Pergamon

Tetrahedron Letters 43 (2002) 9307–9309

TETRAHEDRON
LETTERS

Effect of various acids at different concentrations on the pinacol rearrangement

Monica De Lezaeta,[a] Wajiha Sattar,[a] Paris Svoronos,[a,*] Sasan Karimi[a,*] and Gopal Subramaniam[b,*]

[a]*Department of Chemistry, Queensborough Community College, CUNY, Bayside, NY 11364, USA*
[b]*Department of Chemistry and Biochemistry, Queens College, CUNY, Flushing, NY 11367, USA*

Received 20 September 2002; accepted 21 October 2002

Abstract—The formation of side products in the pinacol–pinacolone rearrangement was studied as a function of concentration and strength of various aqueous acids using ^{1}H NMR spectroscopy. In all cases, pinacolone was the principal product and in most cases, its relative yield decreased with respect to 2,3-dimethyl-1,3-butadiene, when the acid concentration was lowered or the corresponding conjugate base was added. © 2002 Elsevier Science Ltd. All rights reserved.

The acid catalyzed pinacol–pinacolone rearrangement has been well studied for a long time[1] and has served as a standard topic in most undergraduate organic textbooks. With benzopinacol as the diol, tetraphenylethylene oxide was also produced[2] in addition to the expected benzopinacolone. Several non-dehydrative pinacol rearrangements with various Lewis acids have also been reported.[3] More recently, similar rearrangements were observed in the presence of aminium salts.[4] A theoretical study of the mechanism that involves both stepwise and concerted reaction paths has been described by Nakamura and Osamura.[5] Although, the classical pinacol to pinacolone rearrangement is well documented, we were intrigued by some reports[1j] that under certain acidic conditions, 2,3-dimethyl-1,3-butadiene becomes the major product in the reaction. This suggests a shift in the mechanistic pathway (Scheme 1) leading to the preferred formation of **2**. In order to understand the competing reaction pathways, we evaluated the effect of changing the concentration of various acids as well as the effect of added conjugate base. Our results indicate that although the 1,2-migration is the preferred pathway, the alternative route also competes leading to products **2** and **3** (Scheme 1). The change in the ratio of rearrangement to elimination products described in this work is in agreement with the results obtained in the pinacol–pinacolone rearrangement of 2,3-di-(3-pyridyl)-2,3-butanediol in sulfuric acid and the effect of added water.[6]

The classical rearrangement leading to **1** proceeds via protonation of the hydroxyl group and subsequent loss of water to afford the stable carbocation **A**, which undergoes a 1,2-shift to form the more stable intermediate **B** (Scheme 1). Alternatively, **A** can lose a proton to form 2,3-dimethyl-3-buten-2-ol (**3**). Protonation of the hydroxyl group in **3** and loss of water leads to allylic carbocation **C** that yields **2** as the main elimination product. Addition products, 1-halo-2,3-dimethyl-2-butene **4** and 3-halo-2,3-dimethyl-1-butene **5**, were also observed when a hydrogen halide (HX = HCl or HBr) was used as the catalyst. By virtue of resonance structure **C**, reduction product **6** was also obtained when HI served as the acid.

In this study, the reactions were carried out[7] in the presence of various inorganic acids (sulfuric, phosphoric, hydrochloric, hydrobromic, hydriodic) at different concentrations (2 M, 4 M, 6 M), as well as the corresponding conjugate bases (Na_2SO_4, K_3PO_4, NaCl, NaBr and NaI). The identity and the relative ratio of products **1**–**6** were determined by ^{1}H NMR spectroscopy.

The following conclusions may be drawn as a result of treating pinacol with various acids at different concentrations and added conjugate base:

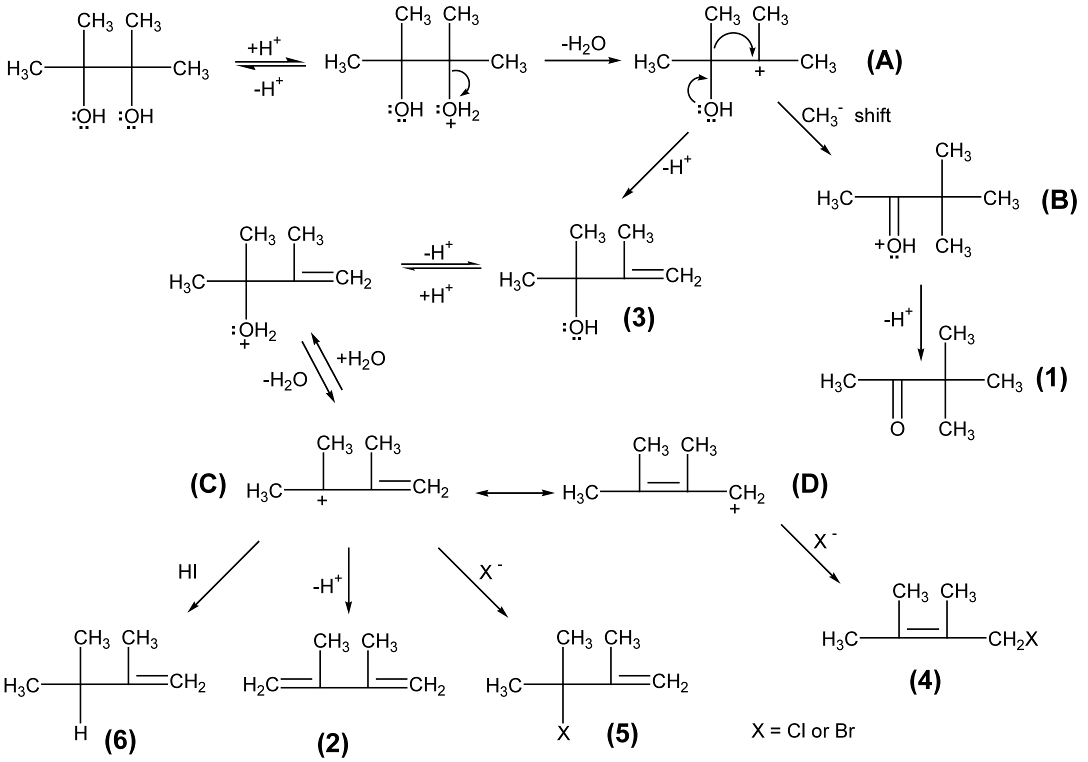
(a) The predominant formation of pinacolone **1** indicates that 1,2-migration is the most favorable process leading to the stable intermediate **B**.

