|                              | ,        | eaction condit             | ion     |  | optically active a            | alcohol         |       |                     |
|------------------------------|----------|----------------------------|---------|--|-------------------------------|-----------------|-------|---------------------|
|                              | reagent, |                            |         | and a second |                               | % e             | e     | he                  |
| ketone                       | equiv    | temp, $^{\circ}\mathrm{C}$ | time    | % yield  | $[\alpha]_{\mathbf{D}}$ , deg | obsd, %         | cor % | config <sup>o</sup> |
| 3-butyn-2-one                | 1.4      | 25                         | 4 h     | 80°  | +37.7 (c 2.3, dioxane)        | 73 <i>d</i>     | 62    |                     |
| 4-phenvl-3-butyn-2-one       | 1.4      | 25                         | 4 h     | $95^{b}$   | +69.9 (neat)                  | $96.5^{e}$      | 105   |                     |
| 4-methyl-1-pentyn-3-one      | 1.4      | 25                         | 8-12 h  | 87 <i>a</i>  | +14.6 (c 2, dioxane)          | $91^{f}$        | 66    |                     |
| trans-4-phenyl-3-buten-3-one | 1.4      | 25                         | 10 days | $80^{b}$   | -22.3 (c 5.2, CHCl,)          | 89\$            | 26    | S                   |
| 1-acetyl-1-cyclohexene       | 1.4      | 25                         | 12 days | 00 <i>a</i>  | -7.47 (c 4.15, CHCI,          | $29^{h}$        | 64    | S                   |
| acetophenone                 | 2        | 25                         | 7 days  | $68^{b}$   | -33.4 (neat)                  | 78'             | 85    | S                   |
| 2-butanone                   | 2        | 25                         | 10 days | 90 <i>a</i>  | -5.4 (neat)                   | $40^{j}$        | 43    | S                   |
| 3-methyl-2-butanone          | 7        | 25                         | 14 days | $100^{a} 78^{b}$   | +3.06 (neat)                  | $57^{k}$        | 62    | S                   |
| 3,3-dimethyl-2-butanone      | 2        | 25                         | 40 days | $40^{b.c}$   | +0.050 (neat)                 | $0.6^{l}$       | 0.7   | S                   |
| 2-octanone                   | 2        | 25                         | 7 days  | $65^{b}$   | +4.12 (neat)                  | 44 m            | 48    | S                   |
| ethyl pyruvate               | 1.4      | 25                         | 4 h     | $50^{b}$   | -8.83 (neat)                  | $16^n$          | 83    | S                   |
| ethyl pyruvate               | 1.4      | 0                          | 24 h    | $50^{b}$   | -9.43 (neat)                  | 82 <sup>n</sup> | 89    | S                   |

## [2 + 2] Cycloadditions of Ynamines with $\alpha,\beta$ -Unsaturated Sulfones: Approach to Versatile Four-Membered Carbocyclic Intermediates<sup>1</sup>

Summary: The interaction of ynamines with various  $\alpha$ ,- $\beta$ -unsaturated sulfones, such as 1-alkenyl, 1-alkynyl, or 1,3-alkadienyl sulfones, leads to the ready formation of the vicinally amino- and sulfonyl-substituted cyclobuta ring in a regiospecific manner. The resulting cyclobutenamines can be hydrolyzed to the corresponding  $\alpha$ -sulfonylcyclobutanones, which can, in turn, be alkylated or desulfonylated to yield substituted cyclobutanones.

Sir: Vinylic sulfones have been recognized recently as versatile synthons, both for the construction of three- and six-membered carbocycles<sup>2,3</sup> and for the generation of ( $\alpha$ -sulfonylvinyl)lithium<sup>4</sup> and ( $\alpha$ -sulfonylalkyl)lithium<sup>5</sup> reagents. As a dienophile in [4 + 2] cycloadditions, phenyl vinyl sulfone has been shown to an excellent ethylene equivalent. The resulting cyclohexenyl sulfones can be sequentially alkylated and desulfonylated to provide 4-alkyl-1-cyclohexenes selectively and in high yield.<sup>3</sup>

