Monatshefte für Chemie 128, 79–83 (1997)

Monatshefte für Chemie
Chemical Monthly

The Rearrangement of 11,13-Dibromo-9,10-dimethoxy-9,10-propanoanthracen-12-ones to the Corresponding *Favorskii* Products

A. A. O. Sarhan

Chemistry Department, Faculty of Science, Assiut University, Assiut 71516, Egypt

Summary. Submitting *cis*- and *trans*-11,13-dibromo-9,10-dimethoxy-9,10-propanoanthracen-12-one (**4a,b**) to *Favorskii* conditions (MeOH/KOH, 60 °C) afforded the *Favorskii* ester **5a** and the α-keto acetal **5b** in 46% overall yield. Almost all reactions resulted in the formation of a single isomer which could be shown to be the most favored one by molecular mechanics calculations (MM2).

Keywords. Allylic rearrangement; Tetrabromoacetone; 9,10-Dimethoxy-9,10-propanoanthracen-12-ones; Ring contraction; Molecular mechanics calculations (MM2).

Umlagerung von 11,13-Dibrom-9,10-dimethoxy-9,10-propanoanthracen-12-onen zu den entsprechenden *Favorskii*-Produkten

Zusammenfassung. Unter *Favorskii*-Bedingungen (MeOH/KOH, 60 °C) entstehen aus *cis*- und *trans*-11,13-Dibrom-9,10-dimethoxy-9,10-propanoanthracen-12-on der *Favorskii*-Ester **5a** und das α-Keto-Acetal **5b** in 46% Gesamtausbeute. Fast alle Reaktionen ergeben ein einziges Isomeres, von dem mittels molekularmechanischer Berechnungen gezeigt werden konnte, daß es sich dabei um das energetisch günstigere Produkt handelt.

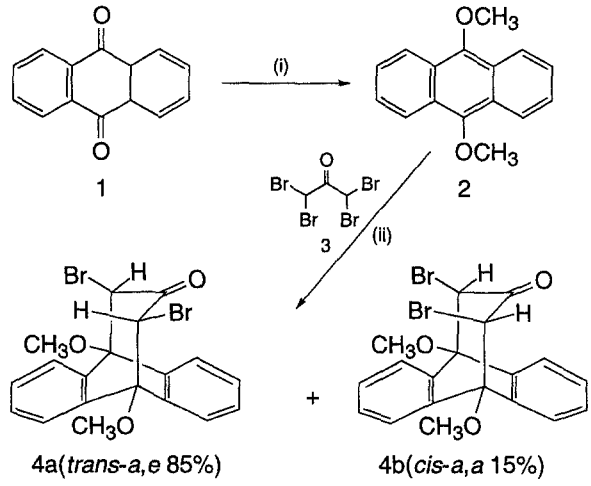
Introduction

The rearrangement of α-halo- and α, α'-dihaloketones under the influence of base was first described by *Favorskii* in 1892 [1, 2]. This rearrangement is usually stereoselective, though subsequent *cis* to *trans* isomerization under the influence of base often obscures this feature. Although the *Favorskii* reaction is pretty well known, studies concerning its mechanism are still in progress.

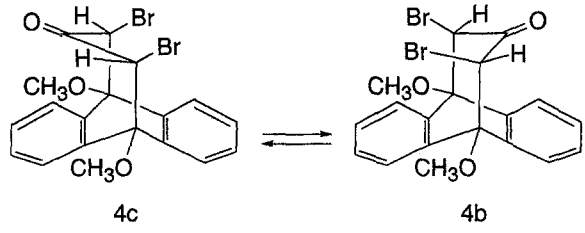
The mechanism of the Favorskii rearrangement has been studied in detail, and the general mechanism proposed by *Bordwell* is in agreement with the reactivity of derivatives in which the bromine atoms can adopt axial positions [3]. However, the use of strong bases generally favours the rearrangement processes [4–10]. Therefore, a detailed investigation of this issue seemed to be of interest.

Results and Discussion

9,10-Dimethoxyanthracene (**2**) was prepared and allowed to add to tetrabromoacetone (**3**) using the Zn-Cu coupling procedure to give the isomeric cycloadducts **4a,b** in 40.5% yield (*trans-axial-equatorial* (*a, e*, **4a**, 85% and *cis-axial-axial* (*e, e*, **4b**, 15%)). The *cis* isomer **4b** is flipped into the isomer **4c** (Schemes 1 and 2). It is interesting that the ^{1}H NMR spectrum of the cycloadduct **4b** displays a long-range coupling between H-11 and H-13, in contrast to the usual behaviour of planar configured H–C–C–C–H chains.

