Ring Expansions and Contractions with Diazonium Betaines. I. Synthesis of Ketones by Ring Expansion of Methylenecycloalkanes with Arenesulfonyl Azides

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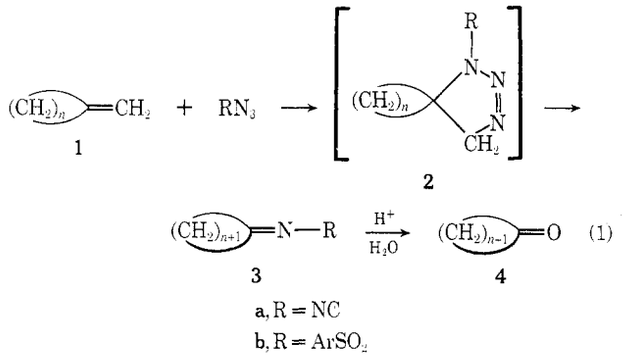
Reactions of methylenecycloalkanes with an aromatic sulfonyl azide proceed practically quantitatively *via* unstable intermediate Δ^2-triazolines **2b** to the ring-expanded arenesulfonimidocycloalkanes **3b** which are then hydrolyzed to the corresponding ketones **4**. The related reaction of 1,2-disubstituted olefins with arenesulfonyl azides provides a convenient route to ketones. Some aspects of the 1,3-dipolar addition of azides to olefins and the thermal decomposition of the resulting Δ^2-triazolines are discussed.

Organic azides react with olefins in a 1,3 cycloaddition to form Δ^2-triazolines **2**, a reaction first reported



by Wolff in 1912.[1,2] McMurry,[3] and recently Hermes and Marsh,[4] have used the reaction between methylenecycloalkane and cyanogen azide as a ring expansion method[5] according to reaction 1 (R = NC). The intermediate Δ^2-triazolines **2a** are unstable in this case and rearrange spontaneously to the ring-enlarged imides **3a** which can be hydrolyzed readily to the corresponding ketones **4**. McMurry obtained cycloheptanone and 2-methylcycloheptanone in this manner from methylenecyclohexane and ethylidenecyclohexane, respectively.[3]

Independently of McMurry's work we have investigated the scope and nature of the analogous reaction using arenesulfonyl azides [reaction 1 (R = $ArSO_2$)] in place of cyanogen azide. The use of arenesulfonyl azides offers the advantages of stability and nonhazardous nature as compared with cyanogen azide.[4]

Results

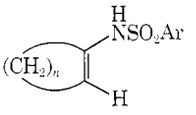
The results obtained are summarized in Table I. All exocyclic olefins examined from methylenecyclobutane to methylenecycloheptane reacted smoothly with aromatic sulfonyl azides to give the corresponding ring-enlarged imides in practically quantitative yield. Of several arenesulfonyl azides tested *o*-nitrobenzenesulfonyl azide was used most extensively because it seemed to give the best crystallizing products.

The identical imidocycloalkane products could also be obtained by the reaction between the corresponding cycloalkene and arenesulfonyl azide. All imides **5–10** show a very strong band around 1600 cm^{-1} in the ir spectrum corresponding to the C=N group (see Table I). This frequency shows a regular decrease when going from the five-membered to the eight-membered ring similar to the conditions found for the corresponding cyclic ketones.[6,7] As expected no band around 3400 cm^{-1} is apparent demonstrating the absence of any NH group.

In the nmr spectra the α protons to the imido function syn and anti to the arenesulfonyl group are generally separately visible with a chemical shift separation between 0.37 and 0.56 ppm. No assignment of these signals with respect to syn and anti was undertaken since no general method for assigning these resonances seems to be available at present.[8] In cyclohexanone oximes and cyclohexanone oxime tosyl esters, the α protons syn to the N substituent are deshielded.[9] It seems perilous, however, to extrapolate from the oxime tosyl esters to the benzenesulfonimido group under consideration.[8]

The sulfonimides **3b**, *i.e.*, **5–10**, were easily hydrolyzed in acidic solution to the corresponding ketones **4** (see reaction 1). The hydrolysis of the related alkylidene cyanamides **3a** has been reported to be catalyzed by silver ion.[4]

From the crude reaction product between cyclohexene and *o*-nitrobenzenesulfonyl azide, in which the imide **7** was the major product as judged by the ir and nmr spectra, an isomeric compound could be isolated in 13% yield to which, on the base of spectral evidence, the enamide structure **11b** was ascribed. The ir spectrum