In our further studies on the utility of vinylic sulfones in synthesis,<sup>1</sup> we have now found that a wide variety of  $\alpha,\beta$ -unsaturated sulfones undergo [2 + 2] cycloaddition reactions with ynamines to form four-membered carbocycles readily. Although thiete 1,1-dioxide (1) had previously been reported to undergo [4 + 2] and [2 + 2] cycloadditions with enamines and ynamines,<sup>6</sup> we have found that such [2 + 2] cycloadditions are not restricted to strained vinylic sulfones, such as 1, but are general for vinylic, acetylenic, and 1,3-dienylic sulfones (eq 1). As

vinylic sulfone participants, phenyl vinyl sulfone (2a), phenyl (E)- $\beta$ -styryl sulfone (2b), (E)-(methoxycarbonyl)ethenyl phenyl sulfone (2c), benzothiophene 1,1-dioxide (2d), and 2-sulfolene (2e) reacted readily with the ynamines 3, N,N-diethyl-1-propynylamine (3a) and N-ethynylmorpholine (3b). Depending on the specific sulfone, the cycloaddition proceeded between 25 and 80 °C, either in methylene chloride solution or without solvent. The acetylenic sulfones, phenyl 1-propynyl sulfone (2f) and phenyl phenylethynyl sulfone (2g), reacted with 3a even more readily than their vinylic counterparts. Finally, it is noteworthy that 1,3-butadien-1-yl phenyl sulfone (5)

Part 4 of the series "Sulfone Reagents in Organic Synthesis"; for previous parts, see J. Org. Chem. 1979, 44, 3277, 3279; 1980, 45, 4534.
Eisch, J. J.; Galle, J. E. J. Org. Chem. 1979, 44, 3277.

<sup>(3)</sup> Carr, R. V. C.; Paquette, L. A. J. Am. Chem. Soc. 1980, 102, 853.

<sup>(4)</sup> Eisch, J. J.; Galle, J. E. J. Org. Chem. 1979, 44, 3279.

<sup>(5)</sup> Eisch, J. J.; Galle, J. E. J. Org. Chem. 1980, 45, 4534.

<sup>(6)</sup> Paquette, L. A.; Houser, R. W.; Rosen, M. J. Org. Chem. 1970, 35, 905.

underwent a [2 + 2] rather than a [4 + 2] cycloaddition with 3a at the olefinic bond remote from the sulfonyl group (eq 2).



The adducts, which are quantitatively formed at 25-50 °C (4 and 6), give NMR spectra in excellent accord with the assigned structures. However, for those adducts formed at 50-100 °C, changes in their NMR spectra indicate that a thermal ring opening of the cyclobutene occurs at a rate comparable to that of the cyclobutene occurs at a rate comparable to that of the cyclobutene (2b) and 3a, for example, exhibited an NMR spectrum resembling a mixture of 4b and the butadiene resulting from ring opening.<sup>7</sup>

The structure of the adducts was further verified in most cases by hydrolysis with dilute acid and by isolation of the expected cyclobutanone (eq 3). The cyclobutanones (7),



which were formed as a mixture of the expected geometrical isomers when R and  $R' \neq H$ , were isolated in good to excellent yields. These ketones displayed carbonyl absorptions at 1785 cm<sup>-1</sup> and appropriate <sup>1</sup>H NMR spectra. The hydrolysis of cycloadduct 6, which was cleanly formed from the dienyl sulfone 5 and ynamine 3a, underwent hydrolysis with rearrangement to form approximately a 1:1 mixture of *E* and *Z* isomers of 9 (eq 4). On the other hand, the quasi-cyclobutadienes formed from the alkynyl sulfones, 2f and 2g, and ynamine 3a exhibited <sup>1</sup>H NMR spectra in excellent agreement with the presence of [2 +



2] cycloadducts, but hydrolysis of the compounds yielded products whose structures still remain to be determined.

These cycloadditions with ynamines take place readily and regiospecifically with a wide variety of open-chain and cyclic (2d)  $\alpha,\beta$ -unsaturated sulfones, thereby providing a facile entree to monocyclic or fused (10) cyclobutanones (eq 5).<sup>8</sup> Furthermore, such sulfonylcyclobutanones con-

(7) For an excellent review of the chemistry of ynamines, in general, and the ring-opening tendency of certain cyclobutenes, in particular, see Ficini, J. Tetrahedron, 1976, 32, 1449 (specifically pp 1464-1475).



stitute versatile intermediates for subsequent functionalization. Excellent methods have been developed for alkylating  $\alpha$  to such sulfonyl groups<sup>3</sup> and for removing sulfonyl groups adjacent to carbonyl linkages.<sup>9</sup> Hence, vinyl sulfones should prove of great value for the synthesis of substituted cyclobutanones and related systems.

