Aminomethylation of hindered 2-propargyl-1,3-diketones

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2-Propargyl-substituted methoxy-1,3-diketones react with alkoxymethylamines or paraform and secondary amines in the presence of CuCl at the acetylene group to afford Mannich bases.

Key words: sterically hindered 2-propargyl-1,3-diketones, aminomethylation; synthesis; copper(I), catalysis.

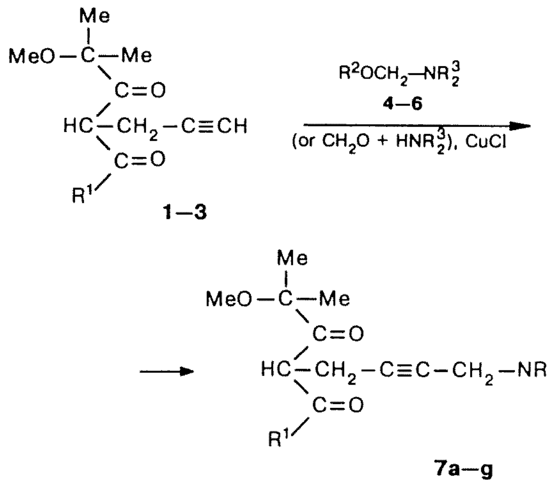
Earlier[1] we showed that methoxy-β-diketones react with propargyl halides under phase transfer catalysis conditions to afford *C*-substitution products. A new type of sterically hindered compounds with two reaction centers, the 1,3-dicarbonyl fragment and the terminal acetylene group, was obtained. Such compounds can be used as synthons for syntheses of both acetylene derivatives of heterocycles and polyfunctional compounds. The introduction of an amino group is one of the possible directions of their functionalization. It is known that polyacetylene derivatives containing amino-, oxo-, or aromatic substituents, offer a wide range of pharmacological properties.[2,3]

In this work, aminomethylation of sterically hindered methoxy-β-diketones **1—3** (Scheme 1) has been studied for the first time.

The possibility of aminomethylation of these ketones was not obvious since copper(I) chloride, which is a catalyst of the Mannich reaction,[4] forms complexes with 1,3-dicarbonyl compounds.[5] Butoxymethyldiethylamine (**4**), isobutoxymethylpiperidine (**5**), and isobutoxymethylmorpholine (**6**) were used as aminoalkylating agents in the synthesis of **7b—g** bases. The reactions were carried out in the presence of catalytic amounts of CuCl in dioxane in a nitrogen atmosphere. Base **7a** was obtained under "classic" Mannich reaction conditions[4] (amine, paraform, and CuCl). The conditions for both reaction procedures are similar (50—60 °C, 2.5—6 h) and both methods result in comparable yields of the target products (Table 1).

There are literature data on non-catalytic aminomethylation of some terminal acetylenes.[6] However, our experiments showed that 2-propargyl-1,3-diketones **1—3** do not enter into this reaction in the absence of a catalyst.

Scheme 1



1: $R^1 = Pr^i$
2: $R^1 = Bu^t$
3: $R^1 = Ph$
4: $R^2 = Bu^n$, $R^3 = Et$
5: $R^2 = Bu^i$, $R^3_2 = (CH_2)_5$
6: $R^2 = Bu^i$, $R^3_2 = (CH_2)_2O(CH_2)_2$

a: $R^1 = Pr^i$, $R^3 = Et$
b: $R^1 = Pr^i$, $R^3_2 = (CH_2)_5$
c: $R^1 = Pr^i$, $R^3_2 = (CH_2)_2O(CH_2)_2$
d: $R^1 = Bu^t$, $R^3 = Et$
e: $R^1 = Bu^t$, $R^3_2 = (CH_2)_2O(CH_2)_2$
f: $R^1 = Ph$, $R^3 = Et$
g: $R^1 = Ph$, $R^3_2 = (CH_2)_2O(CH_2)_2$

Compounds **7a—g** are stable substances. Their structure is confirmed by elemental analysis data and ^{1}H NMR and IR spectroscopy. The IR spectra of β-diketones **7a—e** contain absorption bands of the stretching vibrations of the CO groups (1700 and 1740 cm^{-1}). A shift of one of the bands to the lower frequency area is observed in the spectra of compounds **7f,g**, in which the carbonyl group is linked to the benzene cycle.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 5, pp. 1293—1295, May, 1996.

