Synthesis of 2-[[(p-Nitrophenyl)sulfonyl]oxy] 3-Keto Esters from 3-Keto Esters and (p-Nitrophenyl)sulfonyl Peroxide

Robert V. Hoffman,* Anna Lee Wilson, and Hwa-Ok Kim

Department of Chemistry, Box 3C, New Mexico State University, Las Cruces, New Mexico 88003-0001

Received June 22, 1989

The preparation of 2-[[(p-nitrophenyl)sulfonyl]oxy] β-keto esters from β-keto esters and (p-nitrophenyl)sulfonyl peroxide is described. High yields are obtained for a variety of structural types. One β-diketone was also used and gave comparable success. These materials can serve as precursors to 2-nosyl ketones by decarboxylation, 3-hydroxy-2-nosyl esters by reduction, and tricarbonyl compounds by reductive elimination.

There has been a great deal of recent interest in the preparation and reactions of 2-(sulfonyloxy) carbonyl compounds. This interest stems from the fact that these materials have a more simple and selective reactivity pattern than their 2-halo carbonyl analogues. 2-[(Arylsulfonyl)oxy] ketones can be readily converted to 2-hydroxy ketals, 2-hydroxy ketones in high yields,[1] and reaction with amines such as morpholine and 1,2,3,4-tetrahydroisoquinoline gave 2-amino ketones, also in high yields.[1] 2-(Sulfonyloxy) esters have been used as reactive alkylating agents toward nucleophiles.[2]

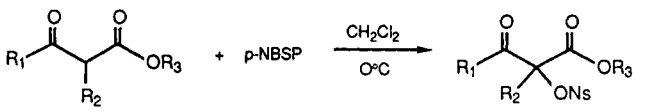
Hypervalent iodine reagents [hydroxy(tosyloxy)iodo]-benzene (1) and [hydroxy(mesyloxy)iodo]benzene (2) have been used to convert simple ketones and β-dicarbonyl compounds directly to 2-(tosyloxy) and 2-(mesyloxy) derivatives.[3] Silyl enol ether derivatives of ketones and esters also give 2-(tosyloxy) and 2-(mesyloxy) carbonyl products with 1 and 2.[4a] Very recently 2-(triflyloxy) ketones have been prepared from silyl enol ethers and the triflate analogue of 1.[4b]

We have reported that enol ester, silyl enol ether, and enamine derivatives of ketones can be converted to 2-[[(p-nitrophenyl)sulfonyl]oxy] and 2-[[[m-(trifluoromethyl)phenyl]sulfonyl]oxy] ketones with the corresponding bis(arylsulfonyl) peroxide, 3 and 4, respectively.[5] Ketene silyl acetals are also readily converted to 2-[[(p-nitrophenyl)sulfonyl]oxy] esters with 3 (pNBSP).[6]

$C_6H_5I(OH)X$ $(YC_6H_4SO_2O)_2$
1: X = OTs 3: Y = p-NO_2
2: X = OMS 4: Y = m-CF_3

The excellent leaving ability of the p-nitrobenzene sulfonate group (nosylate, ONs) results in very clean transformations of 2-(nosyloxy) ketones[1a] and esters.[7] It was thus of interest to prepare 2-(nosyloxy) derivatives of β-keto esters since these highly functionalized compounds might serve as useful precursors for other 1,2,3-functionalized molecules.

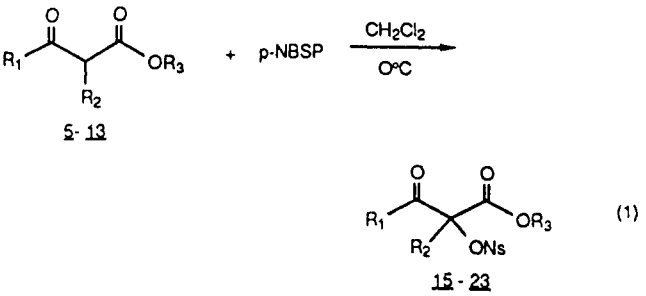
Table I. Yields of 2-[[(p-Nitrophenyl)sulfonyl]oxy] β-Keto Esters from the Reaction of β-Keto Esters and pNBSP



