14.7 (q, *cis*-$\underline{C}H_3C(2)$); 16.4 (s, C(2)); 21.1 (d, C(1), J = 159.3 Hz); 22.6 (d, C(3), J = 162.5 Hz); 27.6 (t, C(1")); 28.5 (q, *trans*-$\underline{C}H_3C(2)$); 29.1 (q, C(3')); 39.1 (t, C(1')); 62.9 (t, C(2")); 210.1 (s, C(2')).

(1*R*,3*S*)-3-(2-Hydroxyethyl)-1-(1-oxoethyl)-2,2-dimethylcyclobutane (4). Yield 2.17 g (87%), colorless liquid (purity 99%, GLC data), $[\alpha]_D^{20}$ +41.2° (*c* 0.4, MeOH).[5] The parameters of the ^{1}H NMR and IR spectra of compound **4** are virtually identical with those described earlier.[1,6] ^{13}C NMR, δ: 16.0 (s, *cis*-$\underline{C}H_3C(2)$); 22.9 (t, C(4), J = 137.3 Hz); 29.7 (q, C(2')); 30.1 (q, *trans*-$\underline{C}H_3C(2)$); 32.8 (t, C(1"), J = 125.31 Hz); 38.5 (d, C(3), J = 133.0 Hz); 43.0 (s, C(2)); 54.1 (d, C(1), J = 132.9 Hz); 60.4 (t, C(2"), J = 143.7 Hz); 208.1 (s, C(1')).

References

1. T. Saton, T. Okuda, Y. Kaneko, and K. Yamakawa, *Chem. Pharm. Bull.*, 1984, **32**, 1401.
2. V. N. Odinokov, V. R. Akhmetova, G. Yu. Ishmuratov, L. P. Botsman, and G. A. Tolstikov, *Zh. Org. Khim.*, 1986, **22**, 953 [*J. Org. Chem. (USSR)*, 1986, **22** (Engl. Transl.)].
3. L. A. Flippia, D. W. Gallagher, and J.-A. Keyvan, *J. Org. Chem.*, 1989, **54**, 1430.
4. J. Gora, K. Smigielski, and J. Kula, *Synthesis*, 1982, **4**, 310.
5. J. Kula, *Lieb. Ann. Chem.*, 1983, **5**, 89.
6. G. W. Shaffer, A. B. Doerr, and K. L. Purzycki, *J. Org. Chem.*, 1972, **37**, 25.

Received April 29, 1998;
in revised form June 26, 1998

Acylation of sterically hindered 2-propargyl-1,3-diketones

S. I. Shergina,* A. S. Zanina, I. E. Sokolov, and M. S. Shvartsberg

Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 2350. E-mail: shvarts@ns.kinetics.nsc.ru

Sterically hindered 2-propargyl-1,3-diketones were acylated at the terminal acetylenic group by acyl chlorides in the presence of CuCl. Some peculiarities of the reaction were revealed.

Key words: 2-propargyl-1,3-diketones, steric hindrances, acylation, Cu and Pd catalysis, isomerization, acetylenic and allenic triketones.

We have described previously[1] the preparation of a new type of sterically hindered compounds containing two reaction centers: 1,3-dicarbonyl fragment and propargyl group. Acylation at the terminal acetylenic group is one of the possible ways of their further functionalization. Products of this reaction (triketones) can find use in the synthesis of polyfunctional heterocyclic compounds.[2,3]

In the present work, we studied for the first time acylation of sterically hindered propargyl-substituted 1,3-diketones in the presence of CuCl.[4]

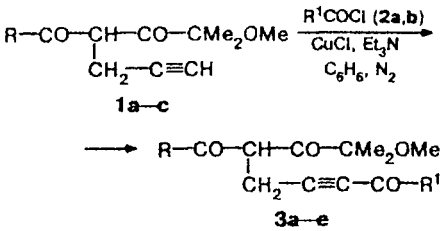
2-Propargyl-1,3-diketones **1a—c**, in which the structure of the substituent bound to one of the carbonyl groups remained unchanged and that of the substituent bound to the second group was sterically hindered, were used as the starting substrates:

The reactions of diketones **1a—c** with chlorides of branched aliphatic carboxylic acids **2a,b** in the presence of catalytic quantities of CuCl afford acetylenic triketones **3a—e** in 67—88% yields. The structures of the compounds obtained were confirmed by the data of elemental analysis and IR and ^{1}H NMR spectra. The IR spectra of triketones **3a—e** contain absorption bands corresponding to stretching vibrations of the CO groups (1670, 1700, and 1740 cm^{-1}) and the triple bond (2210 cm^{-1}). The ^{1}H NMR spectra exhibit signals of diastereotopic protons of the CH_2—C≡C group as two doublets of doublets (ABX system) in the 2.45—3.10 ppm region and a triplet of the methine proton of the β-dicarbonyl fragment at 4.58—5.15 ppm.