11a, Ar = *o*-$NO_2C_6H_4$; *n* = 3 **12**, Ar = *m*-$NO_2C_6H_4$; *n* = 3
b, *n* = 4 **13**, Ar = *p*-$CH_3C_6H_4$; *n* = 6
c, *n* = 5
d, *n* = 6

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(6) (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Wiley, New York, N. Y., 1966, p 147 ff.
(7) L. J. Bellamy, "Advances in Infrared Group Frequencies," Methuen and Co., London, 1968, p 132 ff.
(8) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, New York, N. Y., 1969, p 226.
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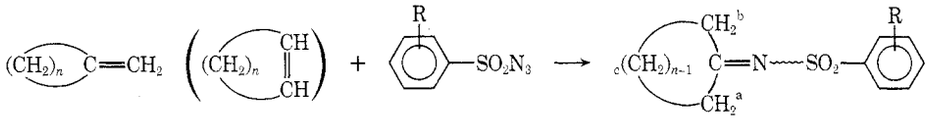
TABLE I

o-NITROBENZENESULFONIMIDOCYCLOALKANES PREPARED FROM METHYLENECYCLOALKANES AND CYCLOALKENES



				Reaction time[a] at	Ir (CH_2Cl_2), cm^{-1}	Nmr ($CDCl_3$)[c]		
n	R	Product	Yield,[a,b] %	60°, days	ν(C=N)	H_a[d]	H_b[d]	H_c
3	*o*-NO_2	**5**	99 (100)	4 (1)	1630	2.99 (t)[e]	2.62 (t)[e]	1.57-2.3 (m)
3	*m*-NO_2	**6**	(100)	(1)	1625	3.02 (t)[e]	2.58 (t)[e]	1.57-2.3 (m)
4	*o*-NO_2	**7**	99 (99.5)	3 (8)	1620	2.99 (m)	2.44 (m)	1.07-2.2 (m)
5	*o*-NO_2	**8**	98[f] (100)[f]	6 (2)	1605	3.10 (m)	2.67 (m)	1.40-2.05 (m)
6	*o*-NO_2	**9**	100 (99)	2 (2)	1595	3.33-2.34 (m)		1.56 (m), 1.96 (m)
6	*p*-CH_3	**10**	(100)	(1)	1598	3.03 (m)	2.47 (m)	1.10-2.24 (m)

[a] Yields and reaction time in parentheses refer to the starting olefins in parentheses. [b] Crude weight yields (with respect to the azide component if an excess of olefin was used). Some products contain small amounts of the isomeric enamide **11-13** (see Discussion). [c] Chemical shifts δ with respect to tetramethylsilane as internal standard. [d] See discussion for assignment of H_a and H_b with respect to syn and anti. [e] Major splitting pattern in actually higher multiplet. [f] The crude material contains up to 13% of the isomeric enamide **11b**.

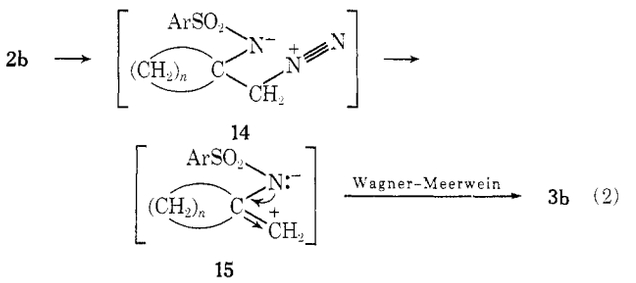
shows a sharp band at 3390 cm^{-1} corresponding to the N–H stretch. There are medium weak bands at 1674 and 1591 cm^{-1} corresponding to the double bond in a monosubstituted cyclohexene and the amide II band.[6] The nmr spectrum shows a pair of one-proton singlets at 6.42 and 5.61 ppm with half-height widths of 6.4 and 7.6 Hz, respectively. The lower field proton is exchangeable with D_2O and can therefore be assigned to the N–H proton. The four α- and four β-methylene protons absorb in two separate signals at 2.00 and 1.52 ppm.

All other crude imide products **5**, **6**, and **8–10** also contained small amounts of the isomeric enamides **11–13**, as judged by their ir and nmr spectra, although the percentage was in all cases much smaller than in the cyclohexane case **7**. No effort was made to isolate these enamides. The imide–enamide equilibrium is quite slow in the cases studied, since the pure compounds in $CDCl_3$ solution at room temperature are stable for weeks.

