Journal of Organometallic Chemistry, 212 (1981) 23—33
Elsevier Sequoia S.A., Lausanne — Printed in The Netherlands

AN OPERATIONAL TEST FOR POSSIBLE ZINCACYCLOBUTANE FORMATION IN THE GUSTAVSON REACTION

THOMAS H. JOHNSON * and ELAINE C. HEFTY

Department of Chemistry, Kansas State University, Manhattan, KS 66506 (U.S.A.)

(Received September 19th, 1980)

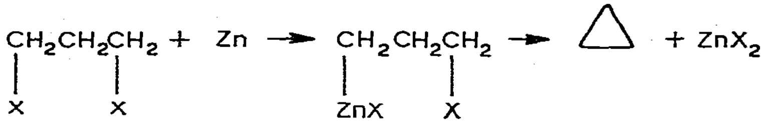
Summary

The possibility of obtaining a zincacyclobutane intermediate in the Gustavson reaction was hypothesized to explain the formation of olefins obtained in this reaction. A select group of substrates was investigated in which the formation of olefin products could be explained if one invoked the intermediacy of a zincacyclobutane, but would be difficult to explain in the absence of such an intermediate. A deuterium-labeled substrate was also investigated and the olefins obtained from its reaction with zinc were found to closely follow the deuterium-labeling pattern obtained from the decomposition of the analogous deuterium-labeled platinacyclobutane.

Introduction

The Gustavson reaction [1] producing cyclopropanes from 1,3-dihalides and zinc in alcohol and the Hass modification [2] using acetamide in place of alcohol have frequently been reported to give olefins in addition to cyclopropanes [3]. Historically, these olefins were viewed as a nuisance and most of the effort employing this reaction was aimed at eliminating the olefin-forming side reaction. We believe, however, that the olefins produced from such reactions may offer insight into some of the mechanistic features of this reaction. A more recent variant [4] employing the addition of 1,3-ditosylates to a heated solution of acetamide containing zinc and sodium iodide increases cyclopropane formation but olefinic contaminants are still present. Certainly one of the advantages of this latter method involves the short contact time of the products with the acetamide solution which prevents cyclopropane decomposition to olefins.

For some time the reaction of zinc with 1,3-dihalides has been depicted as occurring by the sequence outlined in eq. 1. The intermediate **1** is usually depicted as going directly to cyclopropane. Presumably, olefins could form from **1**.



(1)

(X = halogen) (1)

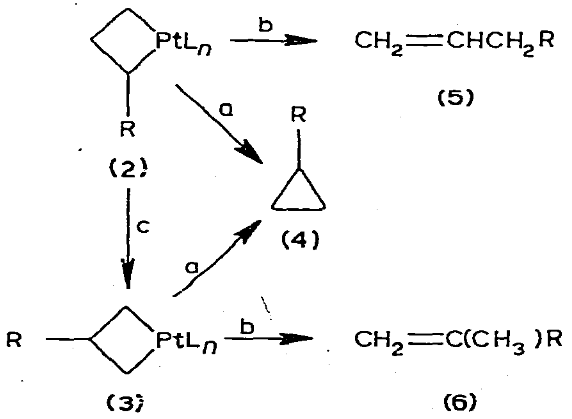
Recently, a fair amount of research has been accumulating on platinacyclobutanes. It is now quite apparent that platinacyclobutanes can undergo reductive elimination to cyclopropane [5,6], β-hydrogen abstraction-reductive elimination to olefins [6,7], and that one platinacyclobutane can rearrange to another isomer [7]. These reactions are outlined in Scheme 1.

The formation of dialkylzinc compounds from alkyl halides and zinc is well known [8]. Thus, it is not difficult to envision the formation of a transitory zincacyclobutane from a 1,3-dihalide and zinc. The observed cyclopropane and olefin products can be reasonably derived from such a zincacyclobutane. However, if zincacyclobutanes behave similarly to platinacyclobutanes with respect to rearrangement, then suitably designed systems might give rise to olefins which could be explained by invoking a zincacyclobutane but could not be easily explained by invoking intermediates such as 1. In Scheme 2 we have depicted a 1,3-dihalide reacting with zinc to form the zincacyclobutane 7 which could undergo further reaction to give the cyclopropane and olefins shown. This zincacycle could also rearrange to 8 which in turn would give the same cyclopropane but a different olefin.

