Communications to the Editor

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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 30.[1] RING ENLARGEMENT OF CYCLOALKANONES WITH BENZYLSULFONYLDIAZOMETHANE AND CONVERSION OF THE RESULTING HOMOLOGATED 2-BENZYLSULFONYLCYCLOALKANONES TO 1-BENZYLSULFONYL-1-CYCLOALKENES VIA CHELETROPIC RING CONTRACTION

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Benzylsulfonyldiazomethane can be used for the ring enlargement of cycloalkanones (1) with various ring sizes. The resulting homologated 2-benzylsulfonylcycloalkanones (2) are easily converted to 1-benzylsulfonyl-1-cycloalkenes (4) by bromination followed by cheletropic ring contraction.

KEYWORDS ——— benzylsulfonyldiazomethane; α-sulfonylcycloalkanone; 1-sulfonyl-1-cycloalkene; ring enlargement; ring contraction; bromination; bromine migration; cheletropic reaction

We have reported recently that trimethylsilyldiazomethane[2] as well as benzylsulfonyldiazomethane[3] can be used as stable and safe substitutes for hazardous diazomethane in the Arndt-Eistert synthesis. Trimethylsilyldiazomethane has been proved to be useful in the homologation of ketones[4] and aldehydes.[5] Here we report that benzylsulfonyldiazomethane can be used for the ring homologation (ring enlargement) of cycloalkanones (1), giving 2-benzylsulfonylcycloalkanones (2) in good yields. The α-sulfonylketones 2 can be conveniently converted to 1-benzylsulfonyl-1-cycloalkenes (4) via α-benzylsulfonyl-α'-bromocycloalkanones (3b) by bromination followed by cheletropic ring contraction, as shown in Chart 1. Although vinylsulfones are generally useful synthetic intermediates,[6] cyclic vinylsulfones like 4 are not readily accessible in contrast to the other vinylsulfones. Thus, the overall process in Chart 1 will offer a convenient way from cycloalkanones to cyclic vinylsulfones.

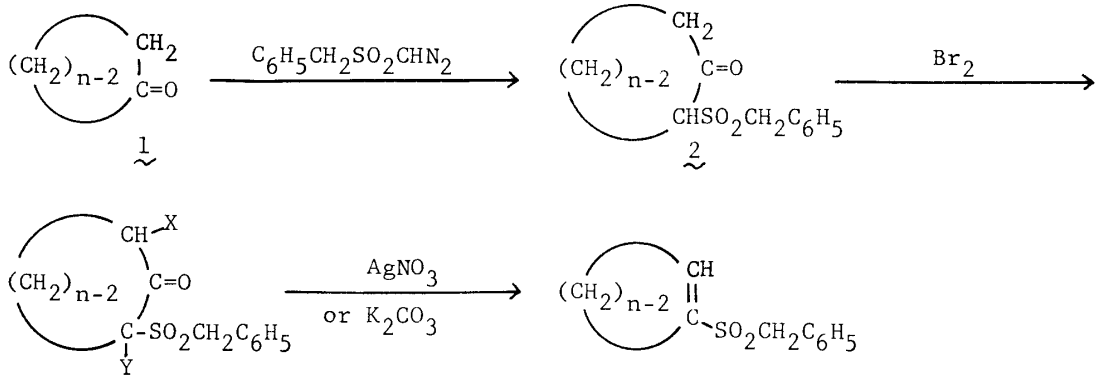


Chart 1

Ring enlargement of various cycloalkanones (1) with benzylsulfonyldiazomethane has been achieved at 0°C by the use of titanium tetrachloride in dichloromethane. Boron trifluoride etherate in dichloromethane, which has been used for the ring enlargement of cycloalkanones (1) with trimethylsilyldiazomethane,[4] was effective for the ring enlargement of cyclohexanone but was not satisfactory for that of cyclododecanone. Of the additives examined so far, titanium tetrachloride was the best though it concomitantly reacted with benzylsulfonyldiazomethane to give benzyl chloromethyl sulfone. The results of the ring enlargement are summarized in Table I.

Table I.[7] Ring Enlargement of Cycloalkanones (1) with Benzylsulfonyldiazomethane

Run	n	Yield, %[a]	Mp, °C
1	6	71	150 (0.3 Torr)[b]
2	7	86	99-100
3	8	27 (73)	200 (0.3 Torr)[b]
4	12	43 (49)	117.5-119
5	14	48 (68)	118-118.5
6	15	54 (98)	122-123
7	16	58 (67)	120

a) Yields in parentheses are based on consumed ketones 1. b) Bp, °C.

Removal of the benzylsulfonyl group from 2 has been easily carried out with Raney nickel W-2 in ethanol or sodium amalgam in phosphate buffer[8] in high yields, proving that benzylsulfonyldiazomethane can be used as a stable and safe substitute for hazardous diazomethane in the ring homologation reaction.