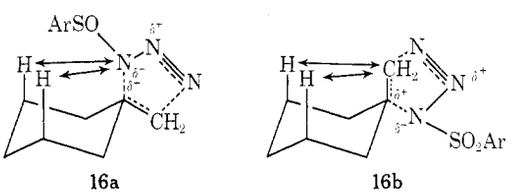
Discussion

While strong electron-withdrawing substituents (R = NC–, ArCO–, ROCO–, picryl, $ArSO_2$–) on the azide facilitate the 1,3-dipolar addition to electron-rich olefins, the resulting triazolines turn out to be relatively unstable and lose nitrogen spontaneously or with slight heating.[2-4,10-14] For this reason the intermediate 1-arenesulfonyl-Δ^2-triazolines **2b** were, analogously to the corresponding 1-cyano compounds **2a**, not isolable.

The probable reaction mechanism proceeds *via* the betaine intermediates **14** and **15** as depicted in reaction 2.[2-4,11-14] The ring-enlargement step is closely related to the classic Demjanov–Tiffeneau reaction.[5] In the case of the reaction with cycloalkenes a hydrogen shift takes the place of the Wagner–Meerwein shift.



With respect to reaction rates methylenecyclohexene proved to be by far the slowest reacting among the exocyclic olefins. A possible explanation is that the transition state probably looks like **16a** or **16b** with



severe 1,3-diaxial interactions. Such 1,3-diaxial interactions are typical of the rigid cyclohexane chair and comparatively absent in other cycloalkanes.

Transition state **16b** resulting from equatorial attack by the bulky azide reagent appears to be the less unfavorable alternative. Among the cycloalkenes cyclohexene was the slowest reacting olefin as has been observed before in cycloadditions with other azides.[13,15-18] No evidence for any aziridine formation[4,14,18] was observed in any of the reported reactions.[19]

Experimental Section

General Procedures.—Melting points were taken on a Fisher–Johns melting point apparatus and are corrected. Ir spectra were taken on a Perkin-Elmer 137 sodium chloride spectrophotometer. Methylene chloride was used as solvent. Gas

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(19) The spirocyclic aziridines under consideration would be derived from the betaine intermediates **14** or **15**. The methylene group of the aziridine ring is expected to absorb at *ca.* δ 2.5–3 ppm.[4,14]

chromatography was done on a Varian Model 90P gas chromatograph. Most of the work was done with a 8-ft column of 10% QF-1 on Gas-Chrom Q. Nmr spectra were taken on a Varian T-60 nmr spectrometer. Tetramethylsilane was used as internal standard. The elemental analyses were performed by the Hoffmann-La Roche Corp., Nutley, N. J., to whom we would like to extend our thanks.

The methylenecycloalkanes not commercially available were prepared from the corresponding ketones by the Wittig reaction modification of Corey and coworkers.[20] The aromatic sulfonyl azides were prepared according to the procedure of Leffler and Tsuno.[21]

General Procedure for Reaction with Aromatic Sulfonyl Azide.—The azide and olefin (1–2 equiv) were combined in a sealed glass pressure tube (Fischer and Porter Co.) and immersed in an oil bath of 60° and protected from light. After all the contents had become liquid, whereby frequently two phases were formed, the contents were stirred magnetically for the time period indicated in Table I, *i.e.*, until an ir spectroscopic analysis indicated that all azide had reacted. The excess olefin was removed *in vacuo* until the sample reached constant weight. Alternatively the reaction may be conducted in acetonitrile as a solvent.

***o*-Nitrobenzenesulfonimidocyclopentane** (**5**) formed as slightly yellowish crystals from absolute ethanol, mp 91–94°.

Anal. Calcd for $C_{11}H_{12}N_2O_4S$: C, 49.25; H, 4.51; N, 10.44; S, 11.95. Found: C, 49.13; H, 4.60; N, 10.28; S, 11.37.

***m*-Nitrobenzenesulfonimidocyclopentane** (**6**).—Imide **6** was obtained as slightly yellowish oil, which according to ir and nmr spectra (see Table I) was practically pure.

Anal. Calcd for $C_{11}H_{12}N_2O_4S$: C, 49.25; H, 4.51; N, 10.44. Found: C, 49.51; H, 4.66; N, 10.65.

***o*-Nitrobenzenesulfonamidocyclohexane** (**7**).—The crude reaction mixture obtained was recrystallized from ether whereupon 69% of crystalline **7**, mp 72–74°, was obtained. This was taken up in warm benzene and filtrated from impurities and the benzene taken off *in vacuo*. The residual oil was treated with ether and a seed crystal whereupon pure imide **7** crystallized as slightly yellowish crystals, mp 73–74°.

