappeared but two new singlets from methyl protons of acetyl group appears at 2.17–2.20 ppm area from keto and enolic forms for compound **11** and for compound **12** appears at 2.34 ppm. The signal of methylene protons of compound **11** looks like a doublet at 3.00 ppm for the ketoform and as a singlet at 3.40 ppm for the enolic form. The signals of the corresponding protons of compound **12** look like a quartet of doublets at 3.0 ppm area.

In the ^{13}C NMR spectra (Table 4) of **11** and **12**, the signals specific to acetylene bond at 70–90 ppm are absent, but the novel signals for central atoms at the 206 ppm and for end's atoms of cumulene structure at 122–125 ppm appear. The signals of the additive acetyl groups appear at 23–30 ppm for methyl and 169–192 ppm for carbonyl atoms.

CONCLUSIONS

Various substances were synthesized by the Glaser reaction for 2-propargyl-1,3-dicarbonyl compounds, for example, the usual diacetylenes and well-known and novel heteroatom compounds such as pyrroles and dipyrroles including cumulenes. Results of the Glaser reaction for 2-propargyl-1,3-dicarbonyl compounds depend on their structures and experimental conditions.

EXPERIMENTAL

Initially 2-propargyl-1,3-dicarbonyl compounds **1, 6**, and **7** were synthesized by a routine method [12]. Physical characteristics of substances **1** and **7** are similar to those described in the literature [12,13]. Characteristics of propargyl benzoyl acetone **6** are given in Tables 1–4 and confirm that its structure.

Solvents were purified by distillation. Melting temperatures were determined by Boetius instrument and not corrected. IR spectra were recorded on Specord M-80 for the solution in CCl_4. ^1H and ^{13}C NMR spectra were measured on a Mercury-300 spectrometer (300 MHz for ^1H, 75.457 MHz for ^{13}C), using HMDS as an internal standard. Mass spectra were measured on a HP 5972 instrument under the standard conditions (EI, 70 eV). The reaction course and purity of the compounds were monitored by the TLC on Silufol UV-254 plates in a benzene: acetone (5:1 or 10:1) mixture using Chromotoscop instrument or I_2 for visualization.

General Procedures of the Glaser Reaction for 2-Propargyl-1,3-dicarbonyl Compounds

In Water–Ethanol Solution of Ammonium Chloride by Cuprous Chloride or Palladium Chloride Catalysis. A solution of **1** (or **6** and **7**) (0.01 mol) in 15 mL of EtOH was added to solution of ammonium chloride (0.1 mol) and catalyst (0.03 mol) in 25 mL water. The mixture was stirred for 5 h at 50–55°C with bubbling by oxygen or air, and after cooling was poured into ammoniated brine and extracted with benzene (5 × 10 mL). Benzene layer was dried over Na_2SO_4, and the solvent was removed by a rotary evaporator. The residue (pyrrole **2** and dipyrrole **3** or diacetylenes **8, 9**) was purified by column chromatography on silica gel with elution by benzene and followed by benzene–acetone in different ratios (20:1, 10:1, 5:1, 2:1, 1:1).

In Pyridine–Methanol Solution by Cupric Acetate Catalysis. Solution of **1**or **7** in 10 mL methanol was mixed with solution of cupric acetate (0.025 mol) in pyridine (30 mL) and methanol (20 mL). Resulting mixture was stirred for 4 h at 50–55°C then cooled, poured into excess of 3 N HCl at 0°C and extracted by ether. Ether layer was dried over Na_2SO_4. Solvent was removed by distillation. Residue was purified by column chromatography on SiO_2.

Diethyl 2-Methyl Ethyleneoxyethylaminomethylene-9 Acetyl deca-4,6-diyndioate **10**

Solution of 0.5 g (0.0015 mol) **9** and vinyl ether of monoethanol amine 0.26 g (0.003 mol) in methylene chloride (20 mL) refluxed under molecular sieves 4 Å for 2 h. Then, reaction mixture was cooled. Solvent was removed on a rotary evaporator. Residue was purified by column chromatography on SiO_2.

REFERENCES

[1] (a) Glaser, C. Chem Ber 1869, 2, 422–429; (b) Glaser C. Liebigs Ann Chem 1870, 154, 137–148; (c) Anchutz, R.; Muller, C. Angew Chem 1927, 40, 273–281; (d) Laue, T.; Plagens, A. Named Organic Reactions, 2nd ed.; Wiley: New York, 2005; pp. 320; (d) Mundy, B. P.; Ellerd, M. G.; Favaloro, F. G., Jr. Name Reactions and Reagents in Organic Synthesis, 2nd ed.; Wiley: New York, 2005, pp. 882.

[2] (a) Eglinton, G.; Jones, E. R. H.; Whiting, M. C. J Chem Soc 1952, 2873–2882; (b) Eglinton, G.; Jones, E. R. H.; Shaw, B. L.; Whiting, M. C. J Chem Soc 1954, 1860–1865; (c) Eglinton, G.; Galbraith, A. R. Chem Ind (London) 1956, 737–739; (d) Behr, O. M.; Eglinton, G.; Raphael, R. A. Chem Ind (London) 1959, 699–700; (e) Eglinton, G.; Galbraith, A. R. J Chem Soc 1959, 889; (f) Eglinton, G.; McCrae, W. In Advances in Organic Chemistry, Vol. 4; Raphael, R. A.; Taylor, E. C.; Wynberg, H. (eds.); Interscience: New York, 1963; pp. 225–328.