Bromination of 2-benzylsulfonylcycloalkanones (2) with bromine in diethyl ether containing acetic acid gave mostly α'-brominated compounds 3b[9] in preference to α-brominated ones 3a, as shown in Table II. The initial products of the bromination reaction are α-brominated ketones 3a, but the bromine atom of 3a migrates to the α'-position during the reaction.[10] In fact, migration of the bromo function of 2-benzylsulfonyl-2-bromocyclooctanone (3a, n=7) has occurred by treatment with 25% hydrogen bromide-acetic acid in diethyl ether to give a mixture of 2-bromo and 8-bromoketones 3a and 3b (n=7).

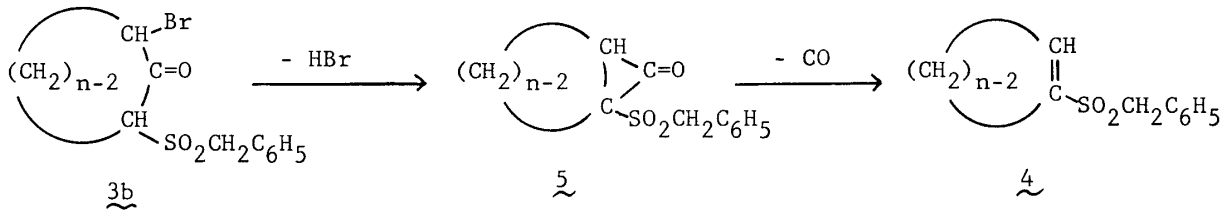
Table II.[7] Bromination of 2-Benzylsulfonylcycloalkanones (2)

Run	n	Yield, %[a] 3a	Yield, %[a] 3b	Mp, °C 3a	Mp, °C 3b
1	6	25 (29)	59 (69)	89-90	134-136
2	7	50	48	98-99	151.5-155
3	8	0	96	-	171-174
4	12[b]	0	32 (100)	-	128-129
5	14[c]	1	99	oil	130-132
6	15	4	94	oil	135-138
7	16	4	95	oil	144-146

a) Yields in parentheses are based on consumed ketones 2. b) Bromination[11] of the sodium enolate of 2 (n=12) with bromine afforded 3b (n=12) in 99% yield. c) Bromination[11] of the sodium enolate of 2 (n=14) with bromine afforded a mixture of 3a (13%) and 3b (84%).

The final step in the preparation of cyclic vinylsulfones 4 involved treatment of α-sulfonyl-α'-bromoketones 3b with either silver nitrate in hot aqueous dioxane or potassium carbonate in refluxing xylene. α-Sulfonyl-α'-bromoketones 3b with larger ring sizes (n>8) afforded a mixture of cis and trans-isomers (4a and 4b), in which the former predominated, while smaller ring size ketones (n≦8) furnished cis-

isomers 4a only.[12] The results are summarized in Table III. It is interesting that no Favorskii rearrangement occurs in either case. The reaction mechanism of this ring contraction probably is as follows: Dehydrobromination of 3b with silver nitrate or potassium carbonate first gives cyclopropanones 5, which loses carbon monoxide[13] by cheletropic reaction[14] to give vinylsulfones 4:



3b 5 4

Table III.[7] Cheletropic Ring Contraction of α-Benzylsulfonyl-α'-bromocycloalkanones (3b)

Run	n	Yield, %[a]		Mp, °C		NMR (CDCl3) δ ppm, vinyl H	
		4a	4b	4a	4b	4a	4b
1	6	27 (41)	0	81-82	-	6.56	-
2	7	21[b] (48)	0	65-66	-	6.82	-
3	8	36 (59)	0	74-76	-	6.68	-
4	12	50 (37)	4 (38)	89-90	63-65	6.36	6.26
5	14	44 (44)	11 (27)	111-112	53	6.33	6.03
6	15	53 (40)	6 (26)	78-80	60	6.33	6.03
7	16	47 (33)	9 (26)	91-92	57-59	6.34	6.02

a) Yields obtained by the reaction with silver nitrate. Yields in parentheses were obtained by the reaction with potassium carbonate. b) Yield becomes 35% based on recovered starting material.

Ring enlargement of cycloalkanones (1) with benzylsulfonyldiazomethane appears to be general with respect to ring size and gives ketones 2 bearing the α-sulfonyl group, which will be useful for other elaboration at the α-position to the carbonyl group. Bromination of 2 followed by the cheletropic ring contraction proceeds in a satisfactory manner and will offer a useful preparative procedure for cyclic vinylsulfones 4.

Typical experimental procedures for each reaction are as follows:

Ring Enlargement of Cycloalkanones (1) with Benzylsulfonyldiazomethane —— To a stirred mixture of cycloalkanone (1, 1 mmole) and titanium tetrachloride (0.11 ml, 1 mmole) in dichloromethane (5 ml) is added benzylsulfonyldiazomethane (216 mg, 1.1 mmole) in dichloromethane (5 ml) at 0°C under nitrogen. After 1 h at 0°C, water (30 ml) is added and the dichloromethane layer is separated. The aqueous layer is extracted with dichloromethane (30 ml x 2), and the combined organic layer is washed with water (30 ml x 2) and saturated aqueous sodium chloride (30 ml x 1), and dried over magnesium sulfate. Concentration in vacuo affords the crude product which is purified by either preparative layer chromatography (Merck silica gel 60 F_{254}, hexane-ethyl acetate 1.5-3:1) or column chromatography (Merck Kieselgel 60, 70-230 mesh, hexane-ethyl acetate 5-7:1) to give 2-benzylsulfonylcycloalkanone (2).