Results and discussion

Although all of the modifications of the Gustavson reaction produced cyclopropanes and olefins, a preliminary analysis revealed that the procedure [4] employing the addition of a 1,3-ditosylate to a heated solution of acetamide containing zinc and sodium iodide gave the most reproducible results. Experimentally, the olefins and cyclopropanes formed in this reaction are volatized away

SCHEME 1. (a) Reductive elimination; (b) β-hydrogen abstraction-reductive elimination; (c) rearrangement.



SCHEME 2

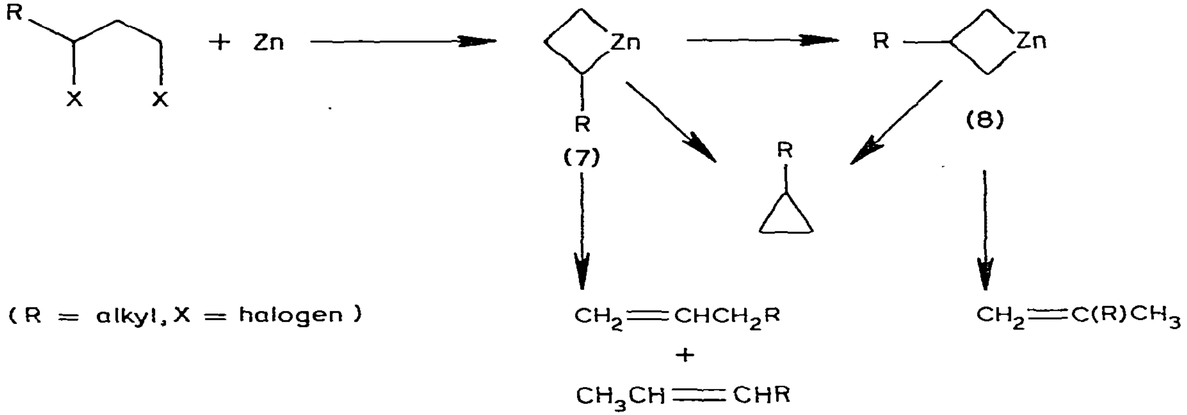
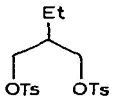
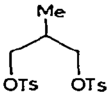
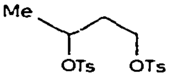
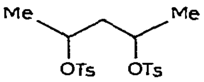
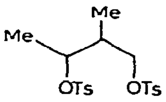
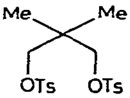


TABLE 1

OLEFINS OBTAINED FROM 1,3-DITOSYLATES WITH ZINC AND SODIUM IODIDE IN ACETAMIDE

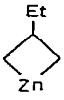
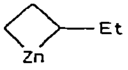
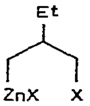
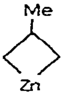
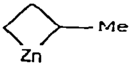
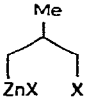
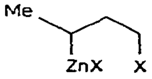
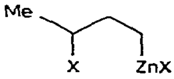
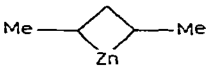
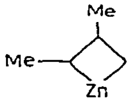
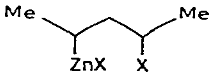
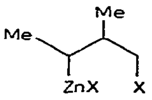
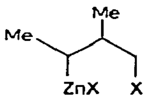
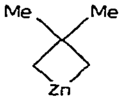
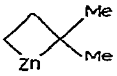
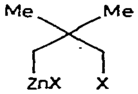
Substrates	Olefins (%) [a,b,c]
 (9)	2-Methyl-1-butene (99%) 1-Pentene (trace)
 (10)	1-Butene (41%) Isobutylene (59%) *cis*-2-butene (trace)
 (11)	1-Butene (95%) Isobutylene (5%) *cis*-2-Butene (trace)
 (12)	1-Pentene (99%) 3-Methyl-1-butene (trace) *cis*-2-Pentene (trace)
 (13)	2-Methyl-2-butene (10%) 3-Methyl-1-butene (80%) 2-Methyl-1-butene (8%) 1-Pentene (2%)
 (14)	3-Methyl-1-butene (35%) 2-Methyl-1-butene (65%)

---

[a] The percentage figure is for percent of olefins. [b] Olefins were isolated and their structures confirmed by spectroscopic comparison to authentic samples except for those olefins present in trace quantities. These latter olefines were identified by VPC retention time and by co-injection with authentic samples. [c] The absolute percent yield of olefins was 12, 12, 15, 21, 18 and 6 percent for 9, 10, 11, 12, 13, and 14, respectively.

