Highly Efficient Synthesis of Methylenecyclopropane

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Abstract: An efficient procedure for the preparation of methylenecyclopropane (**3**), a valuable starting material in organic synthesis, has been developed from methallyl chloride (**1**) and alkali metal [bis(trimethylsilyl)]amide [M(BTMSA) (M = Na, K), **2b**,**c**]. The advantages of this new method are the higher yield of methylenecyclopropane up to 79% and a homogenous reaction mixture, i.e. both substrates are soluble in organic solvents such as toluene and dibutyl ether.

Key words: methylenecyclopropane, methallyl chloride, elimination

Based on a publication of Fisher and Applequist who reported the preparation of 1-methylcyclopropene (**4**) from 3-chloro-2-methylpropene (methallyl chloride, **1**) and sodium amide in refluxing THF,[2] we developed some years ago a synthesis of methylenecyclopropane (**3**) using the same starting materials but modified the solvent and the reaction conditions.[3] With sodium amide, a mixture of **3** and **4** (80:20) was obtained in boiling Bu_2O in a maximum yield of 75% whereas potassium amide in the same boiling solvent produced **3** in 61% yield with 94% purity. The C_4H_6-hydrocarbon mixture of **3** and **4** can be isomerized into pure **3** by bubbling through a solution of *t*-BuOK in DMSO with only little loss.[3,4] Pure **3** has also been synthesized from **1** (43%) by application of the base mixture $NaNH_2$/*t*-BuONa.[5,6,7a] These syntheses suffers from some disadvantages which hinder the preparation of **3** in larger amounts. This, however, is necessary if **3** should be used as starting material in organic synthesis.[7b–d] The most important disadvantages are the following: 1) sodium and potassium amides are insoluble in organic solvents and must be applied as powder, which is too dangerous in technical procedures; and 2) two of the three reaction products, the C_4H_6-hydrocarbons and ammonia are gases at room temperature and must be separated in an additional step, conveniently by bubbling through an aqueous H_2SO_4 solution.[3,6]

To circumvent these disadvantages we looked for soluble bases with similar or even better properties than MNH_2 and found these in the alkali metal [bis(tirmethylsilyl)]amides [M(BTMSA)] **2b** (M = Na) and **2c** (M = K).[8] Amides **2b** and **2c** are strong bases with special properties. They are conveniently available also in larger amounts and are soluble in organic solvents like aromatic hydrocarbons or dialkyl ethers.

Slow addition of methallyl chloride (**1**) to a vigorously refluxing solution of **2b** or **2c** in toluene, *o*-xylene or dibutyl ether immediately causes a gas stream of C_4H_6-hydrocarbons **3** and **4** whose compositions and yields depend mainly on the base used, and to a minor extent on the boiling point of the solvent (Scheme).[9]

The best results are obtained with **2c** (M = K) in refluxing toluene or Bu_2O that directly affords methylenecyclopropane (**3**) in good purity and yield (see Scheme). Amide **2b** (M = Na) produces the C_4H_6-hydrocarbons in comparable yields, but **3** is now contaminated with larger amounts of 1-methylcyclopropene (**4**). To obtain pure **3** it is therefore necessary to isomerize **4** into **3** in a second step that is conveniently performed by bubbling the **3**/**4**-mixture through a 50 °C warm solution of *t*-BuOK in DMSO.[3,4] Interestingly no C_4H_6-hydrocarbons are obtained when $LiN(SiMe_3)_2$ (**2a**) is used as the base under otherwise identical conditions. This is remarkable because it is well known that strong lithium bases, e.g. LDA (lithium diisopropylamide) metalate allyl chlorides in the α-position at low temperatures. Therefore it is reasonable to assume that α-metalation takes place, but subsequent reactions other than α-elimination of LiCl, e.g. C−C-coupling, are faster.[10,11] On the other hand it has been reported that **1** reacts with two equivalents of pure, lithium bisamide-free phenyl lithium to give 1-lithium-2-methylcyclopropene in a yield as high as 60–80%.[12] These difficulties can be circumvented by adding a second base, e.g. *t*-BuOK, to the reaction mixture, e.g. a 1:1 mixture of **2a** and *t*-BuOK in toluene at 110 °C, readily liberates a **3**/**4**-mixture in the ratio 88:12 and a yield of 73%. Addition of *t*-BuOK to **2b** has also a beneficial effect on the yield and **3**/**4**-ratio; e.g. from **1** and the base mixture **2b**/*t*-BuOK in boiling Bu_2O a **3**/**4**-mixture is obtained in the ratio 91:9 and a yield of 81%. The latter observation indicates that a metal–metal exchange occurs and the so formed **2c** acts as the active base.