Bromination of 2-Benzylsulfonylcycloalkanone (2) —— To 2-benzylsulfonylcycloalkanone (2, 1 mmole) in diethyl ether (20 ml) is added glacial acetic acid (66 mg, 1.1 mmole) and bromine (176 mg, 1.1 mmole) and the mixture is stirred at room temperature under nitrogen for 24 h. Water (50 ml) and ethyl acetate (100 ml) are added, and the ethyl acetate layer is washed with water (50 ml x 2) and saturated aqueous sodium chloride (50 ml x 1), and dried over sodium sulfate. Concentration in vacuo followed by separation on a silica gel column (Merck Kieselgel 60, 70-230 mesh, hexane-ethyl acetate

8-13:1) affords α-benzylsulfonyl-α-bromocycloalkanone (3a), then α-benzylsulfonyl-α'-bromocycloalkanone (3b).

Cheletropic Ring Contraction of α-Benzylsulfonyl-α'-bromocycloalkanones (3b) ——— (i) With silver nitrate. To α-benzylsulfonyl-α'-bromocycloalkanone (3b, 1 mmole) in dioxane (20 ml) is added silver nitrate (254 mg, 1.5 mmole) in water (1 ml) under argon. The mixture is refluxed for 6 h. After concentration in vacuo, ethyl acetate (200 ml) is added to the residue and filtered. The filtrate is washed with water (100 ml x 3) and saturated aqueous sodium chloride (100 ml), and dried over sodium sulfate. After concentration in vacuo, the residue is separated by column chromatography over alumina (Merck, Activity II-III, hexane-diethyl ether 1-3:1) to give trans-1-benzylsulfonyl-1-cycloalkene (4b), then cis-1-benzylsulfonyl-1-cycloalkene (4a).

(ii) With potassium carbonate. A mixture of 3b (1 mmole) and potassium carbonate (166 mg, 1.2 mmole) in xylene is refluxed for 2-8 h under argon. The work-up is carried out as in (i).

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3) Y.-C. Kuo, T. Aoyama, and T. Shioiri, Chem. Pharm. Bull., 30, 526 (1982). Cf. Y.-C. Kuo, T. Aoyama, and T. Shioiri, Chem. Pharm. Bull., 30, 899 (1982).
4) N. Hashimoto, T. Aoyama, and T. Shioiri, Tetrahedron Lett., 21, 4619 (1980); Chem. Pharm. Bull., 30, 119 (1982).
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6) T.G. Back and S. Collins, J. Org. Chem., 46, 3249 (1981) and references therein; J.C. Saddler and P.L. Fuchs, J. Am. Chem. Soc., 103, 2112 (1981) and references therein.
7) All the products have been identified by spectral measurements (IR and NMR) as well as elemental analysis. All the crystalline products have been recrystallized from ethanol.
8) For example, the sulfonylketone 2 (n=12) was easily desulfonylated with Raney nickel W-2 in ethanol at room temperature for 2 h or with 5% sodium amalgam in methanol containing disodium hydrogen phosphate (see B.M. Trost, H.C. Arndt, P.E.Strege, and T.R. Verhoeven, Tetrahedron Lett., 1976, 3477) at room temperature for 26 h, giving cyclotridecanone in 82 or 84% yield, respectively. Desulfonylation of 2 (n=14) was similarly achieved with Raney nickel W-2 to give cyclopentadecanone (exaltone) quantitatively.
9) Relative stereochemistry of bromo and benzylsulfonyl groups is undetermined.
10) H.O. House, "Modern Synthetic Reactions," 2nd Ed., W.A. Benjamin, Inc., Menlo Park, 1972, p. 463.
11) Cf. J. Ficini and G. Stork, Bull. Soc. Chim. France, 1964, 723.
12) Assignment of cis and trans-configurations of the products 4a and 4b is based on comparisons of NMR spectra, in which the vinylic hydrogens being cis to the sulfonyl groups appear at lower fields by the anisotropy of the sulfonyl groups, as shown in Table III. Cf. W. Böll, Ann. Chem., 1979, 1655.
13) Detected by a Kitagawa's carbon monoxide detector tube.
14) Cf. G. Büchi and B. Egger, J. Org. Chem., 36, 2021 (1971); J. Bagli and T. Bogri, Tetrahedron Lett., 1972, 3815; F. Kienzle, G.W. Holland, J.L. Jernow, S. Kwoh, and P. Rosen, J. Org. Chem., 38, 3440 (1973); G. Büchi, U. Hochstrasser, and W. Pawlak, J. Org. Chem., 38, 4348 (1973).

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