One-step cyclopropanation of alkynes with diiodomethane and triethylaluminum

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Cyclopropanation of mono- and dialkyl-substituted alkynes under the action of CH_2I_2 and Et_3Al afforded the corresponding 1-alkyl- and 1,2-dialkyl-substituted 1,2-diethylcyclopropanes in 65—80% yields.

Key words: alkynes, cyclopropanes, cyclopropanation.

Cyclopropanation of cyclohexene with CH_2I_2 in the presence of trialkylalanes giving rise to norcarane in 20% yield was first performed in 1964.[1] Later on, the procedures for cyclopropanation of alkenes[2] and allenic alcohols[3,4] were improved, in some cases, cyclopropanation products being obtained in quantitative yields.

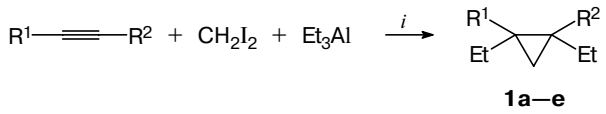
To extend the scope of this approach, we examined the possibility of cyclopropanation of alkynes. Previously, we have developed a two-stage procedure for the conversion of dialkyl-substituted alkynes into the corresponding 1,1-dialkylcyclopropanes by catalytic cycloalumination of the starting alkynes with Et_3Al in the presence of a catalytic amount of Cp_2ZrCl_2 to obtain 2,3-disubstituted aluminacyclopent-2-enes. The latter were converted without isolation into the target cyclopropanes upon treatment with dialkyl sulfates.[5]

In the present study, we examined the possibility of cyclopropanation of internal and terminal alkynes under the action of the CH_2I_2—Et_3Al system with the aim of developing a one-step procedure for cyclopropanation of alkynes.

Preliminary experiments demonstrated that CH_2I_2 reacted with mono- and dialkyl-substituted alkynes (hex-1-yne, hept-1-yne, oct-2-yne, oct-4-yne, and dec-5-yne) in the presence of Et_3Al under mild conditions (20—25 °C) to form the corresponding 1-alkyl- or 1,2-dialkyl-substituted 1,2-diethylcyclopropanes (**1**) in 65—80% yields (Scheme 1).

Analysis of the reaction products by high-performance gas chromatography, GLC-mass spectrometry, and ^{13}C NMR spectroscopy demonstrated that the reactions involving dec-5-yne or oct-4-yne afforded 1 : 1 mixtures of *cis* and *trans* isomers of the corresponding

Scheme 1



1a—e

i. 20—25 °C, hexane.

	a	**b**	**c**	**d**	**e**
R^1	n-C_5H_{11}	Bu	Me	Pr	Bu
R^2	H	Bu	n-C_5H_{11}	Pr	H

1,2-dialkyl-1,2-diethylcyclopropanes **1b** and **1d** (for **1b**, the ^{13}C NMR spectral parameters of the *cis* and *trans* isomers are identical except for the resonance absorption lines of C(3)).

The reactions of terminal alkynes (hept-1-yne and hex-1-yne) with CH_2I_2 and Et_3Al proceeded stereoselectively to form the corresponding 1-alkyl-1,2-diethylcyclopropanes **1a,e**. The reaction with oct-2-yne proceeded analogously to yield the only stereoisomer, which may be indicative of the steric control over stereoselectivity of the reaction pathway. The physical methods used did not allow us to determine the configurations of the resulting tri- and tetra-substituted cyclopropanes.

Based on the published data,[1,6,7] we proposed probable schemes of the reaction. Let us consider the formation of tetrasubstituted cyclopropane **1b** from dec-5-yne (Scheme 2).

Of three reaction pathways presented in Scheme 2, only the path *c* corresponds to the observed formation of two stereoisomers of compound **1b** from dec-5-yne