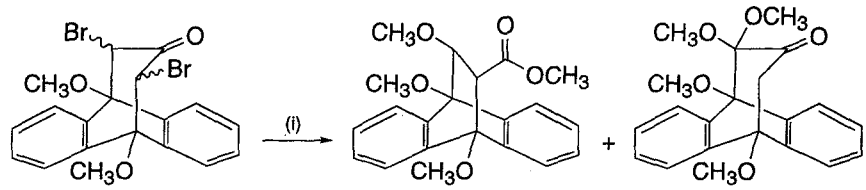


Scheme 1. (i) Zn/NaOH, $(CH_3)_2SO_4$, 51%; (ii) Zn-Cu/dioxane/ultrasound, 10–20 °C, 8 h, 40.5%



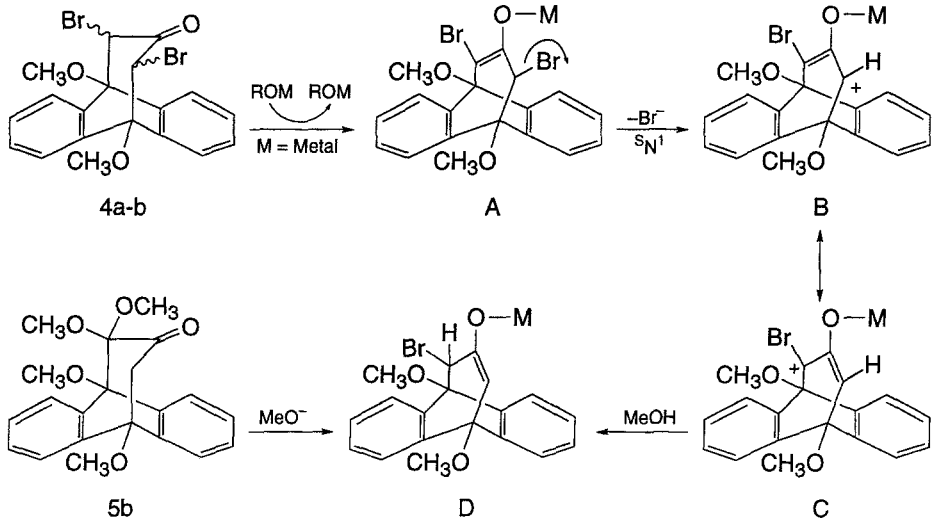
Scheme 2

The MM2 calculations of the conformation **4b** (two possibilities: H-11 and H-13 are *cis-diequatorial* (*e, e*) or H-11 and H-13 are *cis-diaxial* (*a, a*)) favour the formation of **4c**, where H-11 and H-13 again are *cis-diequatorial* (*e, e*). The ^{1}H NMR spectrum (200 MHz, $CDCl_3$) revealed a ^4J coupling of 1.5 Hz for H-11 and H-13. This cannot occur if H-11 and H-13 are not *cis-diequatorial*. MM2 calculations of the isomers **4a-c** agreed with the ^{1}H NMR spectroscopic data. The *Favorskii* rearrangement of the α, α'-dibromocycloadducts **4a, b** lead to the ring contracted cycloadduct **5a** and the α-keto acetal **5b**. Upon reaction of the α, α'-dibromocycloadducts **4a, b** with MeOH/KOH at 60 °C for 3 hours, **5a** and **5b** could be obtained in 46% overall yield (Scheme 3).



Scheme 3. (i) MeOH/KOH, 60 °C, 3 h, **5a**: 75% and **5b**: 25%

The mechanism of the formation of the α-keto acetal can be described by an intramolecular oxidation-reduction reaction. Debromination of **4a, b** is thought to give a bromoallylic bromide (cf. **A**) which suffers S_N1-like heterolysis to result in a resonance stabilized (metal) oxyallyl cation (**B**↔**C**). Recombination with methanol provides the α-bromo ether **D** which, on regioselective methanolysis and ketonization, furnishes the α-keto acetal **5b** and also the *Favorskii* ring contracted dibenzobarrelene **5a** (Scheme 3). Recently, *Hoffmann* and *Sarhan* [11] have discussed this reaction mechanism in detail (Scheme 4).



Scheme 4

Molecular mechanics calculations (MM2 [12]) on the possible conformations of the title compounds gave additional evidence of their stereochemistry (Table 1). From the heats of formation, strain (STR), and molecular minimized energy (MME), the isomers $a^{Br}a^{Br}$-**4c** and *trans*-**5a** are most favoured ones.