TABLE 2

EXPECTED ZINC INTERMEDIATES FROM SUBSTRATES 9—14

	Zincacylobutane			
Substrate	Initial	Rearranged	Organozine	
9	 (15)	 (16)	 (17)	
10	 (18)	 (19)	 (20)	
11	19	18	 (21)	 (22)
12	 (23)	 (24)	 (25)	
13	24	23	 (26)	 (27)
14	 (28)	 (29)	 (30)	

from the reaction medium and trapped downstream. A careful set of control experiments (vide infra) established that cyclopropanes and olefins collected in the downstream traps were obtained without prior isomerization. On the basis of these preliminary investigations it was decided to investigate the olefin-forming aspect of this reaction using the 1,3-ditosylate addition procedure.

We prepared the series of ditosylates 9—14 from known diols and converted these to cyclopropanes and olefins via their addition to a heated acetamide solution containing zinc and sodium iodide. The products were obtained in a downstream cold trap and analyzed by VPC *. The substrates 9—14 gave olefins in addition to cyclopropanes and these are listed in Table 1. Table 2 shows the

---

* The analysis was carried out using a 19′ × 1/8″ $AgNO_3$/ethylene glycol column which we have previously described [6].

expected zincacyclobutane and the expected organozinc species (via eq. 1) for each of these substrates.

A set of control experiments was run where each of the olefins reported in Table 1 and each of the cyclopropanes obtained were subjected, in separate experiments, to the reaction medium and collected in the downstream cold traps. Subsequent analysis revealed that the recovered compounds were unchanged. The recovery of products, however, was only about 60—70%. If the reaction medium was then purged with nitrogen it was possible to reach a mass balance approaching 100%. However, analysis of this recovered fraction revealed that some of the olefins had lost their structural integrity. The worst example of olefin stability was 3-methyl-1-butene which isomerized, 20—30%, to 2-methyl-2-butene in the sample obtained from purging. The sample of 3-methyl-1-butene which was obtained in the traps immediately after introduction into the reaction medium, however, was >99% pure. These control experiments make it quite apparent that a suitable analysis of products could be obtained only from material which was collected in the traps immediately after introduction of the substrates. Apparently, increasing the contact time of the products with the reaction medium leads to rearrangement processes in some instances.

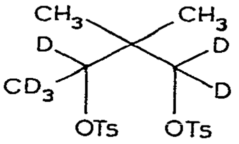
Another source of concern revolved around the fate of the ditosylate substrates which did not enter into reaction with zinc but instead underwent elimination reactions. A set of control experiments was run where the substrates **9**—**14** were introduced into the reaction medium in the absence of zinc. Under these conditions a gradual amount of liquid product was obtained in the downstream traps which, upon analysis, proved to be an assortment of dienes for the substrates **9**, **11**—**13**. Substrates **10** and **14** produced only trace amounts of material having retention times similar to dienes but the small quantities obtained precluded any detailed analysis. Applequist [4] had reported the isolation of dienes in addition to olefins and cyclopropanes in the reaction of 1,3-ditosylates with zinc and sodium iodide in acetamide. Apparently, the source of these dienes is from the ditosylate substrates which do not undergo reaction with zinc but instead undergo elimination reactions. In our reactions, we observed dienes only in that fraction which was collected via nitrogen purge of the reaction medium.