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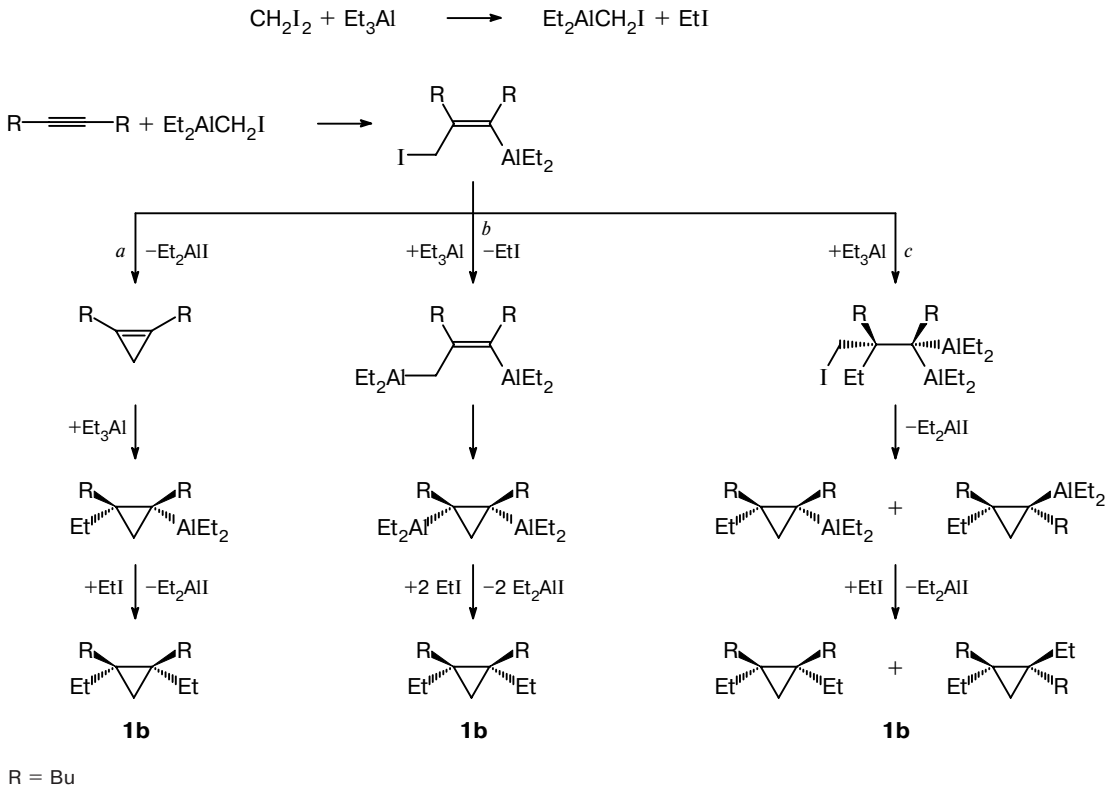
Scheme 2



because the reactions taking the paths *a* or *b* should proceed stereoselectively to give the only stereoisomer (the configuration of the cyclopropane formed in these reactions is determined at the stage of carboalumination proceeding stereospecifically[8]).