A by-product was formed (according to the TLC data) during isolation of triketone **3b**. It has been shown by special experiments that compound **3b** is transformed into this by-product during chromatography on Al_2O_3 (66% yield). Its IR spectrum contains an absorption band at 1550 cm^{-1} characteristic of the C=C bond of the furan cycle,[5] and the ^{1}H NMR spectrum exhibits a singlet at 6.85 ppm corresponding to the proton of this heterocycle.

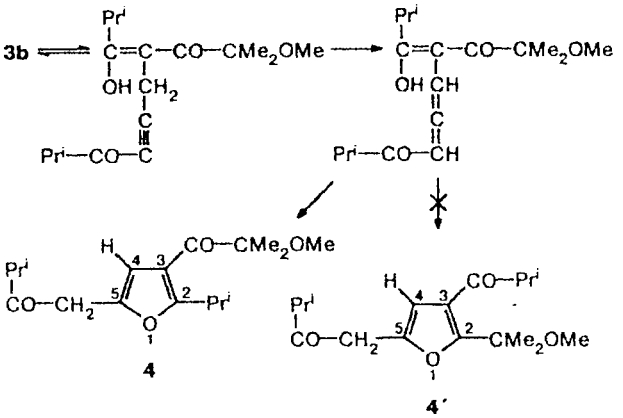
Based on the elemental analysis and spectral data, we ascribed the structure of 2-isopropyl-3-(2-methyl-2-methoxy-1-oxopropyl)-5-(3-methyl-2-oxobutyl)furan (**4**)

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 1, pp. 199—201, January, 1999.

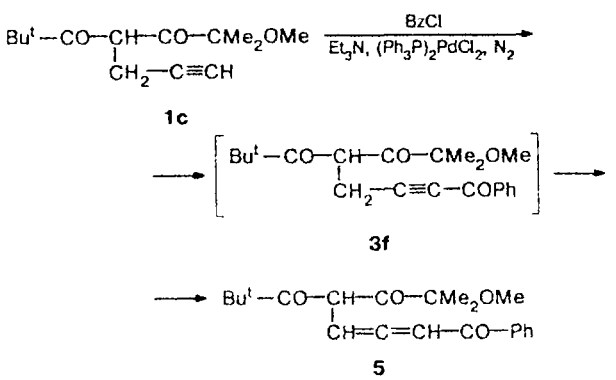


1: R = Ph (**a**); Pr^i (**b**); Bu^t (**c**)
2: R^1 = Pr^i (**a**), Bu^t (**b**)
3: R = Ph, R^1 = Bu^t (**a**); R = R^1 = Pr^i (**b**), R = Pr^i, R^1 = Bu^t (**c**); R = Bu^t, R^1 = Pr^i (**d**), R = R^1 = Bu^t (**e**)

to the compound obtained. An alternative structure of 3-isobutyryl-2-(1-methyl-1-methoxyethyl)-5-(3-methyl-2-oxobutyl)furan (**4'**) seems less probable, since the replacement of one of the isopropyl groups in the starting compound **3b** by the tertiary butyl group (compound **3d**) prevents cyclization.



Acylation of diketone **1c** by BzCl, unlike its reaction with aliphatic acyl chlorides **2a,b**, does not proceed to the end in the presence of catalytic quantities of CuCl. The reaction can be completed only when a threefold excess of CuCl or Pd complex catalyst is used.



The main reaction product coincides in elemental composition with the expected acetylenic ketone **3f**. However, its ^{1}H and IR spectra show that the compound isolated has allenic structure **5** rather than acetylenic structure **3f**.

Probably, ketone **3f** is the primary reaction product. This is confirmed by the presence of minor amounts of **3f** (~6%) in the crude product, which were identified by the ^{1}H and IR spectra. Then, under the reaction conditions, ketone **3f** is isomerized into allenic ketone **5**. Its ^{1}H NMR spectrum contains, along with signals of protons of methyl, methoxyl, and phenyl groups, signals corresponding to protons of the allenic group at 6.06 (s) and 6.32 (d) ppm and to the methine proton at the asymmetric carbon atom as a doublet at 6.62 ppm. The IR spectrum of **5** contains low-intensity absorption bands at 1900 and 1960 cm^{-1}; they are slightly split, which is typical of allenes containing an electron-withdrawing group in the α-position.[5] The formation of allenic ketone **5** can be most likely explained by the fact that the propargyl group is rearranged into the allenic group in a basic medium, and the presence of the benzoyl group facilitates isomerization and stabilizes the allenic structure. The presence of bulky substituents bound to carbonyl groups prevents cyclization of allenic ketone to furan.