Table 1. Characteristics of compounds **7a—g**

Compound	Yield (%)	B.p./°C (*p*/Torr) or m.p./°C (solvent)	n_D (*T*/°C)	Found / Calculated (%)			Molecular formula	^1H NMR, δ
				C	H	N		
7a	72	163—164 (2)	1.4650 (20)	70.10 69.86	10.02 10.01	4.58 4.53	$C_{18}H_{31}NO_3$	0.9—1.20 (m, 18 H, 6 Me); 2.40—2.60 (m, 5 H, $N(CH_2)_2$, $HCHC^*H$); 2.65—2.80 (m, 1 H, $\underline{H}CHC^*H$); 2.95 (m, 1 H, $C\underline{H}Me_2$); 3.20 (s, 3 H, OMe); 3.30 (t, 2 H, NCH_2); 4.50 (t, 1 H, C^*H)
7b	67	184 (2)	1.4860 (18)	70.83 70.99	9.69 9.72	4.15 4.36	$C_{19}H_{31}NO_3$	1.10—1.25 (m, 12 H, 4 Me); 1.38—1.61 (m, 6 H, $(CH_2)_3$); 2.40—2.60 (m, 5 H, $(CH_2)_2N$, $HC\underline{H}C^*H$); 2.65—2.80 (m, 1 H, $\underline{H}CHC^*H$); 2.95 (m, 1 H, $C\underline{H}Me_2$); 3.15 (t, 2 H, NCH_2); 3.20 (s, 3 H, OMe); 4.55 (t, 1 H, C^*H)
7c	74	192 (1)	1.4850 (20)	67.10 66.84	9.32 9.04	4.44 4.33	$C_{18}H_{29}NO_4$	1.13 (d, 6 H, 2 $\underline{Me}CH$); 1.25 (s, 6 H, 2 $\underline{Me}C$); 2.40—2.80 (m, 6 H, $(CH_2)_2N$, $C\underline{H}_2C^*H_2$); 2.92 (m, 1 H, $C\underline{H}Me_2$); 3.15 (t, 2 H, NCH_2); 3.20 (s, 1 H, OMe); 3.60—3.80 (m, 4 H, $(CH_2)_2O$); 4.53 (t, 1 H, C^*H)
7d	71	156—158 (2)	1.4680 (21)	70.35 70.55	10.15 10.28	4.44 4.33	$C_{19}H_{33}NO_3$	0.95 (t, 6 H, 2 $\underline{Me}CH_2$); 1.15—1.30 (m, 15 H, 5 Me); 2.25—2.45 (m, 5 H, $N(C\underline{H}_2)_2$, $HC\underline{H}C^*H$); 2.65—2.75 (m, 1 H, $\underline{H}CHC^*H$); 3.15 (s, 3 H, OMe); 3.25 (m, 2 H, NCH_2); 4.7 (dd, 1 H, C^*H)
7e	82	205—207 (2)		67.70 67.62	9.38 9.26	4.34 4.15	$C_{19}H_{31}NO_4$	1.15—1.25 (m, 15 H, 5 Me); 2.40—2.50 (m, 5 H, $(CH_2)_2N$, $HC\underline{H}C^*H$); 2.70—2.85 (m, 1 H, $\underline{H}CHC^*H$); 3.15 (t, 2 H, NCH_2); 3.25 (s, 3 H, OMe); 3.65—3.70 (m, 4 H, $(CH_2)_2O$); 4.78 (dd, 1 H, C^*H)
7f	73	54—55 (pentane)		73.24 73.44	8.54 8.51	4.12 4.08	$C_{21}H_{29}NO_3$	0.85 (t, 6 H, 2 $\underline{Me}CH_2$); 1.20 and 1.22 (both s, 6 H, 2 Me); 2.20—2.40 (m, 4 H, $N(CH_2)_2$); 2.60—2.80 (m, 2 H, $C\underline{H}_2C^*H$); 2.90 (s, 3 H, OMe); 3.18 (t, 2 H, NCH_2); 5.10 (m, 1 H, C^*H); 7.40—7.60 (m, 3 H, Ph); 7.90—8.10 (m, 2 H, Ph)
7g	66	95—96 (hexane)		70.43 70.56	7.47 7.61	4.03 3.92	$C_{21}H_{27}NO_4$	1.20 (s, 6 H, 2 Me); 2.15—2.30 (m, 4 H, $(CH_2)_2N$); 2.60—2.80 (m, 2 H, $C\underline{H}_2C^*H$); 2.90 (s, 3 H, OMe); 3.0 (t, 2 H, NCH_2); 3.50—3.70 (m, 4 H, $(CH_2)_2O$); 5.0—5.20 (m, 1 H, C^*H); 7.40—7.60 (m, 3 H, Ph); 7.95—8.15 (m, 2 H, Ph)

Experimental

IR spectra were recorded on an UR-20 (Carl Zeiss) instrument in $CHCl_3$, ^1H NMR spectra were obtained on a Jeol FX 90Q instrument (89.55 MHz) in $CDCl_3$ using $SiMe_4$ as the internal standard. TLC analysis was carried out on Silufol UV-254 (Kavalier) plates in dioxane. Alkoxymethylamines **4—6** were synthesized by the previously described procedure.[7]