[3] (a) Hay, A. S. J. Org Chem 1960, 25, 1275–1276; (b) Hay, A. S. J Org Chem 1962, 27, 3320–3321; (c) Xu, G.-L.; Wang, C.-Y.; Ni, Y.-H.; Goodson, T. G., III; Ren, T. Organometallics 2005, 24, 3247–3254; (d) Gibtner, T.; Hampel, F.; Gisselbrecht, J.-P.; Hirsch, A. Chem Eur J 2002, 68, 408–432; (e) Nielsen, M. B.; Utesch, N. F.; Moonen, N. N. P.; Boudon, C.; Gisselbrecht, J.-P.; Concilio, S.; Piotto, S. P.; Seiler, P.; Gunter, P.; Gross, M.; Diederich, F. Chem Eur J 2002, 8, 3601–3613; (f) Anthony, J.; Knobler, C. B.; Diederich, F. Angew Chem, Int Ed Engl 1993, 32, 406–409.

[4] (a) Yadav, J. S.; Reddy, B. V. S.; Reddy, K. B.; Gayathri, K. U.; Prasad, A. R. Tetrahedron Lett 2003, 44, 6493–6496; (b) Boldi, A. M.; Anthony, J.; Gramlich, V.; Knobler, C. B.; Boudon, C.; Gisselbrecht, J.-P.; Gross, M.; Diederich, F. Helv Chim Acta 1995, 78, 779–796; (c) Noji, M.; Nakajima, M; Koga, K. Tetrahedron Lett 1994, 35, 7983; (d) Grudinin, A. L.; Koshkina, I. M.; Domnin, I. N. Zh Org Khim 1993, 29, 408–409 (in Russian); (e) Jones G. E.; Kendrick, D. A.; Holmes, A. B. Org Syn 1987, 65, 52–59.

[5] Li, P.-H.; Yan, J.-C.; Wang, M.; Wang, L. Chin J Chem 2004, 22, 219–221.

[6] Kabalka, G. W.; Wang, L.; Pagni, R. M. Synlett 2001, 1, 108–110.

[7] Fomina, L.; Vazquez, B.; Tkatchouk, E.; Fomine, S. Tetrahedron 2002, 58, 6741–6747.

[8] (a) Setzer, W. N.; Gu, X.; Wells, E. B.; Setzer, M. C.; Moriarity, D. M. Chem Pharm Bull (Tokyo) 2000, 48, 1776–1777; (b) Hoger, S. Macromol Symp 1999, 142, 185–191; (c) Menger, F. M.; Chen, X. Y. Tetrahedron Lett 1996, 37, 323–326; (d) Menger, F. M. US Patent 5391726 A 19950221, 1995 ; (e) Grudinin, A. L.; Koshkina, I. M.; Domnin, I. N. Zh Org Khim (Russia) 1993, 29, 408–409; (f) Augustin, K. E.; Schaefer, H. J. Liebigs Ann Chem 1991, 10, 1037–1040; (g) Jente, R.; Bosold, F.; Bauerle, J.; Anke, T. Phytochemistry 1985, 24, 553–559; (h) Bohlmann, F.; Tietze, B. M. Chem Berichte 1970, 103, 561–563; (i) Doxsee, K. M.; Hutchison, J. E. Green Organic Chemistry—Strategies, Tools, and Laboratory Experiments, 2004; pp. 142–151.

[9] (a) Eguchi, T.; Arakawa, K.; Kakinuma, K. Yuki Gosei Kagaku Kyokaishi 1999, 57, 784–797; (b) Cadiot, P.; Chodkiewicz, W. In Chemistry of Acetylenes; Viehe, H. G. (Ed.); Marcel Dekker: New York, 1969; pp. 597–647; (c) Siemsen, P.; Livingston, R. C.; Diederich, F. Angew Chem, Int Ed Engl. 2000, 39, 2632–2657; (d) Raphael, R. A. Acetylene Compounds in Organic Synthesis; Academic Press: New York, 1955; p. 127.

[10] (a) Vizer, S. A.; Dedeshko, E. H.; Yerzhanov, K. B. Chem Heterocycl Comp (Riga) 2002, 5, 702–703; (b) Vizer, S. A.; Dedeshko, E. H.; Mantchuk, Z. N.; Yerzhanov, K. B.; Dembitsky, V. M. Chemistry and Application of Natural and Synthetic Biologically Active Compounds; Almaty, 2004, 236–240.

[11] (a) Magnanini, G. Gazz Chim Ital 1889, 19, 283; (b) Sprio, V.; Madonia, P. Ann Chim (Rome, Italy) 1960, 50, 1627–1634; (c) Kleinspehn, G. G.; Briod, A. E. J Org Chem 1961, 26, 1652–1654; (d) Ghigi, E.; Drusiani, A. M. Atti Accad Sci Ist Bologna Classe Sci Fis Rend 1962, 251, 5–11 (e) Moffett, R. B. J Med Chem 1968, 11, 1251–1252.

[12] (a) Eglington, G.; Whiting, M. C. J Am Chem Soc 1953, 10, 3052–3059; (b) Arcadi, A.; Giuseppe, S. D. Curr Org Chem 2004, 8, 795–812.

[13] (a) Plouin, D.; Glenat, R. Compt Rend Acad Sci 1972, 274, 2084–2087; (b) Takacs, J. M.; Vayalakkada, S.; Jiang, X. Sci Synth 2002, 1, 265–318; (c) Boya, M.; Marquet, J.; Moreno-Manas, M.; Prior, M. Anal Quimica 1979, 75, 920–926; (d) Makaryan, G. M.; Sargsyan, M. S.; Badanyan, Sh. O. Armyanskii Khim Zh (USSR) 1979, 323, 217–222.