Experimental

IR spectra were recorded on a UR-20 spectrophotometer in $CHCl_3$, and ^{1}H NMR spectra were obtained on Bruker-250 and Jeol FX 90 instruments in $CDCl_3$. The reaction course and purity of products were monitored by GLC and TLC. GLC analysis was carried out on a Chrom-5 instrument (a flame-ionization detector, a glass column 3.6×0.003 m with 5% SE-30 on Inerton N-AW-DMCS 0.2—0.3 mm, and nitrogen as the carrier gas). TLC analysis was carried out on Silufol UV-254 plates using hexane—acetone (3 : 1) as the eluent. 2-Propargyl-1,3-diketones **1a—c** were obtained by the procedure described previously.[1]

7-Benzoyl-2,2,9-trimethyl-9-methoxydec-4-yne-3,8-dione (3a). A solution of diketone **1a** (1.3 g, 0.005 mol), CuCl (50 mg, 0.0005 mol), Et_3N (1.5 g, 0.015 mol), and acyl chloride **2b** (1.5 g, 0.0124 mol) in anhydrous benzene (25 mL) was stirred at 75 °C for 1.5 h in an N_2 atmosphere until **1a** disappeared (TLC monitoring). The reaction mixture was cooled, and MeOH (1 mL) and 0.5 h after ether (25 mL) were added. The organic layer was washed with dilute HCl and water and dried with Na_2SO_4. Compound **3a** with m.p. 64—66 °C (ethanol) was isolated (1.1 g, 67%) by distillation. Found (%): C, 73.55; H, 7.64. $C_{21}H_{26}O_4$. Calculated (%): C, 73.66; H, 7.66. IR, ν/cm^{-1}: 1690, 1730 (C=O), 2220 (C≡C). ^{1}H NMR, δ: 0.95 (s, 9 H, 3 Me); 1.20 (s, 6 H, 2 Me); 2.89 (s, 3 H, MeO); 2.65—3.05 (m, ABX system, 2 H, CH_2—C≡); 5.15 (t, 1 H, HC—CH_2, J = 8.0 Hz); 7.40—7.55 (m, 3 H, Ph); 7.92 (d, 2 H, Ph, J = 8.0 Hz).

7-Isobutyryl-2,9-dimethyl-9-methoxydec-4-yne-3,8-dione (3b) was synthesized similarly to **3a** from compounds **1b** and **2a** (2 h, 30 °C). GLC analysis of crude compound **3b** showed the presence of a minor quantity of a by-product (furan **4**, see below). After chromatography on SiO_2 in benzene followed by

distillation, we obtained **3b** (88%) with b.p. 159—160 °C (1 Torr), n_D^{20} 1.4712. Found (%): C, 69.31; H, 9.03. $C_{17}H_{26}O_4$. Calculated (%): C, 69.36; H, 8.90. ^{1}H NMR, δ: 1.10—1.25 (m, 18 H, 6 Me); 2.45—3.10 (m, 4 H, CH_2—C≡ and 2 C<u>H</u>Me_2); 3.21 (s, 3 H, MeO); 4.65 (t, 1 H, <u>H</u>C—CH_2, J = 7.0 Hz).

7-Isobutyryl-2,2,9-trimethyl-9-methoxydec-4-yne-3,8-dione (3c) was obtained by the procedure for synthesis of **3a** from compounds **1b** and **2b** (3 h, 40 °C) in 71% yield with b.p. 163—164 °C (1 Torr), n_D^{20} 1.4705. Found (%): C, 69.92; H, 9.02. $C_{18}H_{28}O_4$. Calculated (%): C, 70.10; H, 9.15. ^{1}H NMR, δ: 1.11 (s, 9 H, 3 Me); 1.15 (d, 6 H, <u>Me</u>$_2$—CH, J = 7.0 Hz); 1.26 (s, 6 H, 2 Me); 2.65—3.15 (m, 3 H, CH_2C≡ and C<u>H</u>Me_2); 3.20 (s, 3 H, MeO); 4.58 (t, 1 H, C<u>H</u>—CH_2, J = 7.0 Hz).

2,9-Dimethyl-9-methoxy-7-pivaloyldec-4-yne-3,8-dione (3d) was synthesized from compounds **1c** and **2a** (2 h, 25 °C, GLC monitoring) in 74% yield with b.p. 172 °C (1 Torr), n_D^{18} 1.4720. Found (%): C, 70.03; H, 9.13. $C_{18}H_{28}O_4$. Calculated (%): C, 70.10; H, 9.15. ^{1}H NMR, δ: 1.00—1.35 (m, 21 H, 7 Me); 2.45—3.10 (m, 3 H, CH_2—C≡ and $CHMe_2$); 3.22 (s, 3 H, MeO); 4.85 (t, 1 H, <u>H</u>C—CH_2, J = 7.0 Hz).