In summary, we have developed an efficient and simple procedure to synthesize pure **3** in large amounts.

2-Methyl-3-chloropropene (methallyl chloride, **1**) was purchased from Merck KGaA and used without further purification. Amide **2a** was prepared from BuLi and hexamethyldisilazane, (Merck KGaA), and **2b**,**c** were prepared from MNH_2 and hexamethyldisilazane according to a literature procedure.[8] The solvents THF, toluene, *o*-xylene and Bu_2O were dried before use. All reactions were

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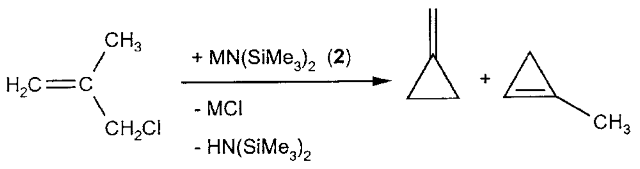

1 **3** **4**

2a: M = Li
2b: M = Na
2c: M = K

Base	Solvent	Reaction temp.	Yield	**3** : **4**
2a	toluene	110°	0	- -
2b	THF	65°	44	80 20
2b	toluene	110°	72	55 45
2b	o-xylene	140°	71	76 24
2b	n-Bu2O	130°	73	84 16
2c	THF	65°	6	100 0
2c	toluene	110°	70	96 4
2c	o-xylene	140°	64	96 4
2c	n-Bu2O	130°	76	96 4

Scheme

carried out under argon. Yield and **3**/**4**-ratio of the C_4H_6-hydrocarbons, as well as the purity of **3** were determined by GC (50 m OV1/3046 capillary column, N_2, FD, 40–260 °C, 8/min).

Methylenecyclopropane (3) from Methallyl Chloride (1); General Procedures

Method 1: With $NaN(SiMe_3)_2$ (**2b**)

Compound **2b** (57.2 g, 0.31 mol) was dissolved in a solvent (THF, toluene, *o*-xylene or dibutyl ether, 100 mL) in a 250 mL three-necked flask, equipped with a 25 mL dropping funnel, water-cooled Dimroth condenser, magnetic stirrer, an argon gas bubbler and an inlet tube connected to a –80 °C cold trap. To this vigorous boiling solution was added **1** (22.7 g, 0.25 mol) over ca. 20 min. Product **3** or a mixture of **3** and **4** that escaped from the flask through the condenser was condensed via the inlet tube in a trap at –80 °C as a colorless liquid. After an additional 30 min reflux, the reaction was over.

In THF: A mixture of **3** and **4** (GC: 80% **3** and 20% **4**) was obtained from **1** (22.6 g, 0.25 mol) and **2b** (57.2 g, 0.31 mol); yield: 5.9 g (8.2 mL, *d* = 0.72 g/mol, 44%).

In Bu_2O: A mixture of **3** and **4** (GC: 85.8% **3** and 14.2% **4**) was obtained from **1** (22.6 g, 0.25 mol) and **2b** (57.2 g, 0.31 mol); yield: 9.9 g (13.8 mL, *d* = 0.72 g/mol, 73%).

In Toluene: A mixture of **3** and **4** (GC: 55% **3** and 45% **4**) was obtained from **1** (22.6 g, 0.25 mol) and **2b** (57.2 g, 0.31 mol); yield: 9.8 g (13.6 mL, 72%).

In o-Xylene: A mixture of **3** and **4** (GC: 76% 3, 24% **4**) was obtained from **1** (25.5 g, 0.28 mol) and **2b** (64.3 g, 0.38 mol); yield: 10.8 g (15.0 mL, 71%).