The substrate **9** when exposed to zinc in acetamide gave mostly 2-methyl-1-butene with a trace of 1-pentene. The major olefin could be seen as arising from either **15** or **17** by standard β-hydrogen abstraction reactions, although **17** would require some reaction in which the iodide is replaced by a hydrogen. The small amount of 1-pentene can be easily accounted for from the rearranged zincacyclobutane **16**. The substrates **10** and **11** both gave methylcyclopropane but produced a different percentage distribution of olefins. From **10** one would anticipate obtaining only isobutylene but one observes that 41% of the olefin fraction also contains 1-butene which can be nicely accounted for from the rearranged zincacyclobutane **19**. The trace amount of *cis*-2-butene can also be accounted for from **19**. It is difficult to envision the formation of these two olefins as arising from **18** or **20**. In the substrate **11** we would now anticipate the formation of 1-butene but we also see 5% of isobutylene. Again, these non-anticipated olefins are nicely accounted for by invoking a zincacyclobutane which has undergone partial rearrangement to another zincacycle.

The substrates 12 and 13 are analogous to 10 and 11 in that 12 and 13 produce the same cyclopropane but a different distribution of olefins. The olefin 1-pentene is the expected major olefin from 12 but was also found as 2% of the composition in the reaction of 13 with zinc. Likewise the 3-methyl-1-butene found in trace amounts from 12 became the major olefin in the zinc reaction with 13. A rearrangement of 23 to 24 in the reaction of 12 and the rearrangement of 24 to 23 in the reaction of 13 produces zincacyclobutanes that are capable of producing the non-anticipated olefins. The substrate sets 10, 11 and 12, 13 also demonstrate that the rearrangement processes being invoked here are reversible. However, the major olefin in these instances is formally derived from the proposed first-formed zincacyclobutane. It would appear that olefin formation from a zincacyclobutane (along with cyclopropane formation) is favored over the rearrangement process for these substrates.

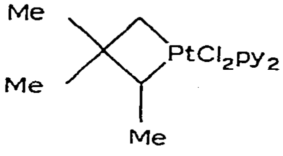
The substrate 14 is different from the previous substrates in that the first-formed zinc species, 28 or/and 30, do not have any β-hydrogens available for abstraction. Hence, no olefins are expected from 28 and 30. The rearranged zincacyclobutane, 29, however, could give rise to three different olefins and we observed two of these: 3-methyl-1-butene and 2-methyl-1-butene.

Earlier in this paper we alluded to possible similarities between platinacyclobutanes and zincacyclobutane intermediates. In order to explore this possibility further we subjected the deuterium-labeled substrate 31 to the reaction conditions. Interestingly, only one structural olefin, 2,3-dimethyl-1-butene, was obtained. None of the expected 3,3-dimethyl-1-butene was observed. This is the same result obtained for the platinacyclobutane 32 which rearranges to 33 and gives olefin products derived only from 33 [6a]. Compound 33 produced two differently labeled isomers of 2,3-dimethyl-1-butene [6a] and, likewise, the reaction of 31 with zinc and sodium iodide in acetamide produced the same two isomers, 34 and 35. The ration of 34/35 derived from 33 was 1/1 while the ratio of 34/35 derived from 31 was ca. 1/2.

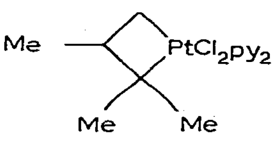


(31)

The analysis and ratio determination of the olefinic products were aided by ^{13}C NMR and ^{1}H NMR spectroscopy. For this purpose the unlabeled olefin served as a standard for comparison and its peaks are shown in Table 3. The various carbons and protons are designated as shown in Fig. 1.



(32)



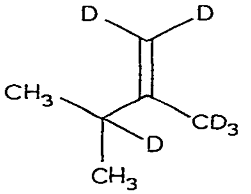
(33)

TABLE 3

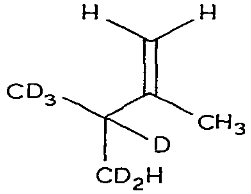
CHEMICAL SHIFTS FOR CARBONS AND PROTONS FOR 2,3-DIMETHYL-1-BUTENE

Proton [b]	Shift [a] (ppm)	Carbon [b]	Shift [a] (ppm)
a	4.71 [c]	α	107.47
b	1.78 [c]	β	151.07
c	2.35 [d]	γ	20.02
d	1.09 [e]	δ	35.13
		ϵ	21.35

[a] Downfield from Me_4Si in $CDCl_3$. [b] The proton and carbon designations are shown in Fig. 1. [c] Singlet. [d] Septulet. [e] Doublet, J 6.5 Hz.