(b) Generally, as the concentration of the acids decreased, a decreasing trend in the formation of **1** and a steady increase of both **2** and **3** was observed. This may be attributed to the involvement of the

---

* Corresponding authors. E-mail: skarimi@qcc.cuny.edu

PII: S0040-4039(02)02379-1



Scheme 1.

increasingly larger quantity of water present, which can act as a base to remove the adjacent protons from both intermediates **C** and **A** to afford **2** and **3**, respectively.

(c) In most reactions, addition of the corresponding conjugate base also increased the formation of **2** and **3**. This may be interpreted by the fact that as the ionic strength of the mixture increases, the anion present can act as a base and favor elimination.

(d) With addition of hydrogen halides (chloride or bromide), two addition products **4** and **5** were also formed, with **4** being the predominant isomer (thermodynamic product). The quantities of **4** and **5** also increased with increasing acid concentration (Tables 1 and 2).

(e) Phosphoric is the weakest of all acids used ($K_a = 7.5\times10^{-3}$). Although the relative trend of product ratio compares well with all other cases, the overall mass yield of products decreased with decreasing concentration of the acid (Table 1). This suggests that the hydronium ion concentration is not sufficient to affect protonation and subsequent rearrangement. Furthermore, addition of the conjugate base reduced the mass yield of products even further, presumably by reducing the effective concentration of the hydronium ion (Table 2).

Table 1. Ratio of pinacolone to various alkenes in the **absence** of added conjugate base

Acid	Measured quantity	2 M	4 M	6 M
HCl	Product ratio	100:33:10:0:0:0	100:14:0:0:0:0	100:26:0:8:7:0
	Product mass (g)	1.07	1.16	1.13
	Distillation range (°C)	84–94	84–94	84–94
HBr	Product ratio	100:25:7:0:0:0	100:18:2:0:0:0	100:16:2:2:0:0
	Product mass (g)	0.90	1.00	1.09
	Distillation range (°C)	80–85	80–85	80–85
HI	Product ratio	100:16:5:0:0:0	100:2:0:0:0:0	100:0:0:0:0:10
	Product mass (g)	1.06	0.77	0.66
	Distillation range (°C)	84–93	74–88	63–72
H_2SO_4	Product ratio	100:18:4:0:0:0	100:15:1:0:0:0	100:10:0:0:0:0
	Product mass (g)	1.06	1.08	0.83
	Distillation range (°C)	84–87	83–85	83–85
H_3PO_4	Product ratio	100:25:15:0:0:0	100:31:10:0:0:0	100:16:5:0:0:0
	Product mass (g)	0.05	0.41	1.08
	Distillation range (°C)	85–87	83–97	80–95

Table 2. Ratio of pinacolone to various alkenes in the **presence** of added conjugate base

Acid	Measured Quantity	2 M	4 M	6 M
HCl	Product ratio	100:42:10:11:0:0	100:31:4:3:4:0	100:22:0:13:10:0
	Product mass (g)	1.01	0.75	1.12
	Distillation range (°C)	84–94	84–94	84–94
HBr	Product ratio	100:26:5:0:0:0	100:21:2:0:0:0	100:22:4:3:0:0
	Product mass (g)	1.06	0.97	0.95
	Distillation range (°C)	80–85	80–85	80–85
HI	Product ratio	100:19:5:0:0:0	100:2:0:0:0:0	100:0:0:0:0:11
	Product mass (g)	1.09	0.70	0.68
	Distillation range (°C)	80–93	81–87	63–74
H_2SO_4	Product ratio	100:23:5:0:0:0	100:18:1:0:0:0	100:11:0:0:0:0
	Product mass (g)	1.04	1.06	1.05
	Distillation range (°C)	77–92	83–85	83–85
H_3PO_4	Product ratio	No reaction	100:25:20:0:0:0	100:33:6:0:0:0
	Product mass (g)	0	0.06	0.42
	Distillation range (°C)	NA	83–97	80–95

Product ratio represents the relative amounts of pinacolone (**1**), 2,3-dimethyl-1,3-butadiene (**2**), and 2,3-dimethyl-3-buten-2-ol (**3**), 1-halo-2,3-dimethyl-2-butene (**4**), 3-halo-2,3-dimethyl-1-butene (**5**), 2,3-dimethyl-1-butene (**6**).