Experimental

Column chromatography (silica gel, 0.02–0.63 mm, Merck) was carried out under weak positive pressure; TLC: precoated plates, Macherey-Nagel, Merck; IR spectra: Electrophotometer 580 and FT

Table 1. Molecular mechanics (MM2) data of **4a, c** and **5a, b**

	MME	STR	BND	S-B	TOR	VDW	DD/QQ	DP MOM	HF	SE
4a ($a^{Br}e^{Br}$)	53.52	3.81	11.01	0.54	22.20	26.05	−10.10	4.36	163.75	42.40
4b ($a^{Br}a^{Br}$)	50.83	3.44	11.21	0.49	22.95	23.89	−11.16	4.11	161.06	39.71
4c ($a^{Br}a^{Br}$)	49.54	3.30	10.18	0.51	22.67	23.40	−10.53	4.61	159.78	38.42
5a, *trans*	62.24	3.41	13.66	0.22	20.11	25.11	−0.27	1.96	78.02	42.49
5a, *cis*	64.44	3.52	13.91	0.28	20.68	25.74	0.30	3.09	80.22	44.69
5b	66.89	4.69	11.45	0.54	26.27	29.24	−5.03	3.82	87.12	39.91

spectrometer 1710, Perkin-Elmer; ^{1}H NMR: WP 200 SY and AM 300, Bruker; ^{13}C NMR: WP 200 SY, AM 300, Bruker; APT (attached proton test): spin echo based selection of multiplicities of ^{13}C signals; MS: spectrometer MAT 312, Finnigan company; elementary analyses: Microanalytical Laboratory of the Department of Organic Chemistry (Spectral Unit, Hannover University, D-30167 Hannover, Germany), measured and calculated values agreed satisfactory. The starting 9,10-dimethoxyanthracene (**2**) was prepared according to Ref. [13].

cis- and *trans-11, 13-Dibromo-9, 10-dimethoxy-9, 10-propanoanthracen-12-ones* (**4a, b**; $C_{19}H_{16}Br_2O_3$)

A mixture of Zn powder (4 mmol), CuCl (0.4 mmol), and 9, 10-dimethoxy-anthracene (**2**, 2.38 g 10 mmol) in absolute dioxane (20 ml) contained in a three-necked flask was sonicated under nitrogen in an ultrasonic bath. A solution of 7.48 g **3** (20 mmol) and chlorotrimethylsilane (20 mmol) in dry dioxane (10 ml) was added dropwise over a period of 30 minutes. The bath temperature was maintained below 20 °C for the first hour and then allowed to reach slowly room temperature. The reaction mixture was then sonicated for another 6–8 hours, filtered over silica gel, and washed several times with dichloromethane. The filtrate was dried ($MgSO_4$) and chromatographed on silica gel (ether/petrolether = 1:5) to give the cycloadducts **4a, b** as colourless crystals in 40.5% yield.

IR (KBr): ν = 3072w, 2968w, 2944m, 2840w, 1708s, 1464m, 1176w, 1104s, 728s cm^{-1}.

^{13}C NMR (50 MHz, $CDCl_3$): δ = 53.42, 53.52 (q, OMe-9, 10), 56.42, 56.59 (d, C-11, 13), 66.28, 66.43 (s, C-9, 10), 125.58–129.86 (d, arom-C), 132.69–135.25 (s, arom-C), 193.59, 194.06 (s, 2 C = O); MS: m/z(%) = 454(5)[M^{+2}], 452(9)[M^+], 450(5)[M^{-2}], 408(7), 373(25), 371(24), 341(5), 327(13),

Table 2. ^{1}H NMR spectra of **4a, b** in $CDCl_3$, CDC_3N, and C_6D_6

	$CDCl_3$	CD_3CN	C_6D_6
trans-ae-**4a**	δ = 3.58 (s, 6H, OCH_3-9, 10), 4.32 (s, 2H, H-11, 13), 7.48–7.77 (m, 8H, arom-H) ppm	δ = 3.51 (s, 6H, OCH_3-9, 10), 4.48 (s, 2H, H-11, 13), 7.57–7.78 (m, 8H, arom-H) ppm	δ = 3.07 (s, 6H, OCH_3-9, 10), 4.62 (s, 2H, H-11, 13), 6.95–7.70 (m, 8H, arom-H) ppm
cis-aa-**4b**	δ = 3.59 (s, 6H, OCH_3-9, 10), 4.33–4.42 (dd, J = 1.5 Hz, J = 16 Hz, 2H, H-11, 13), 7.48–7.77 (m, 8H, arom-H) ppm	δ = 3.52 (s, 6H, OCH_3-9, 10), 4.37–4.46 (dd, J = 1.5 Hz, J = 16 Hz, 2H, H-11, 13), 7.57–7.78 (m, 8H, arom-H) ppm	δ = 3.08 (s, 6H, OCH_3-9, 10), 4.53–4.60 (dd, J = 1.5 Hz, J = 16 Hz, 2H, H-11, 13), 6.95–7.70 (m, 8H, arom-H) ppm

295(6), 277(3), 251(25), 238(100), 223(91), 208(6), 193(16), 176(10), 165(19), 152(10), 119(5), 95(4), 76(4), 63(2), 49(2).