(34)



(35)

In the olefin set 34 and 35, the ^{13}C NMR spectrum showed a triplet centered at 34.41 ppm in place of the peak at 35.13 ppm, consistent with complete deuterium substitution of carbon δ (see Fig. 1). The carbon α was now represented by a singlet at 107.5 ppm and a pentuplet centered at 106.94 ppm consistent with a mixture of 34 and 35. Both of the peaks at 21.35 and 20.02 ppm have clusters of smaller peaks at their base line which overlap with one another and make the exact assignment of the multiplicity difficult. One would expect two different septuplets and one pentuplet in addition to the two singlets for 34 and 35. The ^1H NMR spectrum confirms the complete deuteration at carbon δ as the signal at 2.35 ppm was no longer present. The height of the integrated area for the vinylic protons (H_a) was 49 mm while the height of the integrated area for the methyl protons (H_d) was 108 mm. The ratio of 34 to 35 can be determined from the above integrals by the following procedure. The vinylic protons (H_a) are due only to 35 and correspond to 24 mm per proton. The methyl protons (H_d) are due to both 34 and 35. The olefin 35, however, has one proton per five deuteriums substituted at the carbons a and, therefore, 24 mm (the value for one proton, see above) was subtracted from 108 mm to give a value of 84 mm for the protons due to 34. Compound 34 has six protons

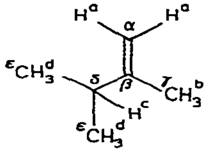
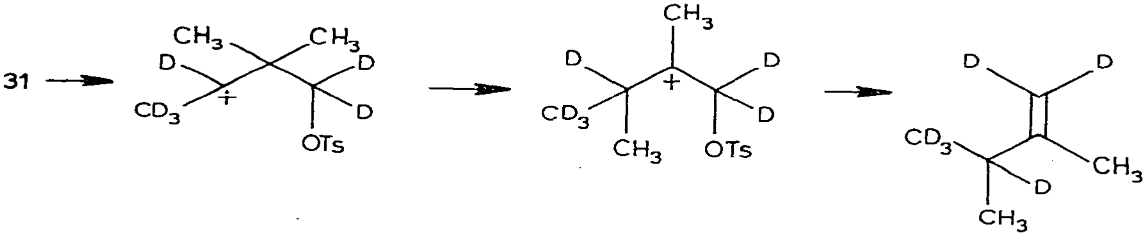


Fig. 1. Designation of protons (Roman) and carbons (Greek) for 2,3-dimethyl-1-butene.

and this corresponds to a height for the integrated area of 14 mm per proton. Taking these values per proton we arrived at the ratio of 34 to 35 as ca. 1/2.

As it is known that reactions involving zinc can undergo carbonium-ion rearrangements in some instances [10], we examined our results with a view toward carbonium ion-mediated formation of olefins. The reaction of 31 with zinc is particularly instructive in this regard. A carbonium ion derived from 31 should give the neopentyl ion 36 which upon classical neopentyl rearrangement pathways should give 37. It is known that the only olefin obtained from 31 is 2,3-dimethyl-1-butene and thus if 36 was formed, its rearrangement to 37 would have to be highly favored as the observed olefin can not derive from 36 but could be envisioned as deriving from 37. However, the labeling pattern of the olefin formed from 37 should be 38 not 34 or 35 as found. The compound 38 can be distinguished from 34 and 35 and from a mixture containing all three by the following process:



(36) (37) (38)

The key difference between the olefins 34, 35, and 38 is that the carbons α and γ are always labeled with the same hydrogen isotope in 34 and 35 but with opposite isotopes in 38. This same type of spectroscopic distinction was required in our earlier studies of platinacyclobutanes [6]. The height of the integrated area for H_a to H_b must be 2/3 if the observed olefins are 34 and 35. The height of the integrated areas of H_a and H_b were 48 and 74 mm, respectively. If 38 were present instead of 34, then this ratio would deviate from a 2 : 3 ratio. If 38 were present in addition to 34 and 35, then the ratio would also deviate. Thus, we conclude that 38 is not formed. Further, it would seem unlikely that a carbonium-ion intermediate is responsible for the olefins observed.