Method 2: With $KN(SiMe_3)_2$ (**2c**)

Apparatus and procedure were the same as described under Method 1. A slight excess of **2c** (**1**:**2c** = 1:1.2) was used. The Table summarizes the results obtained in different solvents.

Method 3; With Base Mixture **2a** and *t*-BuOK: The base **2a** (58.3 g, 0.35 mol) and *t*-BuOK (51.0 g, 0.46 mol) were dissolved in toluene (150 mL) whereby a heat evolution to ca. 40 °C was observed. The mixture was heated to a rigorous reflux (110 °C) and at this temperature **1** (31.6 g, 0.35 mol) was added within 45 min. Immediately C_4H_6-hydrocarbons escaped which were condensed in a –80 °C cold trap; yield: 19 mL (13.7 g, 73%); colorless liquid containing 88% **3** and 12% **4** (GC). When this procedure was carried out with a slightly molar excess of **2a** or *t*-BuOK no C_4H_6-hydrocarbon was obtained.

Method 4; With **2b** and *t*-BuOK: The base **2b** (62.2 g, 9.34 mol) and *t*-BuOK (10.1 g, 0.09 mol) were dissolved in Bu_2O (100 mL). The mixture was heated to a vigorous reflux (ca. 130 °C) and the chloride **1** (20.8 g, 0.23 mol) was added within 30 min. The C_4H_6-hydrocarbons were condensed in a –80 °C trap: 14 mL [10.1 g, 81%, composition (GC): 90.8% **3** and 9.2% **4**]. The above procedure carried out with equimolar amounts of **2b** (48g, 0.20 mol), *t*-BuOK (22.6, 0.20 mol) and **1** (18.1 g, 0.20 mol) led to the formation of 8.8 g (82%) of 97% **3** contaminated with 3% of **4**.

Large Scale Preparation of Methylecyclopropane (3)

The base **2b** (500 g, 2.73 mol) was dissolved in toluene (700 mL) in a 3 L four-necked flask, equipped with a 250 mL dropping funnel, a water-cooled Dimroth condenser, a KPG-stirrer, an argon gas bubbler and an inlet tube connected to a –80 °C cold 250 mL trap. The mixture was heated to a vigorous reflux and at this temperature **1** (199 g, 2.2 mol) was added under stirring within 4 h. From the beginning of the addition of **1**, a continuous gas stream of **3** and **4** escaped via the condenser and the inlet tube, which was condensed in the trap at –80 °C. After an additional 1 h reflux, whereby a slow stream of argon transported the rest of **3** and **4** into the trap, a mixture of **3** and **4** (138 mL, *d* = 1.72 g/mL, 99.4 g; 84%, GC: 78% **3** and 22% **4**) was collected as a colorless liquid. From the remaining reaction mixture, a white suspension, all volatiles were removed at r.t. and 0.01 bar; the colorless distillate (921 g) had the composition (GC): 61.5% toluene and 38.5% hexamethyldisilazane [calcd 355 g

Table Reaction of Methallyl Chloride (**1**) with **2c**

1		**2c**		Solvent	C_4H_6-Hydrocarbons				
g	mol	g	mol	(100 mL)	mL	g	Yield (%)	**3**	**4**
22.6	0.25	61.7	0.31	THF	1.2	0.86	6.4	100	0
22.6	0.25	61.7	0.31	Bu_2O	14.3	10.3	76	96	4
25.3	0.28	67.6	0.34	toluene	13.0	9.4	70	96	4
22.6	0.25	61.7	0.31	*o*-xylene	12.0	8.6	64	96	4

(100%)]. The remaining residue (275 g) was a white powder. The above described procedure carried out with **1** (390 g, 4.3 mol) and **2b** (791 g, 4.3 mol) in Bu_2O (1.5 L) led to the formation of 199 g (77%) of C_4H_6-hydrocarbons with the composition (GC): 91.6% **3** and 8.4% **4**.

Pure Methylenecyclopropane (3)

A mixture of **3** and **4** (138 mL, 99.4 g, 1.84 mol) was bubbled through a solution of *t*-BuOK (9.8 g, 88 mmol) in DMSO (60 mL) at 50 °C and recondensed in a –80 °C flask. The resulting **3** (130 g, 94%) was 99.4% pure (GC).

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