11-Methoxycarbonyl-9, 10, 12-trimethoxy-9, 10-propanoanthracen-12-one (**5a**; $C_{21}H_{22}O_5$) and *9, 10, 11, 11-Tetramethoxy-9, 10-propanoanthracen-12-one* (**5b**; $C_{21}H_{22}O_5$)

A mixture of the dibromocycloadduct **4a b** (0.452 g, 1.0 mmol) and KOH (0.56 g, 10 mmol) was refluxed in methanol (15 ml) with stirring under nitrogen for 4 hours. The reaction mixture was cooled, diluted with water, extracted with dichloromethane, and dried ($MgSO_4$). The filtrate was concentrated under reduced pressure and chromatographed (silica gel, ether/petrolether = 1:5) to give an unseparable mixture of the *Favorskii* ester **5a** (25%) and the α-keto acetal **5b** (75%) in 46% overall yield.

IR (KBr): $\nu = 3080$w, 3040w, 2990m, 2950s, 2840s, 1740s, 1725s, 1460s, 1430s, 1220s, 1100s, 1070s, 1005s, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): Ester **5a** $\delta = 3.18$ (d, $J = 3$Hz, 1H, H-11), 3.35 (s, 3H, OCH_3-9(10)), 3.36 (s, 3H, OCH_3-9(10)), 3.88 (s, 3H, OCH_3-12), 3.98 (s, 3H, $COOCH_3$-11), 4.15 (d, $J = 3$ Hz, 1H, H-12), 7.15–7.75 (m, 8H, arom-H) ppm; α-keto acetal **5b**: $\delta = 2.8$ (s, 2H, CH_2-13), 3.45 (s, 3H, OCH_3-9(10)), 3.59 (s, 3H, OCH_3-9(10)), 3.63 (s, 6H, OCH_3-11, 11), 7.15–7.75 (m, 8H, arom-H) ppm; MS: m/z (%) = 352 [M^{-2}](9), 339(5), 323(63), 308(9), 281(14), 263(4), 249(6), 239(29), 238(100), 223(34), 208(5), 193(4), 189(4), 178(5), 165(9), 155(24), 149(14), 135(33), 117(32), 107(17).

Acknowledgements

Thanks are due to Prof. *H.M.R. Hoffmann* (Organic Chemistry Department, Hannover University, D-30167 Hannover, Germany) for his kind help.

References

[1] Favorskii AE (1892) Zh Russ Fiz-Khim O-Va **24**: 254
[2] Favorskii AE (1894) Zh Russ Fiz-Khim O-Va **26**: 556
[3] Bordwell FG, Carlson MW (1970) J Am Chem Soc **92**: 3370
[4] Favorskii AE (1894) J Soc Chem Phys R **26**: 590
[5] Jacquier R (1950) Bull Soc Chem Fr: 35
[6] Tohoubar B (1955) Bull Soc Chem Fr: 1363
[7] Kende AS (1960) Org React **11**: 261
[8] Kakhrem AA, Ustynyuk TK, Titiv YA (1970) Russ Chem Rev **39**: 732
[9] Chenier PJ (1978) J Chem Educ **55**: 286
[10] Reviews: Mann J (1992) In: Trost BM, Fleming I, Pattenden G (eds) Comprehensive Organic Synthesis, vol 3. Pergamon Press, Oxford, p 839; Baretta A, Waegell B, Abramovitch RA (1982) Reactive intermediates, vol. 2. Plenum Press, New York, p 527–585
[11] a) Sarhan AAO, Hoffmann HMR (1994) Chem Ber **127**: 1755; b) Sarhan AAO, Hoffmann HMR (1996) (submitted); c) Sarhan AAO (1994) Thesis, Universities of Hannover and Assiut; d) Sarhan AAO (1995) 5th Ibn Sina International Conference, Cairo, Egypt, p 140; e) Sarhan AAO (1996) (submitted)
[12] a) Molecular mechanics calculations (MM2) were performed using the computer program PCMODEL 486 version 6, available from Serena Software; b) Schwartz MH, Rosenfeld SM, Lee CI, Jasinski JP, Dardon EH (1992) Tetrahedron Lett **33**(42): 6275; c) Okada K, Kawai H, Oda M (1992) Tetrahedron Lett **33**(2): 257; d) Sakakibara K, Allinger NL (1995) J Org Chem **60**: 4044
[13] Sauer J, Schroder B, Wiener R (1967) Chem Ber **100**: 306

Received August 20, 1996. Accepted (revised) September 16, 1996