entry	substrate	prod.	mp °C	yield,[a] %
1	5, R_1 = CH_3, R_2 = H, R_3 = CH_3	15	86–88	62–65
2	6, R_1 = CH_3, R_2 = H, R_3 = Et	16	84–86	56–57
3	7, R_1 = i-Pr, R_2 = H, R_3 = Et	17	70–72	61–67
4	8, R_1 = CH_3, R_2 = H, R_3 = $CH_2CH_2OCH_3$	18	67–69	51–67
5	9, R_1 = CH_3, R_2 = H, R_3 = t-Bu	19	83–85	46–51
6	10, R_1 = C_6H_5, R_2 = H, R_3 = Et	20	106–108	62–65
7	11, R_1 = 4-$NO_2C_6H_4$, R_2 = H, R_3 = Et	21	101–103	70–89
8	12, R_1 = CH_3, R_2 = CH_3, R_3 = Et	22	55–58	43–57
9	13, R_1, R_2 = $(CH_2)_3$, R_3 = Me	23	84–86	46–51
10	14, 2,4-pentanedione	24	83–85	67–72

[a] Percent yields of recrystallized, analytically pure products given as the range observed in several replicate experiments.

The reaction of β-keto esters with pNBSP (3) in dichloromethane at 0 °C proceeds smoothly to give good yields of 2-(nosyloxy)-β-keto esters 15–23 (Eq 1). The



5-13 15-23 (1)

yields in Table I, which are yields of recrystallized, analytically pure products, show that a range of structural variations in the β-keto ester have little influence on the yield. The crude yields of products were very good (80–95%). The crude products contained trace amounts of unreacted starting materials as the only detectable impurities, and thus they might be suitable for a variety of subsequent transformations without further purification. The purified products were stored for extended periods at 0 °C without loss of purity.

When *tert*-butyl ester 9 was reacted with pNBSP under the standard conditions, only low yields of 19 were obtained. Since p-nitrobenzene sulfonic acid is a byproduct of the reaction, it was reasoned that the high acidity of the reaction mixture caused loss of the *tert*-butyl group from

(1) (a) Hoffman, R. V.; Jankowski, B. J.; Carr, S. C. *J. Org. Chem.* **1986**, *51*, 130. (b) See also: Creary, X. *Acc. Chem. Res.* **1985**, *18*, 3.
(2) (a) Flynn, G. A.; Giroux, E. L.; Dage, R. C. *J. Am. Chem. Soc.* **1987**, *109*, 7914. (b) Urbach, H.; Henning, R. *Tetrahedron Lett.* **1984**, *25*, 1143. (c) Effenberger, F.; Burkard, U.; Willfahrt, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 65. (d) Shiosaki, K.; Fels, G.; Rappoport, H. *J. Org. Chem.* **1981**, *46*, 3230. (e) Vedejs, E.; Engler, D. A.; Mullins, M. *J. Org. Chem.* **1977**, *42*, 3109.
(3) (a) Lodaya, J. S.; Koser, G. F. *J. Org. Chem.* **1988**, *53*, 210. (b) Koser, G. F.; Relenyi, A. G.; Kalos, A. N.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1982**, *47*, 2487. (c) Koser, G. F.; Wettach, R. H. *J. Org. Chem.* **1977**, *42*, 1476.
(4) (a) Moriarty, R. M.; Penmasta, R.; Awasthi, A. K.; Epa, W. R.; Prakash, I. *J. Org. Chem.* **1989**, *54*, 1101. (b) Moriarty, R. M.; Epa, W. R.; Penmasta, R.; Awasthi, A. K. *Tetrahedron Lett.* **1989**, *30*, 667.
(5) (a) Hoffman, R. V. *Synthesis* **1985**, 760. (b) Hoffman, R. V.; Carr, C. S.; Jankowski, B. J. *J. Org. Chem.* **1985**, *50*, 5148. (c) Hoffman, R. V.; Carr, C. S. *Tetrahedron Lett.* **1986**, *27*, 5811.
(6) Hoffman, R. V.; Kim, H.-O. *J. Org. Chem.* **1988**, *53*, 3855.
(7) Kim, H.-O., unpublished results.

0022-3263/90/1955-1267$02.50/0

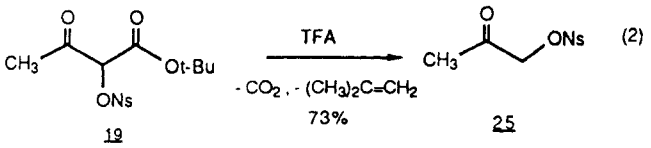
the product. When potassium carbonate (1 equiv) was suspended in the reaction mixture to neutralize the sulfonic acid, good yields of **19** were obtained (entry 5). 2,4-Pentanedione (**14**) was also converted to its 3-(nosyloxy) derivative **24** in good yield (entry 10), and it is expected that other 1,3-diketones should react similarly. Malonate esters failed to deliver products.