While these studies do not exclude species such as 1 from being present in the reaction of 1,3-ditosylates with zinc and sodium iodide in acetamide, they do require an additional intermediate to account for the number of olefins which can not be formally derived from species such as 1. The presence of a zincacyclobutane would account for the observed cyclopropane and expected olefins. In addition, a competitive but slower side reaction involving rearrangement of the initially-formed zincacyclobutane to another zincacyclobutane would account for all of the unexpected, and unaccountable by species such as 1, olefins. The formation and rearrangement of metallocycloalkanes along with the formation of olefins from such species has ample precedent in platinacyclobutane chemistry. Indeed, in the case of 31 reacting with zinc and sodium iodide in acetamide there is a good correlation with the chemistry obtained from platinacyclobutanes.

Experimental

The substrates 9—14 were all prepared by the method of Applequist [4] from commercially available diols. Analysis of the olefinic products was accomplished using a Varian 940 gas chromatograph equipped with a 19′ × 1/8″ $AgNO_3$/ ethylene glycol on 80/100 Chromosorb P column at 50° C. The olefins were isolated by the use of a Varian A-90-P3 preparative gas chromatograph and their structures confirmed by spectroscopic comparison to authentic samples except for those olefins present in trace quantities. These latter olefins were identified by VPC retention time and by co-injection with authentic samples. The results are given in Table 1. The ^{13}C NMR spectra were recorded on a Varian XL-100 spectrometer and the ^{1}H NMR spectra were recorded on either a Varian T-60 or Varian XL-100 spectrometer. All of the NMR spectra are reported relative to Me_4Si using $CDCl_3$ as solvent.

General procedure for zinc reactions

To a mechanically stirred suspension of 160 g of zinc dust, 60 g of sodium carbonate, 30 g of sodium iodide, and 400 g of acetamide in a 1000-ml, 3-necked, round-bottomed flask maintained at 170—175° C, was added, portionwise, 0.19 mol of a ditosylate, 9—14, from a 250-ml Erlenmayer flask which was connected by means of Gooch tubing to the reaction flask. The products were allowed to distill out of the reaction into a trap which had been pre-cooled to —78° C. After the addition of the ditosylate was completed, the flask containing the trapped products was removed and a new flask was inserted and cooled to —78° C. Then, the reaction mixture was thoroughly purged with nitrogen to expel any residual products. The products obtained without purging of the reaction medium are reported in Table 1. The composition of the two traps (purged and non-purged) was not always the same, as noted in the text. Control experiments, vide infra, established that olefins experiencing significant residence times in the reaction medium sometimes underwent rearrangement reactions.

Control experiment for determining olefin stability in the reaction medium

A reaction was performed as described in the general procedure except that only one-half or 0.085 mol of the ditosylate was used. The reaction medium was then purged until no more products were trapped. Then, in separate experiments, each of the observed olefins was introduced into the reaction medium by means of a glass tube which excited beneath the surface of the reaction. Some of the olefin distilled off immediately and was controlled in a trap cooled to —78° C. Characterization of the olefins obtained immediately after introduction into the reaction medium showed that they were unchanged. Purging of the reaction medium after 30 min resulted in the recovery of additional olefin(s). However, the olefin did not always maintain its structural integrity after remaining in the reaction for this time. The worse case was 3-methyl-1-butene which isomerized, 20—30%, to 2-methyl-2-butene.

Methyl 2,2-dimethyl-3-oxobutanoate-4,4,4-d_3 (5a)

To a 1000-ml, three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and addition funnel were added 500 ml of anhydrous

THF and 50.5 g (0.5 mol) of diisopropylamine. The flask was cooled to −78°C and 210 ml (0.5 mol) of 2.4 *M* n-butyllithium was added. After the mixture was stirred at −78°C for 2 h, 51 g (0.5 mol) of methyl isobutyrate was added over a period of 2 h. After the addition was completed, the reaction mixture was stirred for 0.5 h and then 36 ml (0.5 mol) of acetyl-d_3 chloride (Aldrich) was added over a period of 1.5 h. Then the mixture was allowed to warm to room temperature and was stirred for 3 h, after which time 125 ml of 6 *N* HCl and 200 ml of H_2O were added to the reaction mixture. The organic layer was separated, washed four times with 100 ml portions of saturated sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and evaporated in vacuo. The residue was distilled, giving 29.2 g (41%) of 5a: b.p. 90—93°C (30 mmHg); ^1H NMR ($CDCl_3$) δ 3.6 (s, 3 H) and 1.3 (s, 6 H) ppm.