Some typical procedures for the cycloaddition and the hydrolysis of cycloadducts are as follows.

a. Benzothiophene 1,1-Dioxide (2d). Under an argon atmosphere, a solution of 2.5 g (15 mmol) of 2d dissolved in 15 mL of chloroform was allowed to react with 3.1 mL (20 mmol) of 3a over a 96-h period. By spectral examination the reaction was shown to be complete and then the excess of 3a was removed in vacuo. The cycloadduct 4d had the following <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>): 0.85 (6 H, d), 3.95 (1 H, m), 4.45 (4 H, t), 4.95 (1 H, d of d), 7.2-7.7 (4 H, m).

Hydrolysis of 4d dissolved in ether was accomplished in essentially quantitative yield with dilute HCl. The resulting ketone, 1,2-dihydro-2-oxo-1-methylcyclobuta-[b]benzothiophene 3,3-dioxide, melted at 131-133 °C: NMR (CDCl<sub>3</sub>)  $\delta$  0.85 (3 H, d), 3.9 (1 H, m), 4.45 (1 H, t), 4.95 (1 H, d of d), 7.2-7.7 (4 H, m); IR (mineral oil) 1780 cm<sup>-1</sup> (C=O).

b. Phenyl Vinyl Sulfone (2a). In a similar manner, 2.0 g (12 mmol) of 2a and 1.5 g (13 mmol) of 3a gave a quantitative yield of cycloadduct 4a after 48 h at 25 °C. After removal of excess 3a in vacuo, 4a showed the following <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>):  $\delta$  0.9–1.3 (6 H, t), 1.6 (3 H, s), 2.0–2.2 (2 H, m), 2.8–3.5 (4 H, m), 4.15–4.3 (1 H, m), 7.4–8.1 (5 H, m). Hydrolysis with 0.1 N HCl in an ether-water mixture (30:20 mL) and usual workup gave almost 100% of 7a. Recrystallization from a benzenehexane pair twice gave 84% of 7a, 2-methyl-4-(phenylsulfonyl)cyclobutanone, as a 55:45 mixture of stereoisomers: mp 65–70 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.05 (d, 0.45 H), 1.2 (d, 0.55 H), 2.0–3.8 (3 H, br m), 4.5–4.9 (1 H, m), 7.4–7.9 (5 H, m); IR (mineral oil) 1785 cm<sup>-1</sup> (C=O).

c. Phenyl 1-Propynyl Sulfone (2f). A noticeable exotherm resulted from admixing 1.0 g (9 mmol) of 2f with 1.6 g (9 mmol) of 3a. After 48 h at 25 °C and removal of volatiles in vacuo, the cycloadduct 4f was shown by NMR spectroscopy to have formed quantitatively (CDCl<sub>3</sub>):  $\delta$ 0.7-1.0 (6 H, t), 1.8 (3 H, s), 2.2 (3 H, s), 2.8-3.4 (4 H, m), 7.2-7.8 (5 H, m).

d. 1,3-Butadien-1-yl Phenyl Sulfone (5).<sup>10</sup> Admix-

<sup>(8)</sup> Assignment of the exo configuration to the methyl group in 10 is based upon the <sup>1</sup>H coupling constant of the proton  $\alpha$  to the C=O group with the adjacent bridgehead proton: J = 6.8 Hz. The cis bridgehead protons have J = 8.0 Hz. Such cis and trans vicinal proton coupling constants are typical for cyclobutanones: Kagan, H. B. "Stereochemistry: Fundamentals and Methods"; Georg Thieme Verlag, Stuttgart, 1977; Vol. 1 p. 85

p 85.
(9) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. Tetrahedron Lett. 1976, 3857.