Tables 1 and 2 show the mass balance and distillation range for all the reactions. The data shown in Tables 1 and 2 is an average of two independent experiments. The relative amounts of products were normalized with respect to pinacolone. The maximum concentration of HI was only 5.6 M.

(f) Use of concentrated hydriodic acid (5.6 M) led to a dark solution which was indicative of iodine formation (verified by oxidation of $NaHSO_3$). The ^{1}H NMR spectrum of the distillate indicated the surprising formation of 2,3-dimethyl-1-butene **6**, and the complete absence of **2** (Tables 1 and 2). Apparently the allylic carbocation **C** underwent reduction to form molecular iodine as a byproduct.

In conclusion, this study demonstrates that there exists a competition between the favorable 1,2-migration and the alternative reaction paths leading to products **2** and **3**. With both increasing dilution of the acid as well as added conjugate base, the mechanistic pathway is shifted toward elimination. The observation of the two addition products **4** and **5**, especially with 6 M HCl, reflect the relative stability of the resonance-stabilized intermediate allylic cations **C** and **D**. The highest ratio of elimination to rearrangement products observed with added NaCl can be correlated with the strongly basic character of chloride ion. In contrast, the much weaker nature of the iodide ion did not lead to the formation of either **2** or **3**; instead, reduction product **6** was obtained.

Acknowledgements

This work was supported by the Research Foundation of the City University of New York. The authors thank Professors W. F. Berkowitz and R. Bittman of Queens College–CUNY and Professor N. McKelvie of City College–CUNY for their valuable suggestions.

References

1. (a) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, *Part B*, 3rd ed.; Plenum, 1993; p. 499; (b) March, J. *Advanced Organic Chemistry: Reactions*, *Mechanisms*, *and Structure*, 4th ed.; Wiley-Interscience, 1992; p. 1072; (c) Partridge, D. A. *Edu. Chem.* **1983**, *20*, 12; (d) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper & Row, 1981; p. 373; (e) Sykes, P. *A Guidebook to Mechanism in Organic Chemistry*, 5th ed.; Longmans, 1975; p. 112; (f) Pocker, Y. In *Molecular Rearrangements*; De Mayo, P., Ed.; Wiley-Interscience: New York, 1963; pp. 15–25; (g) Deno, N. C.; Perizzolo, C. *J. Org. Chem.* **1957**, 836; (h) Duncan, J. F.; Lynn, K. R. *J. Chem. Soc.* **1956**, 3512; (i) Gebhart, H. J.; Adams, K. H. *J. Am. Chem. Soc.* **1954**, *76*, 3925; (j) Allen, C. F. H.; Bell, A. *Organic Synthesis*, *Coll. Volume 3* **1955**, 312 and references cited therein.
2. Kakimoto, M.; Seri, T.; Imai, Y. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2643 and references cited therein.
3. (a) Kita, Y.; Yoshida, Y.; Mihara, S.; Furukawa, A.; Higuchi, K.; Fang, D.; Fujioka, H. *Tetrahedron* **1998**, *54*, 14689; (b) Bhushan, V.; Chandrasekaran, S. *Chem. Lett.* **1982**, 1537.
4. Lopez, L.; Mele, G.; Mazzeo, C. *J. Chem. Soc.*, *Perkin Trans. 1* **1994**, *7*, 779.
5. Nakamura, K.; Osamura, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9112.
6. Loeser, E.; Chen, G. P.; He, T.; Prasad, K.; Repic, O. *Tetrahedron Lett.* **2002**, *43*, 2161.
7. The following procedure was used: 1.47 g (12.5 mmol) of pinacol hexahydrate (Aldrich) was combined with 5.0 mL of the acid and the mixture was distilled using a constant-temperature oil bath (130–135°C). The mass balance and temperature range for the mixture of distillate are listed in Tables 1 and 2. The distillate was collected (15–20 min) in an ice-water bath in a closed system, dried, and its ^{1}H NMR spectrum was obtained ($CDCl_3$, Bruker Avance-DPX 400 MHz NMR). For experiments that involved the use of conjugate base, 0.44 g of the corresponding anhydrous conjugate base was dissolved in 5.0 mL of the acid before mixing with 1.47 g of pinacol hexahydrate. The conjugate bases used include sodium sulfate, potassium phosphate, sodium chloride, sodium bromide and sodium iodide. The acid solutions were made by diluting commercially available concentrated sulfuric (18 M), phosphoric (15 M), hydrochloric (12 M), hydrobromic (8.8 M), and hydriodic (5.6 M) acids.