2-Methyl-2-methoxy-4-pivaloyl-8-diethylaminooct-6-yne-3-one (7d). A mixture of alkyne **2** (4.8 g, 0.02 mol), amine **4** (4.0 g, 0.024 mol), and CuCl (0.02 g, 0.02 mol) in dioxane (25 mL) was stirred at 60 °C for 7 h in a nitrogen atmosphere (TLC control). The reaction mixture was then cooled, water (10 mL) was added, and the reaction mixture was extracted with ether. The ethereal layer was washed with water and treated with 50 mL of diluted (1 : 1) HCl. The ethereal layer was separated and a solution of NH_3 (25 %) was gradually added to the residue. The ammonium solution was extracted with ether, the ethereal extract was dried with Na_2SO_4, the ether was distilled off, and the residue was distilled *in vacuo* to afford 4.4 g of **7d**. 4-Isobutyryl-2-methyl-2-methoxy-8-piperidinooct-6-yne-3-one (**7b**), 4-isobutyryl-2-methyl-2-methoxy-8-morpholinooct-6-yne-3-one (**7c**), 2-methyl-2-methoxy-8-morpholino-4-pivaloyloct-6-yne-3-one (**7e**), 4-benzoyl-2-methyl-2-methoxy-8-diethylaminooct-6-yne-3-one (**7f**), and 4-benzoyl-2-methyl-2-methoxy-8-morpholinooct-6-yne-3-one (**7g**) were synthesized by similar procedures.

4-Isobutyryl-2-methyl-2-methoxy-8-diethylaminooct-6-yne-3-one (7a). A mixture of alkyne **1** (4.48 g, 0.02 mol), paraform (0.5 g, 0.02 mol), CuCl (0.02 g, 0.02 mol), and diethylamine (1.46 g, 0.02 mol) in dioxane (50 mL) was stirred for 3 h at 50 °C. The product was isolated as described above for compound **7d** to afford 4.4 g of **7a**.

The yields, constants, elemental analysis data, and ^1H NMR spectra of β-diketones **7a—g** are given in Table 1.

References

1. A. S. Zanina, S. I. Shergina, and I. E. Sokolov, in *Mezhfaznyi kataliz, novye idei i metody* [*Phase Transfer Catalysis, New Ideas and Methods*], Moscow, 1994, 31 (in Russian).
2. N. Bohlman, *Angew. Chem.*, 1955, **67**, 389.
3. E. K. Andrievskaya and I. L. Kotlyarevskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1970, 2809 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1970, **19** (Engl. Transl.)].
4. L. B. Fisher, *Usp. Khim.*, 1958, **27**, 578 [*Russ. Chem. Rev.*, 1958, **27** (Engl. Transl.)].
5. D. Gibson, B. F. G. Johnson, and J. Lewis, *J. Chem. Soc. A.*, 1970, 367.
6. J. L. Dumont, A. Metge, W. Chodkiewicz, and P. Cadiot, *Compt. Rend.*, 1965, **260**, 215.
7. R. I. Kruglikova, G. R. Kalinina, and P. S. Leonova, *Zh. Org. Khim.*, 1966, **2**, 1155 [*J. Org. Chem. USSR*, 1966, **2** (Engl. Transl.)].

Received October 12, 1995

A synthesis of chlorofluoro(*N*-trimethylsilyl)imidophosphates

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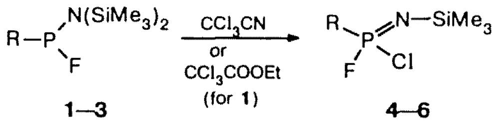
Reaction of bis(trimethylsilyl)amidofluorophosphites with the derivatives of trichloroacetic acid affords chlorofluoro(*N*-trimethylsilyl)imidophosphates.

Key words: chlorofluoro(*N*-trimethylsilyl)imidophosphates; bis(trimethylsilyl)amidofluorophosphites, ethyl trichloroacetate, trichloroacetonitrile, reactions.

Halo(*N*-trimethylsilyl)imidophosphates (*N*-trimethylsilyl-*P*-halophosphazenes) are of interest as the intermediates in the synthesis of various phosphazenes and polyphosphazenes.[1,2]

We have shown previously that the "halophilic"[3] reaction of bis(trimethylsilyl)amidophosphites with the derivatives of trichloroacetic acid is useful for the synthesis of compounds of such type. In the present work, it is found that in the case of bis(trimethylsilyl)amidofluorophosphites, this reaction affords the poorly studied[4] chlorofluoro(*N*-trimethylsilyl)imidophosphates. Thus, the reaction of bis(trimethylsilyl)amidofluorophosphites **1—3** with CCl_3CN gives phosphazenes **4—6**, respectively, whereas in the reactions with CCl_3COOEt, the desired product **4** is formed only from phosphite **1**.



1—3 **4—6**

1, 4: R = Et_2N
2, 5: R = Pr^iO
3, 6: R = Bu^iO

Compounds **4—6** are colorless, nonviscous liquids fuming on air. Even when thoroughly protected from the moisture of air, they turn brown after several hours. The composition and structure of compounds **4—6** were established by the elemental analysis data and ^1H, ^{19}F, and ^{31}P NMR and IR spectroscopy (Table 1) and mass spectrometry.

One can assume that the considered reaction proceeds *via* the stage of the positive halogen atom abstraction; this pathway was proposed previously by us for the silylated derivatives of phosphorous acid.[3]

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 1295—1296, May, 1996.

1066-5285/96/4505-1234 $15.00