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Triisobutylaluminum (TIBA) as a reagent to convert 2,2-dimethoxyalkanes to 2-methoxy-1-alkenes

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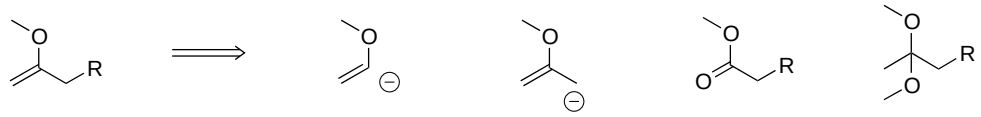
Abstract—Methanol ketals undergo methanol elimination by reaction with triisobutylaluminum to yield the corresponding less substituted 2-methoxyolefins; the experimental conditions are compatible with the presence of other functional groups.

Vinyl ethers such as **1** are valuable synthetic intermediates: they can give regiospecifically α-functionalized ketones by reaction with electrophiles under mild conditions and behave as olefinic compounds in a variety of electrocyclic reactions.[1] We became particularly interested in 2-alkoxy-1-alkenes of general structure **1** as dipolarophiles in the reaction with cyclic nitrones leading to 2-(2-ketoalkyl) substituted nitrogen heterocycles.[2]

Compounds of general structure **1** can be obtained by a number of approaches, including alkylation of metallated vinyl ethers **2**,[3] alkylation of metallated alkoxypropenes **3**,[4] methylidenation of esters **4**,[5] and elimination of alcohol from ketals of methyl ketones **5**.[6] This last method, although not regiospecific in general, is perhaps the most attractive because methyl ketones are easy to prepare and convert into the corresponding ketals.

Triisobutylaluminum (TIBA, a relatively inexpensive reagent, easily handled as solution in hydrocarbon solvents) has been extensively used to cleave cyclic acetals with different levels of stereocontrol.[7] In a study mainly focused on the use of TIBA to generate allyl 2-propenyl ethers from 2-methoxy-2-propyl allyl ethers and to catalyze their subsequent Claisen rearrangement in a one-pot process,[8] it has been marginally noted that TIBA can also promote the efficient and highly regioselective elimination of methanol from benzylacetone dimethyl acetal **6** to give 2-methoxy-4-phenyl-1-propene **22** under very convenient experimental conditions. However, to the best of our knowledge, no report has so far appeared on the scope of this interesting reaction. We wish to report herein (Eq. (1) and Table 1) the results of a brief investigation of TIBA induced elimination of methanol from dimethyl acetals, particularly focused on the preparation of compounds of general formula **1**.

When allowed to react in methylene chloride with a two- to five-fold molar excess of TIBA (as a 2 M solution in hexane) dimethyl acetals of 2-alkanones **6**–**14** underwent a clean methanol elimination affording the corresponding 2-methoxy-1-alkenes **20**–**28** as the sole products. An excess of TIBA was generally required in order to achieve complete conversion within 18 h at room temperature. Before work up, the excess of TIBA was quenched with an excess of 20% aq. trisodium citrate (3 h stirring), and the crude product



1 2 3 4 5

Keywords: elimination; vinyl ethers; methoxyolefins; acetals; organometallics; triisobutylaluminum; ketals.
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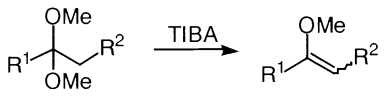
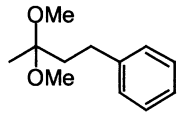
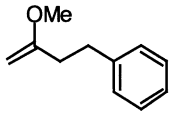
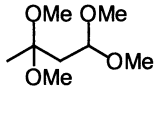
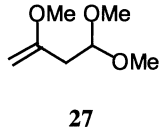
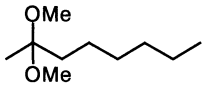
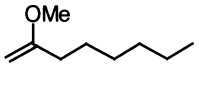
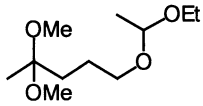
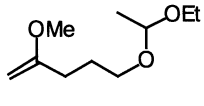
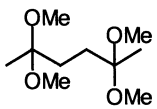
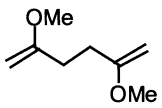
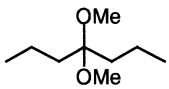
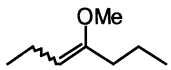
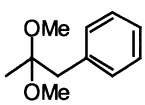
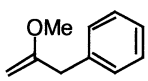
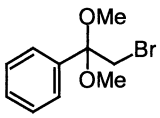
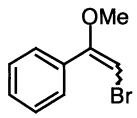
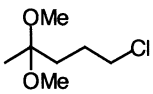
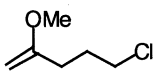
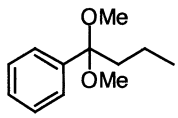
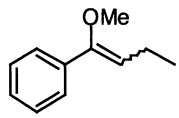
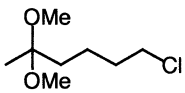
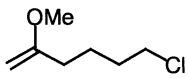
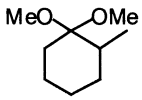
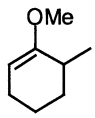
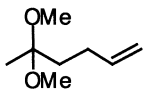
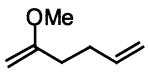
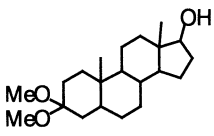
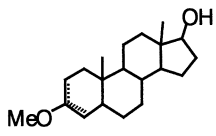
Table 1. Elimination of methanol from dimethyl acetals promoted by triisobutylaluminum (TIBA)