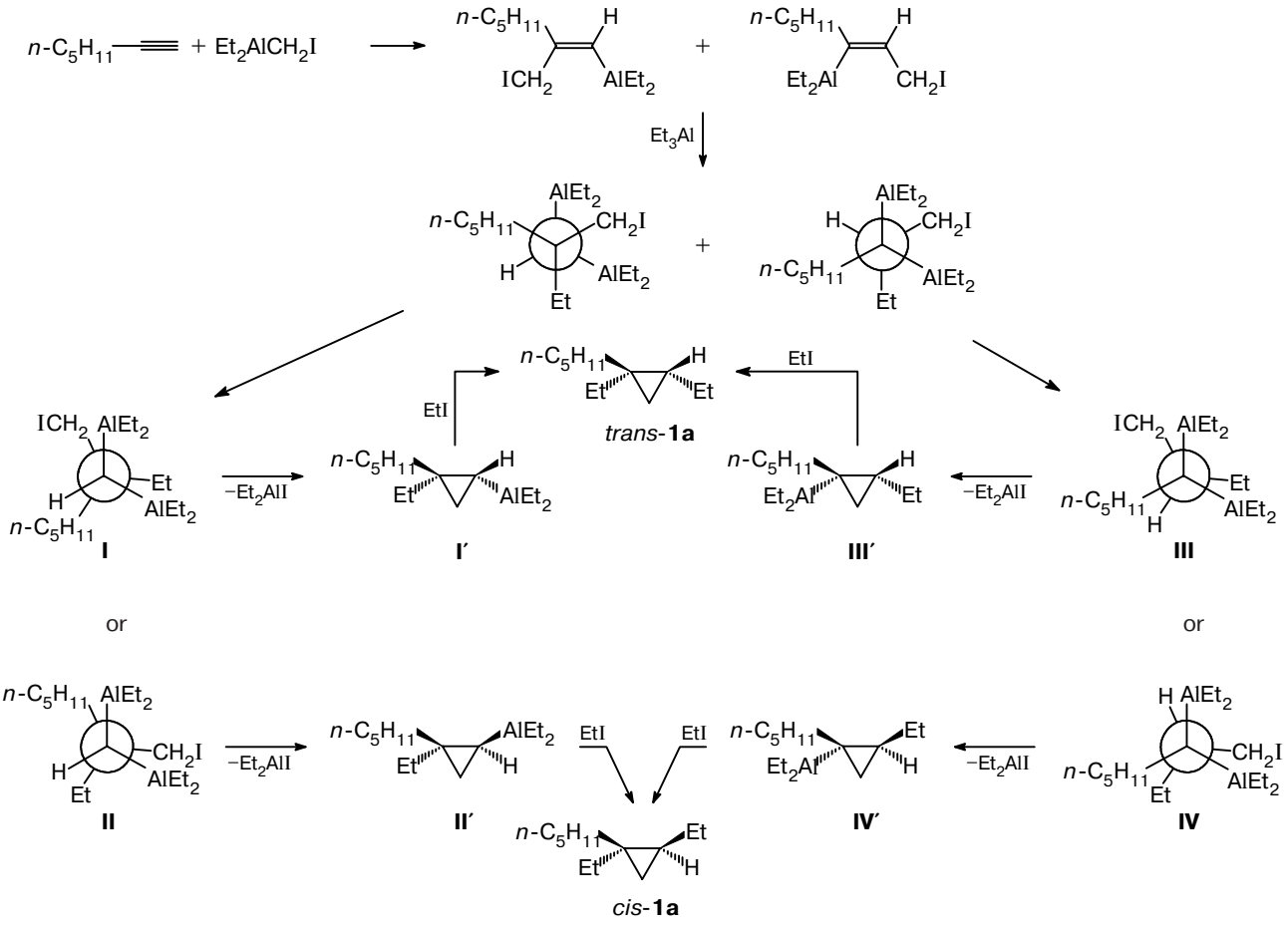
In the case of unsymmetrical alkynes (hex-1-yne, hept-1-yne, and oct-2-yne), the formation of the only stereoisomer of compounds **1a,c,e** does not contradict the reaction path *c* (Scheme 3). Thus according to Scheme 3, the configuration of the final product **1a** generated from hept-1-yne is determined at the stage of elimination of Et_2AlI from the dialuminum compound and, to a first approximation, depends on the relative stability of eclipsed conformations **I**—**IV**. Since steric interactions in structures **I′**—**IV′** are identical with those in eclipsed conformations **I**—**IV** (provided that conformations **I** and **II** and conformations **III** and **IV** are compared), conformations **I′**—**IV′** were considered for simplicity. Calculations of the strain energies of structures **I′**, **II′**, **III′**, and **IV′** by molecular mechanics (6.37, 6.70, 3.37, and 9.87 kcal mol^{-1}, respectively) demonstrated that the formation of the *trans* isomer of compound **1a** is energetically more favorable. It should be noted that qualitative analysis of conformations **I**—**IV** led us to the same conclusion.

Based on analogous reasoning, it can be suggested that the reactions of hex-1-yne or oct-2-yne also afforded *trans* isomers of compounds **1c,e**.

With the aim of extending the scope of the reaction under consideration and revealing the effect of the structure of the starting alkyne on the yield and selectivity of the formation of substituted cyclopropanes, we studied this process involving mono- and disubstituted alkynes containing alkyl, phenyl, and allylic substituents at the triple bond. Under the conditions found previously, alkylphenyl-substituted alkynes, for example, methylphenylacetylene and phenylpropylacetylene, exhibit low reactivity. The reactions involving allyl-containing alkynes, for example, allylphenylacetylene, crotylphenylacetylene, allylamylacetylene, and amylcrotylacetylene, gave rise to complex mixtures of products due, apparently, to side reactions proceeding with the participation of the double bond. The reaction with phenylacetylene also proceeded nonselectively to form a complex mixture of products.