2,2-Dimethyl-1,3-butanediol-1,1,3,4,4,4-d_6

To a 1000 ml, three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and addition funnel were added 500 ml of anhydrous ether and 9.0 g (0.2 mol) of lithium aluminum deuteride (Stohler Isotopes). To this stirred mixture was added a solution of 33.5 g (0.23 mol) of 5a in 250 ml of anhydrous ether. The solution was added at a rate which maintained reflux. After the addition was completed, the reaction mixture was refluxed for 3 h. The reaction mixture was then cooled and worked up by adding dropwise amounts of the following reagents: 9 ml of H_2O, then 9 ml of 15% aqueous NaOH, and then 12 ml of H_2O. This gave a precipitate which was removed by filtration. The filtrate was washed once with 200 ml of H_2O, the layers were separated, and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was distilled, giving 17.9 g (63%) of the product: b.p. 78—79°C (0.3 mmHg); ^1H NMR ($CDCl_3$) δ 4.11 (br, 2 H), and 0.82 (s, 6 H) ppm.

2,2-Dimethyl-1,2-butanediol-1,1,3,4,4,4-d_6 ditosylate (31)

To a 1000-ml Erlenmeyer flask, cooled to 0°C, were added 300 ml of dry pyridine, 53.2 g (0.28 mol) of tosyl chloride, and 16.8 g (0.14 mol) of the above diol. The Erlenmeyer flask was stoppered and refrigerated for 3 days. The resultant solid was removed by filtration and the filtrate was poured into 1500 ml of ice water. The aqueous solution was extracted with two 450 ml portions of chloroform. The chloroform extract was then washed with eight 150 ml portions of 5% aqueous potassium bisulfate and once with 150 ml of water. The chloroform solution solution was dried over anhydrous sodium sulfate and then concentrated in vacuo. The resultant oil was taken up in 12 ml of warm methanol and then cooled, whereupon crystallization took place. Filtration of crystals gave 36.1 g (95%) of the product which was used without further purification, m.p. 68—69°C.

References

1 G. Gustavson, J. Prakt. Chem., 35 (1887) 300.
2 H.B. Hass, E.T. McBee, G.E. Hinds and E.W. Gluessenkamp, Ind. Eng. Chem., 28 (1936) 1178.
3 J.D. Bartleson, R.E. Burk and H.P. Lankelma, J. Amer. Chem. Soc., 68 (1946) 2513 and ref. contained therein.

4 For example, see G.G. Maynes and D.E. Applequist, J. Amer. Chem. Soc., 95 (1973) 856.

5 C.F.H. Tipper, J. Chem. Soc., (1955) 2045; P.W. Hall, R.J. Puddephatt, K.R. Seddon and C.F.H. Tipper, J. Organometal. Chem., 81 (1974) 423.

6 (a) T.H. Johnson and S.-S. Cheng, J. Amer. Chem. Soc., 101 (1979) 5277; (b) T.H. Johnson and E.C. Hefty, J. Org. Chem., 44 (1979) 4896.

7 T.H. Johnson, J. Org. Chem., 44 (1979) 1356; R.J. Puddephatt, M.A. Quyser and C.F.H. Tipper, Chem. Commun., (1976) 626; R.H. Al-Essa, R.J. Puddephatt, M.A. Quyser and C.F.H. Tipper, J. Amer. Chem. Soc., 101 (1979) 364; R.J. Al-Essa and R.J. Puddephatt, Inorg. Chim. Acta, 34 (1979) L187.

8 E. Frankland, Ann., 71 (1849) 171, 213; 85 (1953) 329; 99 (1856) 333; A.M. Butlerow, ibid., 144 (1867) 2; A. Kaulfuss, Chem. Ber., 20 (1887) 3104; C. Pape, ibid., 14 (1881) 1873; H. Wichelhaus, Ann., 152 (1869) 321; J.A. Wanklyn, J. Chem. Soc., 13 (1861) 124.

9 D.E. Applequist, G.F. Fanta and B.W. Henrikson, J. Org. Chem., 23 (1958) 1715.