(1)

Reagent	Conditions TIBA equiv. time yield	Product	Reagent	Conditions TIBA equiv. time yield	Product
 **6**	2 5 h 78% yield	 **20**	 **13**	5 eq. 18 h 75 %	 **27**
 **7**	2 eq 5 h 71%	 **21**	 **14**	5 eq. 18 h 75 %	 **28**
 **8**	4 eq. 2 h 66 %	 **22**	 **15**	2 5h 75%	 **29** (Z:E=3:1)
 **9**	2 eq. 5 h 76%	 **23**	 **16**	2 eq. 5 h 75%	 **30** (Z:E=3:1)
 **10**	2 eq. 5 h 71%	 **24**	 **17**	2eq 1 h (0 °C) 80%	 **31** (Z:E=5:1)
 **11**	2 eq. 5 h 75%	 **25**	 **18**	2 eq 5 h 72%	 **32**
 **12**	2 eq. 5 h 68%	 **26**	 **19**	4 eq 5 h 85% Δ^2:Δ^3=1:1	 **33**

was isolated by evaporation of the organic phase. The yields of crude methoxyolefins were uniformly high and the lower yields of purified product listed in Table 1 are due to evaporation losses. Regioselectivity (by ^{1}H NMR)[9] was uniformly higher than 95%. Methanol elimination leading to the formation of the less substituted methoxyolefin, which is likely to be determined by steric factors, is the preferred reaction pathway even in those cases (as for the conversion of **9** to **23**) in which the alternative mode of elimination would lead to a particularly stable conjugated olefin. The elimination conditions are compatible with the presence of other functional groups: aliphatic chlorides (**10** and **11**), a double bond (**12**), and, quite surprisingly, acetals (**13** and **14**) are stable to TIBA; thus, bifunctional compounds **24**–**28** could be readily prepared. Phenylacetaldehyde dimethyl acetal and 2-phenylpropionaldehyde dimethylacetal were completely inert to elimination, even under forcing conditions (18 h, reflux). Acetals containing a nitrile or an ester (such as methyl 4,4-dimethoxypentanoate or the corresponding nitrile) gave complex mixtures upon exposure to TIBA.

A few ketals from ketones other than methyl ketons were also studied (**15**–**19**). The aliphatic ketal **15** and the aromatic one **16** were converted to the respective methoxyolefins **29** and **30** under conditions similar to those used for ketals of simple methyl ketones; the aromatic acetal **17**, on the other hand, underwent a much more rapid elimination and the conditions had to be optimized to avoid further reaction of the desired elimination product **31**. The elimination occurred with a low degree of stereoselectivity and, except for the halogenated derivative **30**, the preferred product had the methoxy group *cis* to the vinyl hydrogen, as established by means of NOESY experiments. A very high regioselectivity was observed in the reaction of cyclohexanone derivative **18**, in which the acetal group is flanked by a methylene and a methyne, the less substituted olefin **32** being the preferred product. The elimination from steroidal ketone **19** to give **33** was, however, non-regioselective, probably due to the similar hindrance of the two carbon atom α to the ketal.

In conclusion, TIBA can bring about the regio- and chemoselective elimination of methanol from 2,2-dimethoxyalkanes; the reaction is efficient, occurs under mild conditions, is compatible with other functional groups (most noteworthy, aldehyde acetals are not affected by the reagent), and affords valuable products such as 2-methoxy-1-alkenes from readily prepared starting materials.