According to the probable scheme of the reaction, one of its key stages involves carboalumination of alkyne with diethyl(iodomethyl)aluminum. It is known that Cp_2ZrCl_2 is an efficient catalyst of carboalumination of substituted alkynes.[9] We found that phenyl- and allyl-containing alkynes reacted with Et_3Al and CH_2I_2 in the presence of catalytic amounts of Cp_2ZrCl_2 to form 2,3-disubstituted alumacyclopent-2-enes, which indicates that the processes performed under these conditions involve cycloalumination of alkynes discovered by us previously.[10,11] However, the zirconium-catalyzed

Scheme 3



reactions of mono- and dialkyl-substituted alkynes (hept-1-yne and dec-5-yne) with Et_3Al and CH_2I_2 afforded the cyclopropanation products of alkyne, the reaction with hept-1-yne proceeding with lower selectivity.

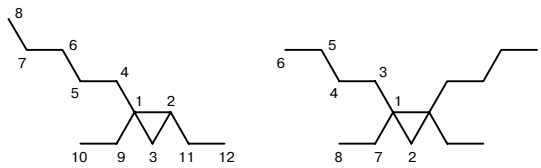
To summarize, we studied for the first time cyclopropanation of mono- and disusbtituted alkynes with the CH_2I_2—Et_3Al system. An efficient one-step procedure was developed for cyclopropanation of mono- and dialkyl-substituted alkynes giving rise to tri- and tetraalkyl-substituted cyclopropanes, respectively.

Experimental

The experiments were carried out under an atmosphere of dried argon. Hexane was distilled over $LiAlH_4$ immediately before use. The reaction products were analyzed on a Carlo Erba chromatograph (a 25 m×0.2-mm Ultra-1 glass capillary column (Hewlett—Packard); flame ionization detector; 50—170 °C; helium as the carrier gas). The mass spectra were measured on a Finnigan 4021 instrument; the energy of ionizing electrons was 70 eV; the temperature of the ionization chamber was 200 °C. The ^1H and ^{13}C NMR spectra were recorded on Jeol FX-90Q (22.5 MHz for ^{13}C and 90 MHz for ^1H) and Bruker AM-300 (75.46 MHz for ^{13}C and 300 MHz for ^1H) spectrometers with Me_4Si and $CDCl_3$, respectively, as the internal standard. The ^{13}C NMR spectra were recorded in the fully and partially proton-decoupled modes and using the INEPT technique. The strain energies were calculated with the use of the MMFF94 force field taking into account the conformer distribution at 25 °C.

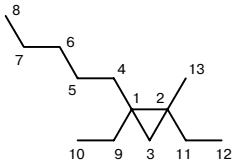
Synthesis of 1-alkyl-1,2-diethylcyclopropanes 1a,e (general procedure). A mixture of hexane (50 mL), monoalkylacetylene (10 mmol, Et_3Al (30 mmol), and CH_2I_2 (20 mmol) was stirred at 20—25 °C for 8 h. After completion of the reaction, the mixture was hydrolyzed with a 10% aqueous solution of HCl. The aqueous layer was extracted with diethyl ether, combined with the organic layer, and kept over anhydrous $CaCl_2$.

1-(*n*-Amyl)-1,2-diethylcyclopropane (1a). The yield was 69%, b.p. 90 °C (20 Torr). Found (%): C, 85.42; H, 14.23. $C_{12}H_{24}$. Calculated (%): C, 85.63; H, 14.37. ^{13}C NMR ($CDCl_3$), δ: 10.71 (q, C(10), $^1J_{CH}$ = 124.64 Hz); 14.22 (q, C(8), $^1J_{CH}$ = 123.78 Hz); 14.67 (q, C(12), $^1J_{CH}$ = 124.27 Hz); 18.31 (t, C(3), $^1J_{CH}$ = 156.30 Hz); 22.54 (t, C(7), $^1J_{CH}$ = 124.95 Hz); 22.87 (t, C(11), $^1J_{CH}$ = 125.74 Hz); 24.82 (s, C(1)); 26.25 (d, C(2), $^1J_{CH}$ = 154.82 Hz); 26.64 (t, C(5), $^1J_{CH}$ = 126.54 Hz); 29.82 (t, C(9), $^1J_{CH}$ = 125.39 Hz); 30.47 (t, C(4), $^1J_{CH}$ = 124.96 Hz); 32.55 (t, C(6), $^1J_{CH}$ = 123.72 Hz). ^1H NMR ($CDCl_3$), δ: 0.18—0.42 (m, 3 H, C(2)H, $C(3)H_2$); 0.85 (t, 6 H, $C(10)H_3$, $C(12)H_3$, $^3J_{CH}$ = 4.89 Hz); 0.97 (t, 3 H, $C(8)H_3$, $^3J_{CH}$ = 6.84 Hz); 1.07—1.50 (m, 12 H, $C(4—7)H_2$,