Anal. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.05; H, 5.00; N, 9.92; S, 11.36. Found: C, 51.02; H, 4.90; N, 9.86; S, 11.36.

***o*-Nitrobenzenesulfonimidocycloheptane** (**8**) formed as slightly yellowish crystals from benzene–petroleum ether, mp 90–90.8°.

Anal. Calcd for $C_{13}H_{16}N_2O_4S$: C, 52.69; H, 5.44; N, 9.45; S, 10.82. Found: C, 52.70; H, 5.42; N, 9.33; S, 10.86.

***o*-Nitrobenzenesulfonimidocyclooctane** (**9**) formed as slightly yellowish crystals from isopropyl alcohol, mp 95.5–97°.

Anal. Calcd for $C_{14}H_{18}N_2O_4S$: C, 54.18; H, 5.85, N, 9.03; S, 10.33. Found: C, 53.96; H, 5.79; N, 8.93; S, 10.13.

***p*-Toluenesulfonimidocyclooctane** (**10**). **A.**—A mixture of tosyl azide (0.59 g, 3.0 mmol) and cyclooctene (1.65, g, 15 mmol) was kept for 5 weeks at room temperature in a tightly stoppered reaction flask with occasional release of pressure. Removal of the olefin *in vacuo* until constancy of weight afforded 892 mg (100%) of a colorless oil. According to the ir and nmr spectra (see Table I) this consisted of practically pure title compound **10**.

B.—The same compound was obtained in the same yield by heating the two reagents in a sealed pressure tube at 65° for 24 hr.

Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.58; N, 5.01. Found: C, 64.18; H, 7.66; N, 4.82.

***o*-Nitrobenzenesulfonamido-1-cyclohexene** (**11b**).—A mixture of *o*-nitrobenzenesulfonyl azide (3.42 g, 15 mmol) and cyclohexene (2.46 g, 30 mmol) was treated as described in the general procedure, for 8 days at 60°. Evaporation *in vacuo* yielded 4.20 g of a yellowish oil, which was triturated with five 20-ml portions of petroleum ether. After addition of *ca.* 30 ml of cold ether crystals formed. Filtration and washing with ether afforded 553 mg (13%) of yellowish crystals, mp 99–107°. Repeated recrystallization from benzene–petroleum ether raised the melting point to 105–107°: ir (CH_2Cl_2) 3390 (N–H), 2905 (C–H), 1674 (C=C), 1591 (amide II), 1538 (NO_2, asym), 1361 (NO_2, sym), 1328 (SO_2, asym), 1171 cm^{-1} (SO_2, sym); nmr δ ($CDCl_3$) 8.08 (m, 1, arom), 7.80 (m, 3, arom), 6.42 (s, 1, N–H), 5.61 (m, 1, >C=C—H), 2.00 (m, 4, α-CH_2), 1.52 (m, 4, β-CH_2).

Anal. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.05; H, 5.00; N, 9.92; S, 11.36. Found: C, 50.95; H, 4.95; N, 9.78; S, 11.24.

General Procedure for Hydrolysis.—The arenesulfonimidocycloalkane was treated with an excess of cold 2 *N* hydrochloric acid. The mixture was kept at room temperature for 24 hr with occasional shaking, and the ketone then was isolated according to methods A or B.

A.—The mixture was steam distilled. The distillate was extracted with ether, and the ethereal extracts were dried with magnesium sulfate. After filtration, evaporation of the ether yielded the ketone. For low-boiling ketones the ether was removed through a fractionating column.

B.—The mixture was made alkaline with 2 *N* sodium hydroxide and then extracted three times with ether. The subsequent work-up was as described under method A.

Yields for the hydrolysis under methods A or B were better than 80%. The resulting ketones were identified by their ir and nmr spectra and gas chromatographic retention times.

Acknowledgment.—We wish to thank the Rutgers Research Council for financial support.

Registry No.—**1** (n = 3), 1120-56-5; **1** (n = 4), 1528-30-9; **1** (n = 5), 1192-37-6; **1** (n = 6), 2505-03-5; **5**, 41700-94-1; **6**, 41700-95-2; **7**, 41700-96-3; **8**, 41700-97-4; **9**, 41700-98-5; **10**, 41700-99-6; **11b**, 41701-00-2; cyclopentene, 142-29-0; cyclohexene, 110-83-8; cycloheptene, 628-92-2; cyclooctene, 931-88-4; *o*-nitrobenzenesulfonyl azide, 6655-31-8; *m*-nitrobenzenesulfonyl azide, 6647-85-4; tosyl azide, 941-55-9.

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