| Table I. | Cycloadditions | of Ynamines | with $\alpha, \beta$ . | Unsaturated | Sulfones |
|----------|----------------|-------------|------------------------|-------------|----------|
|----------|----------------|-------------|------------------------|-------------|----------|

| sulfone 2  | ynamine<br>3 | % yield of<br>adduct 4 | % yield of<br>ketone 7 | mp, <sup>a</sup> °C |
|--|--------------|------------------------|------------------------|---------------------|
| phenyl vinyl sulfone (2a)                        | 3a           | 95                     | 84                     | 65-70 <sup>b</sup>  |
| phenyl (E)- $\beta$ -styryl sulfone (2b)         | 3a           | 60 <i>°</i>            |                        |                     |
| benzothiophene 1,1-dioxide (2d)                  | 3a           | $100^{d}$              | 95                     | 131-133             |
| (E)-(methoxycarbonyl)ethenyl phenyl sulfone (2c) | 3a           | 100 <sup>d,e</sup>     |                        |                     |
| 2-sulfolene (2e)                                 | 3a           | 35 <i>f</i>            |                        |                     |
| phenyl 1-propynyl sulfone (2f)                   | 3a           | 100 <sup>d,e</sup>     |                        |                     |
| 1,3-butadien-1-yl phenyl sulfone (5)             | 3a           | 90-100                 | 72                     | 82-85               |
| phenyl vinyl sulfone (2a)                        | 3b           | 75                     | 64                     | (oil) <sup>g</sup>  |

<sup>a</sup> The cycloadducts 4 were characterized by <sup>1</sup>H NMR, IR, and MS; the isolated ketones gave satisfactory spectral and elemental analyses. <sup>b</sup> A cis-trans mixture of 7 results. <sup>c</sup> At 100 °C cycloaddition and ring opening of 4 occurred. <sup>d</sup> By NMR analysis no starting sulfone was discernible after reaction. <sup>e</sup> Cycloaddition occurs exothermically at 25 °C, but attempted hydrolysis to 7 took an undetermined course. <sup>f</sup> Cycloaddition and isomerization to 3-sulfolene were competitive above 60 °C. <sup>g</sup> This product was purified by column chromatography.

ture of 1.0 g (5 mmol) of sulfone 5, either dissolved in 10 mL of methylene chloride or neat, with 0.97 mL (7 mmol) of ynamine 3a led to an exotherm after a few minutes. After standing several h, the solvent and excess ynamine were removed in vacuo at 50 °C and 0.1 mmHg. For the neat reaction the starting sulfone was consumed; in  $CH_2Cl_2$  medium, 10% of 5 remained. When acetonitrile was used as a solvent, 40% of 5 was unconsumed. Product 6: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.06 (6 H, m, J = 7 Hz), 1.62 (3 H, sl br), 2.25–2.6 (2 H, m), 2.85 (4 H, g, J = 7 Hz), 3.30 (1 H, m), 6.46 (1 H, d, J = 15 Hz), 7.1 (1 H, d of d, J = 8, 15 Hz), 7.66 (3 H, m), 7.9 (2 H, m); IR (neat) sharp, intense absorptions at 1605 and 1660 cm<sup>-1</sup>.

Hydrolysis of product 6 from a 30-mmol run was carried out in 30 mL or ether with 3 mL of concentrated HCl for 1 h. The ether layer was washed with water, dried with anhydrous MgSO<sub>4</sub>, and evaporated to yield isomers of 9; column chromatography on silica gel and elution with an ether-hexane pair (1:1) gave a colorless solid, which was recrystallized from methanol to give one isomer of 9, mp 82-85 °C, presumably having the C=O and SO<sub>2</sub>Ph groups E: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  2.02 (2 H, d, J = 7 Hz), 2.59 (1 H, m), 3.0-4.2 (2 H, m), 4.46 (2 H, d, J = 7 Hz), 6.56 (1 H, m), 7.8-8.3 (5 H, m); IR (mineral oil) 1750 (C=O), 1680 (C=C) cm<sup>-1</sup>.

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## $\beta'$ Metalation of $\alpha,\beta$ -Unsaturated Tertiary Amides

Summary: Novel  $\beta'$  metalations of the  $\alpha,\beta$ -unsaturated tertiary amides N,N-diisopropyl-1-cyclohexenecarboxamide (3), (E)-N,N-diisopropyl-2-methyl-2-butenamide (7), and N,N-diisopropyl-6-(trimethylsilyl)-1-cyclohexenecarboxamide (10) are reported. Additions of the  $\beta'$ lithio- $\alpha,\beta$ -unsaturated tertiary amides 4, 8, and 11 to a variety of electrophiles, including in the case of 8 subsequent formation of five-membered rings, illustrate the value of this approach for achieving substitution at the  $\beta'$  position of  $\alpha,\beta$ -unsaturated carboxylic acid derivatives.