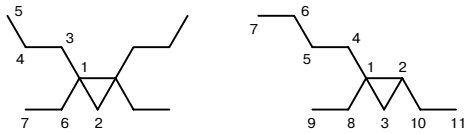


1a

1b



1c



1d **1e**

C(9)H_2, C(11)H_2). MS, *m/z* (I_{rel} (%)): 168 $[M]^+$ (4), 139 $[M - C_2H_5]^+$ (3), 126 (3), 112 (11), 97 $[M - C_5H_{11}]^+$ (41), 83 (39), 70 (52), 69 (67), 55 (100).

1-(*n*-Butyl)-1,2-diethylcyclopropane (1e). The yield was 64%, b.p. 73 °C (20 Torr). Found (%): C, 85.51; H, 14.40. $C_{11}H_{22}$. Calculated (%): C, 85.63; H, 14.37. ^{13}C NMR, ($CDCl_3$), δ: 10.60 (q, C(9)); 14.18 (q, C(7)); 14.50 (q, C(11)); 18.27 (t, C(3)); 22.44 (t, C(10)); 23.28 (t, C(6)); 26.14 (s, C(1)); 26.79 (t, C(5)); 29.13 (d, C(2)); 29.46 (t, C(4)); 30.37 (t, C(8)). ^1H NMR ($CDCl_3$), δ: −0.16—0.35 (m, 3 H, C(2)H, C(3)H_2); 0.68—1.02 (m, 9 H, C(7)H_3, C(9)H_3, C(11)H_3); 1.14—1.49 (m, 10 H, C(4—6)H_2, C(8)H_2, C(10)H_2). MS, *m/z* (I_{rel} (%)): 154 $[M]^+$ (5), 125 $[M - C_2H_5]^+$ (4), 97 $[M - C_4H_9]^+$ (57).

Synthesis of 1,2-dialkyl-1,2-diethylcyclopropanes 1b—d (general procedure). A mixture of hexane (50 mL), dialkyl-substituted alkyne (10 mmol), Et_3Al (40 mmol), and CH_2I_2 (20 mmol) was stirred at 20—25 °C for 18 h. Then the reaction mixture was hydrolyzed with a 10% aqueous solution of HCl. The aqueous layer was extracted with diethyl ether, combined with the organic layer, and kept over anhydrous $CaCl_2$.

1,2-Di(*n*-butyl)-1,2-diethylcyclopropane (1b). The yield was 78%, b.p. 69 °C (1 Torr). Found (%): C, 85.31; H, 14.56. $C_{15}H_{30}$. Calculated (%): C, 85.63; H, 14.37. ^{13}C NMR ($CDCl_3$), δ: 11.18 (q, C(8), $^1J_{CH}$ = 124.96 Hz); 14.22 (q, C(6), $^1J_{CH}$ = 124.40 Hz); 23.30 (t, C(5), $^1J_{CH}$ = 125.42 Hz); 24.27 (t, C(2), $^1J_{CH}$ = 155.64 Hz); 24.27 (t, C(7), $^1J_{CH}$ = 126.13 Hz); 29.24 (t, C(4), $^1J_{CH}$ = 125.36 Hz); 30.04 (s, C(1)); 30.72 and 30.77 (both t, C(3), $^1J_{CH}$ = 124.05 Hz). ^1H NMR ($CDCl_3$), δ: 0.68—1.10 (m, 14 H, C(2)H_2, C(6)H_3, C(8)H_3); 1.17—1.53 (m, 16 H, C(3—5)H_2, C(7)H_2). MS, *m/z* (I_{rel} (%)): 210 $[M]^+$ (5), 181 $[M - C_2H_5]^+$ (39), 153 $[M - C_4H_9]^+$ (39), 125 (12), 111 (21), 97 (60), 83 (54), 69 (100).