References

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9. Selected spectroscopic properties of products; ^{1}H NMR (200 MHz, benzene-d_6); **20** 7.2–7.0 (m, 5H), 3.90 and 3.85 (2m, 2H), 3.25 (s, 3H), 2.83 and 2.41 (2m, 2×2H); **21** 3.93 and 3.85 (2m, 2×1H), 3.24 (s, 3H), 2.15 (t, J=7.2 Hz, 2H), 1.56 (m, 2H), 1.22 (m, 6H), 0.85 (m, 3H); **22** 3.90 and 3.79 (2m, 2×1H), 3.19 (s, 3H), 2.41 (s, 4H); **23** 7.48–7.15 (m, 5H), 3.90, 3.85 (2m, 2H), 3.42 (s, 2H), 3.15 (s, 3H); **24** 3.81 and 3.79, 3.15 (s, 3H), 3.16 (m, 2H), 2.12 and 1.72 (2t, J=7.0 Hz, 2×2H); **25** 3.82 and 3.85 (2m, 2×1H), 3.21 (s, 3H), 3.13 (m, 2H), 1.98 (m, 2H), 1.50 (m, 4H); **26** 5.68–5.89 (m, 1H), 5.03–4.94 (m, 2H), 3.83 and 3.80 (2m, 2×1H), 3.19 (s, 3H), 2.13–2.28 (m, 4H); **27** 4.81 (t, J=6 Hz, 1H), 4.04, 3.92 (2m, 2H), 3.22 (s, 3H), 3.18 (s, 6H), 2.59 (d, J=6 Hz, 2H); **28** 4.60 (q, 5.3 Hz, 1H), 3.97 and 3.86 (2m, 2×1H), 3.55 (m, 2H), 3.38 (m, 2H), 3.23 (s, 3H), 2.32 (t, J=7.2 Hz, 2H), 1.88 (m, 2H), 1.25 (d, J=5.3 Hz, 3H), 1.24 (t, J=6.8 Hz, 3H); **29** (Z:E=3:1); Z: 4.28 (t, J=8.0 Hz, 1H), 3.25 (s, 3H); E: 4.48 (t, J=8.0 Hz, 1H), 3.29 (s, 3H); **30**: Z: 5.63 (s, 1H), 3.03 (s, 3H); E: 5.18 (s, 1H), 3.03 (s, 3H); **31** (Z:E=5:1); Z: 4.62 (t, J=8.0 Hz, 1H), 3.35 (s, 3H); E: 5.28 (t, J=8.0 Hz, 1H), 3.32 (s, 3H); **32**: 4.46 (t, J=3.8 Hz, 1H), 3.25 (s, 3H), 2.35 (m, 1H), 2.03 (m, 2H), 1.25–1.75 (m, 4H), 1.19 (d, J=6.9 Hz, 3H); **33** Δ^2: C(2)-H 4.45; Δ^3: C(4)-H 4.23; ^{13}C NMR (50 MHz, benzene-d_6); **20**: 165.1, 140.4, 130.7, 130.6, 129.9, 129.5, 129.0, 128.0, 83.6, 56.0, 43.3; **21**: 164.7, 80.2, 54.3, 35.4, 32.0, 29.1, 27.7, 22.9, 14.2; **22**: 163.4, 80.2, 54.3, 33.2; **23**: 163.2, 139.3, 130.7, 128.5, 126.8, 80.9, 56.4, 42.3; **24**: 162.6, 81.3, 54.3, 44.1, 32.3, 30.4; **25**: 163.5, 80.5, 54.4, 44.2, 34.1, 32.0, 24.3; **26**: 163.7, 138.3, 114.7, 80.6, 54.3, 34.7, 31.3; **27**: 160.3, 102.4, 82.9, 54.4, 52.3, 39.3; **27**: 164.0, 99.59, 80.58, 64.18, 60.39, 54.35, 32.18, 31.90, 28.21; **29** (Z:E=3:1); Z: 156.7, 98.3, 53.5, 32.4, 21.2, 20.4, 16.1, 13.8. E: 154.8, 111.7, 55.9, 33.7, 20.7, 18.6, 15.6, 13.7; **30**: Z: 158.85, 90.37, 79.67. E: 158.85, 79.66, 57.23; **31** (Z:E=5:1) Z: 147.5; E: 146.9; **32**: 159.43, 92.64, 53.59, 32.63, 31.91, 24.48, 20.79, 14.32; **33** Δ^2: C(2) 91.30; Δ^3: C(4)-H 4.23; C(4) 81.85.