Electrophilic addition of **3** to the enol tautomers of dicarbonyl compounds accounts for product formation.[5b] It follows that β-keto esters and β-diketones, which contain significant amounts of enol tautomer at equilibrium, react readily with **3**. In contrast, β-diesters that enolize very little[8] do not react effectively with **3**. The same behavior was observed for enolizable ketones.[5b]

The starting keto esters **5**, **6**, **9**, and **10** are known to enolize to measurable extents (5–22%)[8] while *p*-nitrobenzoyl substrate **11** contains 49% of the enol tautomer at equilibrium in chloroform solution.[9] The 2-(nosyloxy)-β-keto esters **15–20**, **22**, and **23** gave signals in the ^{1}H NMR spectrum that corresponded only to the keto tautomers. Likewise, the IR spectra of these materials included only two carbonyl absorptions, one at higher frequency (1755–1780 cm^{-1}) due to the ester carbonyl and one at lower frequency (1735–1750 cm^{-1}, 1685 cm^{-1} for **20**) corresponding to the ketone carbonyl group. No evidence for a measurable amount of the enol tautomer was observed. The single exception was *p*-nitrophenyl compound **21**. Proton signals for the ethyl group of both the keto and enol forms were visible in the ^{1}H NMR spectrum in chloroform-*d* and acetone-d_6, and a third, weak carbonyl absorption at 1650 cm^{-1} was assigned as an enol carbonyl absorption. The extent of enolization in chloroform was found to be 32%.

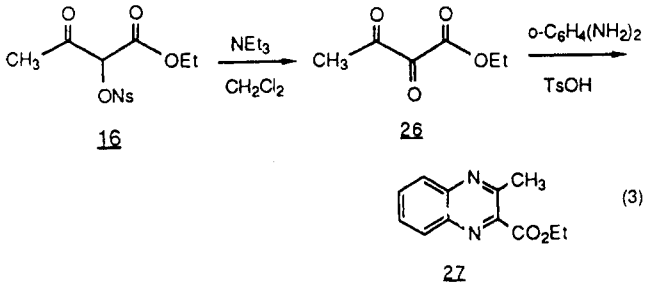
It is somewhat surprizing that attachment of a [(*p*-nitrophenyl)sulfonyl]oxy group to the 2-position of β-keto esters decreases enolization. Normally electron-withdrawing groups at the 2-position of β-keto esters increase the extent of enolization.[8a] While sulfonyloxy groups are good electron-withdrawing groups inductively,[10] Stang has shown that they are also capable of electron donation by resonance in unsaturated systems.[11] It is this electron-donating ability by resonance that apparently destabilizes the enol form and leads to a decrease in enolization when attached to the 2-position.

Preliminary results demonstrate the utility of 2-(nosyloxy)-β-keto esters as synthetic intermediates. Treatment of *tert*-butyl derivative **19** with trifluoroacetic acid in methylene chloride gave acetone derivative **25** (73%) (eq 2). Extension to 2-, 4-, and 2,4-alkylated *tert*-butyl β-keto esters permits the regiospecific synthesis of α-nosyloxy ketones without the need for regiospecifically prepared enol derivatives.[4,5c]



19 25 (2)

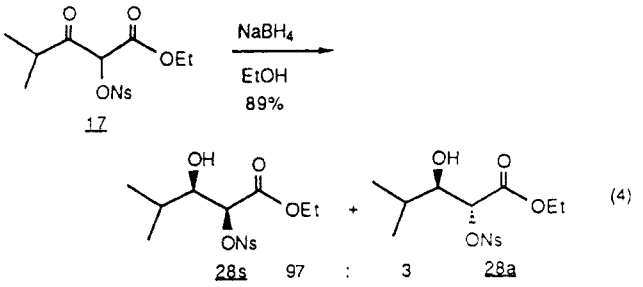
Treatment of **16** with triethylamine in dichloromethane led to the production of tricarbonyl product **26**, which was isolated as its quinoxaline derivative **27** (74%) (eq 3). Reductive elimination of *p*-nitrobenzenesulfinate from the anion of **16** could account for the production of **26**. Similar base-promoted reductive eliminations have been observed in some α-(sulfonyloxy) ketones,[1b] and Koser has observed that α-(tosyloxy) derivatives of β-diketones give triketones upon treatment with base.[12]



16 26 27 (3)

The elegant work of Wasserman has demonstrated the utility of tricarbonyl compounds in synthesis.[13] The preparation of these materials from 2-(nosyloxy)-β-keto esters offers a simple and practical alternative to singlet oxygen cleavage of enamino ketones,[14] ozonolysis of 2-iodonium β-keto esters,[15] ozonolysis of 2-phosphorous ylide derivatives of β-keto esters,[13b] hydrolysis of 2-oximino β-keto esters,[13e] or singlet oxygen cleavage of 2-phosphorous ylide derivatives of β-keto esters,[13f] which are methods in current use.