1-(*n*-Amyl)-1,2-diethyl-2-methylcyclopropane (1c). The yield was 75%, b.p. 82 °C (10 Torr). Found (%): C, 85.47; H, 14.39. $C_{13}H_{26}$. Calculated (%): C, 85.63; H, 14.37. ^{13}C NMR ($CDCl_3$), δ: 11.36 (q, C(12)); 11.49 (q, C(10)); 14.22 (q, C(8)); 18.96 (q, C(13)); 22.93 (t, C(7)); 25.08 (t, C(3)); 25.73 (s, C(2)); 26.90 (t, C(5)); 29.04 (t, C(4)); 29.56 (s, C(1)); 30.80 (t, C(9)); 32.68 (t, C(6)); 34.38 (t, C(11)). ^1H NMR ($CDCl_3$), δ: −0.07—0.06 (m, 2 H, C(3)H_2); 0.61—0.98 (m, 9 H, C(8)H_3, C(10)H_3, C(12)H_3); 1.02 (s, 3 H, C(13)H_3); 1.06—1.47 (m, 12 H, C(4—7)H_2, C(9)H_2, C(11)H_2). MS, *m/z* (I_{rel} (%)): 182 $[M]^+$ (5), 153 $[M - C_2H_5]^+$ (23), 111 $[M - C_5H_{11}]^+$ (33), 97 (24), 83 (62), 69 (95), 55 (100).

1,2-Diethyl-1,2-di(*n*-propyl)cyclopropane (1d). The yield was 72%, b.p. 93 °C (15 Torr). Found (%): C, 85.79; H, 14.25. $C_{13}H_{26}$. Calculated (%): C, 85.63; H, 14.37. ^{13}C NMR ($CDCl_3$), δ: 11.29 (q, C(7)); 14.74 (t, C(5)); 20.20 (t, C(4)); 24.43 (t, C(2)); 24.43 (t, C(6)); 30.02 (s, C(1)); 33.47 and 33.60 (both t, C(3)). ^1H NMR ($CDCl_3$), δ: 0.73—1.00 (m, 14 H, C(2)H_2, C(5)H_3, C(7)H_3); 1.05—1.48 (m, 12 H, C(3)H_2, C(4)H_2, C(6)H_2). MS, *m/z* (I_{rel} (%)): 182 $[M]^+$ (5), 153 $[M - C_2H_5]^+$ (41), 139 $[M - C_3H_7]^+$ (45), 97 (10), 83 (28).

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References

1. D. B. Miller, *Tetrahedron Lett.*, 1964, **17**, 989.
2. K. Maruoka, Y. Fukutani, and H. Yamamoto, *J. Org. Chem.*, 1985, **50**, 4412.
3. J. M. Russo and W. A. Price, *J. Org. Chem.*, 1993, **58**, 3589.
4. D. Li, H.-q. Zhou, S. Dakoji, I. Shin, E. Oh, and H.-W. Liu, *J. Am. Chem. Soc.*, 1998, **120**, 2008.
5. U. M. Dzhemilev, A. G. Ibragimov, I. R. Ramazanov, M. P. Luk′yanova, A. Z. Sharipova, and L. M. Khalilov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1092 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1086].
6. H. Hoberg, *Lieb. Ann.*, 1962, **656**, 1.
7. A. T. Stoll and E. Negishi, *Tetrahedron Lett.*, 1985, **26**, 5671.
8. R. Schimpf and P. Heimbach, *Chem. Ber.*, 1970, **103**, 2122.
9. D. E. Van Horn and E. Negishi, *J. Am. Chem. Soc.*, 1978, **100**, 2252.
10. U. M. Dzhemilev, A. G. Ibragimov, and A. P. Zolotarev, *Mendeleev Commun.*, 1992, **4**, 135.
11. U. M. Dzhemilev, A. G. Ibragimov, I. R. Ramazanov, M. P. Luk′yanova, and A. Z. Sharipova, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 465 [*Russ. Chem. Bull., Int. Ed.*, 2001, **50**, 484].

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