Sir: Recent communications which report that  $\alpha,\beta$ -unsaturated secondary amides and thioamides react with 2 equiv of alkyllithiums to give a species which is dilithiated at the nitrogen and  $\beta'$ -carbon provide the basis for a newapproach to  $\beta'$  substitution of  $\alpha,\beta$ -unsaturated carboxylic acid derivatives.<sup>12</sup> In view of the interest in the novel  $\beta'$ -lithiomethacrylate synthon 1, we now communicate our observation that diisopropyl tertiary amides bearing potentially acidic  $\beta$ - and  $\gamma$ -hydrogens undergo  $\beta'$  metalation at low temperatures to give stable  $\beta'$ -lithio- $\alpha,\beta$ -unsaturated amides 2 which can subsequently react with a variety of electrophiles.<sup>3</sup>



Addition of N,N-diisopropyl-1-cyclohexenecarboxamide (3) to 1.1 equiv of sec-butyllithium-tetramethylethylenediamine in tetrahydrofuran at -78 °C followed by addition of an electrophile leads to  $\beta'$ -substituted amides 5 via the substituted allyllithium 4. As shown in Table I, deuteration, alkylation, silylation, sulfenylation, oxidation, and condensation with carbonyl compounds proceed in useful yields. Products resulting from  $\beta$ - or  $\gamma$ -hydrogen removal are not observed; however, reaction of 4 with dimethylformamide gives the conjugated product 6 in which isomerization of the double bond has occurred. A typical experimental description is given at the end of this report.

<sup>(10)</sup> Sulfone 5 was prepared from 1,3-butadiene in three steps: (a) 1,3-butadiene and PhSO<sub>2</sub>Cl at -78 °C in CH<sub>2</sub>Cl<sub>2</sub> with CuCl and Et<sub>3</sub>NHCl yielded 1-chloro-4-(phenylsulfonyl)-2-butene; (b) treatment of the chloro compound with Et<sub>3</sub>N and Me<sub>2</sub>NH provided 1-amino-4-(phenylsulfonyl)-2-butene, which was a convenient, storable source of 5; (c) quaternization of the amino compound with MeI in MeOH and treatment of the resulting quaternary salt with aqueous NaOH liberate 5.

<sup>(1)</sup> For cases in which potentially acidic  $\beta$ - and  $\gamma$ -hydrogens are present, see: (a) Beak, P.; Kempf, D. J. J. Am. Chem. Soc. 1980, 102, 4550. (b) Tamaru, Y.; Kagotani, M.; Yoshida, Z. Tetrahedron Lett. 1981, 3409. (c) Tamaru, Y.; Kagotani, M.; Furukawa, Y.; Amino, Y.; Yoshida, Z. Ibid. 1981, 3413. For cases in which only  $\beta$ -hydrogens are present, see: (a) Fitt, J. J.; Gschwend, H. W. J. Org. Chem. 1980, 45, 4257. (b) Tamaka, K.; Nozaki, Y.; Tamura, N.; Tanikaga, R.; Kaji, A. Chem. Lett. 1980, 1567. (2) For  $\beta'$ -certhanionic methorcruic acid synthoms see: (a) Löffler A.:

<sup>(2)</sup> For  $\beta$ -carbanionic methacrylic acid synthons, see: (a) Löffler, A.; Pratt, R. D.; Pucknat, J.; Gelbard, G.; Dreiding, A. S. Chimia 1969, 23, 413. (b) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. J. Org. Chem. 1975, 40, 593. (c) Carlson, R. M.; Oyler, A. R. Ibid. 1976, 41, 4065. (d) Carlson, R. M. Tetrahedron Lett. 1978, 111.

<sup>(3)</sup> For a report of the transient  $\beta'$  metalation of the tertiary amide 18, see: Bannwarth, W.; Eidenschink, R.; Kauffman, T. Angew. Chem., Int. Ed. Engl. 1974, 13, 468.