Reduction of isobutyryl derivative **17** with sodium borohydride in ethanol gives the 3-hydroxy-2-(nosyloxy) esters **28s** and **28a** (72%). The reduction was highly stereoselective, favoring the syn isomer 97:3 (eq 4). A variety of 1,2,3-functionalized materials are accessible by replacement of the nosylate group by nucleophiles.



17 28s 97 : 3 28a (4)

In summary, it has been shown that 2-(nosyloxy)-β-keto esters can be easily prepared from β-keto esters and pNBSP (**3**). These materials can serve as precursors to 2-(nosyloxy) ketones, 3-hydroxy-2-(nosyloxy) esters, and tricarbonyl compounds. Further transformations of these versatile compounds are presently under investigation.

Experimental Section

Melting points were obtained on a Mel Temp apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 283 spectrophotometer as potassium bromide disks. Proton NMR spectra were obtained on a Varian XL-200 instrument. Chemical shifts are reported for chloroform-*d* solution in ppm relative to

(8) (a) Rogers, M. T.; Burdett, J. L. *J. Am. Chem. Soc.* **1964**, *86*, 2105. (b) Rogers, M. T.; Burdett, J. L. *Can. J. Chem.* **1965**, *43*, 1516.
(9) Zhlegova, D. K.; Ershov, B. A. *Zh. Org. Khim.* **1974**, *10*, 18.
(10) Lambert, J. B.; Mark, H. W.; Holcomb, A. G.; Magyar, E. S. *Acc. Chem. Res.* **1979**, *12*, 317.
(11) Stang, P. J.; Anderson, A. G. *J. Org. Chem.* **1976**, *41*, 781.
(12) Koser, G. F., unpublished results.
(13) (a) Wasserman, H. H. *Aldrichimica Acta* **1987**, *20*, 63. (b) Wasserman, H. H.; Amici, R.; Frechette, R.; van Duser, J. H. *Tetrahedron Lett.* **1989**, *30*, 869. (c) Wasserman, H. H.; Kuo, G.-H. *Tetrahedron Lett.* **1989**, *30*, 873. (d) Wasserman, H. H.; Cook, J. D.; Fukuuyama, J. M.; Rotello, V. M. *Tetrahederon Lett.* **1989**, *30*, 1721. (e) Wasserman, H. H.; Lombardo, L. J. *Tetrahedron Lett.* **1989**, *30*, 1725. (f) Wasserman, H. H.; Rotello, V. M.; Williams, D. R.; Benbow, J. W. *J. Org. Chem.* **1989**, *54*, 2785.
(14) Wasserman, H. H.; Fukuyama, J.; Murugesan, N.; van Duzer, J.; Lombardo, L.; Rotello, V.; McCarthy, K. *J. Am. Chem. Soc.* **1989**, *111*, 371.
(15) Schank, K.; Lick, C. *Synthesis* **1983**, 392 and references therein.

Me_4Si. Elemental analyses were performed by Desert Analytics, Tuscon, AZ. Thin-layer chromatography was performed on silica gel 60 F_{254} plates from EM Reagents and visualized by UV irradiation and/or iodine. Flash column chromatography was performed on silica gel 60 (230–400 mesh).[16] All β-keto ester starting materials were obtained from Aldrich Chemical and used as received. (p-Nitrophenyl)sulfonyl peroxide (pNBSP) was prepared by the literature method.[17]

General Procedure for the Preparation of 2-[[(p-Nitrophenyl)sulfonyl]oxy] β-Keto Esters. To a cooled (0 °C) solution of the β-keto ester (2.1–3.2 mmol) in dichloromethane (50 mL) was added pNBSP (2.1–3.2 mmol). The mixture was stirred at 0 °C until the peroxide was consumed (normally 4–5 h) as determined by iodometric titration of small aliquots (0.1 mL) of the reaction mixture that were removed periodically. The reaction mixture turned yellow and a white precipitate formed. After being stored overnight at 0 °C, the solution was washed with water (2 × 25 mL) and once with saturated sodium chloride (10 mL). The organic layer was dried ($MgSO_4$) and the solvent removed by rotary evaporation to give a yellow oil, which crystallized when the last traces of solvent were removed under high vacuum. The solid was then recrystallized twice with ethyl acetate/hexane (1:5) to give the analytically pure product.