2,2,9-Trimethyl-9-methoxy-7-pivaloyldec-4-yne-3,8-dione (3e) was obtained similarly to **3a** from compounds **1c** and **2b** (3 h, 27 °C) in 85% yield with b.p. 176—177 °C (1 Torr), n_D^{22} 1.4695. Found (%): C, 70.76; H, 9.52. $C_{19}H_{30}O_4$. Calculated (%): C, 70.78; H, 9.38. ^{1}H NMR, δ: 1.12 (s, 6 H, 2 Me); 1.21 (s, 18 H, 6 Me); 2.45—2.98 (two dd, ABX system, 2 H, CH_2—C≡); 3.25 (s, 3 H, MeO); 4.80 (t, 1 H, <u>H</u>—C—CH_2, J = 7.0 Hz).

2-Isopropyl-3-(2-methyl-2-methoxy-1-oxopropyl)-5-(3-methyl-2-oxobutyl)furan (4). A solution of triketone **3b** (0.2 g) in benzene was passed through the Al_2O_3 layer (h = 1.5 cm, d = 7.5 cm). After the solvent was removed, we obtained individual (according to the GLC and TLC data) furan **4** (0.13 g, 66%) with m.p. 39 °C (hexane). Found (%): C, 69.38; H, 8.96. $C_{17}H_{26}O_4$. Calculated (%): C, 69.36; H, 8.90. IR, ν/cm^{-1}: 1720, 1670 (C=O); 1550 (C=C of ring). ^{1}H NMR, δ: 1.16—1.65 (m, 18 H, 6 Me); 2.50—2.90 (m, 2 H, 2 C<u>H</u>Me_2); 3.12 (s, 3 H, MeO); 3.65 (s, 2 H, CH_2CO); 6.85 (s, 1 H, HC of ring).

Benzoylation of 2,2,6-trimethyl-6-methoxy-4-propargylheptane-3,5-dione (1c). A mixture of **1c** (1.2 g, 0.005 mol), $(Ph_3P)_2PdCl_2$ (100 mg), and Et_3N (1.4 g, 0.014 mol) in benzene (15 mL) was stirred for 5 min, and BzCl (0.9 g, 0.0064 mol) was added. The mixture was stirred at 40 °C for 7 h until **1c** disappeared (TLC monitoring), cooled, and extracted with benzene. The organic layer was washed with dilute HCl and water to the neutral reaction and dried with $MgSO_4$. The solvent was removed. Crude compound **5** containing (according to the ^{1}H NMR data) ~10% admixture of **3f** was obtained in 94% yield (1.6 g). ^{1}H NMR, δ: 2.72—3.10 (two d.d, ABX system, 2 H, CH_2—C≡); 4.95 (t, 1 H, <u>H</u>C—CH_2). IR, ν/cm^{-1}: 2210 (C≡C). After recrystallization from EtOH, compound **5** with m.p. 81—84 °C (EtOH) was obtained in 56.4% yield (0.96 g). Found (%): C, 73.40; H, 7.61. $C_{21}H_{26}O_4$. Calculated (%): C, 73.66; H, 7.66. ^{1}H NMR, δ: 1.15 (s, 9 H, 3 Me); 1.30, 1.35 (both s, 6 H, 2 Me); 3.26 (s, 3 H, MeO); 6.06 (s, 1 H, COCH=); 6.32 (d, 1 H, HC=, J = 3.5 Hz); 6.62 (d, 1 H, <u>H</u>CCH=, J = 3.5 Hz); 7.25—7.40 (m, 3 H, Ph); 7.63 (d, 2 H, Ph, J = 7.0 Hz).

References

1. A. S. Zanina, S. I. Shergina, I. E. Sokolov, and M. S. Shvartsberg, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2518 [*Russ. Chem. Bull.*, 1996, **45**, 2389 (Engl. Transl.)].
2. Jih Ru Hwu, Himatkumar V. Patel, Ren Jye Lin, and Maris O. Gray, *J. Org. Chem.*, 1994, **59**, 1577.
3. J. A. Ciller, N. Martin, M. Quintero, C. Seoane, and I. L. Soto, *Organic Preparation and Procedure Int.*, 1986, **18**, 227.
4. A. S. Zanina, S. I. Shergina, I. E. Sokolov, and I. L. Kotlyarevskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 2551 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 2307 (Engl. Transl.)].
5. K. Nakanishi, *Infrared Absorption Spectroscopy*, Holden-Day, Inc., San Francisco and Nankovo Company Ltd., Tokyo, 1962, 216 pp.

Received May 7, 1998;
in revised form June 9, 1998