Methyl 2-[[(p-nitrophenyl)sulfonyl]oxy]acetoacetate (15) was prepared from methyl acetoacetate (0.37 g, 3.2 mmol) and pNBSP (1.27 g, 3.2 mmol). The crude product was an off-white solid (0.84 g, 84%) that was recrystallized from ethyl acetate/hexane (1:5) to give small white needles (0.62–0.65 g, 62–65%) with mp 86–88 °C: IR (KBr) cm^{-1} 1765 (COOR), 1735 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.42 (AB q, 4 H, J = 8.3 Hz, Ar H), 5.42 (s, 1 H, C*H*), 3.78 (s, 3 H, OCH_3), 2.36 (s, 3 H, $C(O)CH_3$). Anal. Calcd for $C_{11}H_{11}NO_8S$: C, 41.64; H, 3.49; N, 4.41. Found: C, 41.35; H, 3.49; N, 4.32.

Ethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]acetoacetate (16) was prepared from ethyl acetoacetate (0.39 g, 3.1 mmol) and pNBSP (1.22 g, 3.1 mmol). The crude product was an off-white solid (0.88–0.95 g, 88–95%) that was recrystallized with ethyl acetate/hexane (1:5) to give white plates (0.56–0.57 g, 56–57%) with mp 83–86 °C: IR (KBr) cm^{-1} 1758 (COOR), 1733 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.3 (AB q, 4 H, J = 8.3 Hz, Ar H), 5.39 (s, 1 H, C*H*), 4.21 (d, J = 7.0 Hz, 2 H, CH_2), 2.37 (s, 3 H, $C(O)CH_3$), 1.23 (t, J = 7.0 Hz, 3 H, CH_3). Anal. Calcd for $C_{12}H_{13}NO_8S$: C, 43.46; H, 3.66; N, 4.23, S, 9.68. Found: C, 43.31; H, 3.80; N, 4.29; S, 9.87.

Ethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]-2-isobutyrylacetate (17) was prepared from ethyl 2-isobutyrylacetate (0.44 g, 2.8 mmol) and pNBSP (1.23 g, 2.8 mmol). The crude product was an off-white solid (0.92 g, 92%) that was recrystallized from ethyl acetate/hexane (1:5) to give fine white prisms (0.61–0.67 g, 61–67%) with mp 70–72 °C: IR (KBr) cm^{-1} 1758 (COOR), 1727 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.31 (q, 4 H, J = 8.4 Hz, Ar C*H*), 5.56 (s, 1 H, C*H*), 4.24 (q, J = 7.2 Hz, 2 H, -OCH_2-), 3.07 (sept, J = 7.0 Hz, 1 H, $(CH_3)_2CH$), 1.25 (t, J = 7.2 Hz, CH_2CH_3), 1.13 (d, J = 7.0 Hz, 6 H, $CH(CH_3)_2$). Anal. Calcd for $C_{14}H_{17}NO_8S$: C, 46.79; H, 4.78; N, 4.00. Found: C, 46.20; H, 4.78; N, 4.03.

2-Methoxyethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]acetoacetate (18) was prepared from 2-methoxyethyl acetoacetate (0.44 g, 2.8 mmol) and pNBSP (1.12 g, 2.8 mmol). The crude product was an off-white solid (1.10 g, 100%), that was recrystallized twice from ethyl acetate/hexane (1:5) to give thin off-white needles (0.51–0.67, 51–67%) with mp 66–69 °C: IR (KBr) cm^{-1} 1755 (COOR), 1738 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.41 (AB q, 4 H, J = 9.0 Hz, Ar C*H*), 5.44 (s, 1 H, C*H*), 4.32 (t, J = 4.2 Hz, 2 H, OCH_2), 3.60 (t, J = 4.2 Hz, 2 H, OCH_2), 3.35 (s, 3 H, OCH_3), 2.36 (s, 3 H, $C(O)CH_3$). Anal. Calcd for $C_{13}H_{15}NO_9S$: C, 43.21; H, 4.18; N, 3.88. Found: C, 43.39; H, 4.21; N, 3.81.

***tert*-Butyl 2-[[(p-nitrophenyl)sulfonyl]oxy]acetoacetate (19)** was prepared by the same general procedure except that 1 equiv of solid, ground potassium carbonate (0.38 g, 2.8 mmol) was suspended in the solution of *tert*-butyl acetoacetate (0.44 g, 2.8 mmol). Addition of pNBSP (1.13 g, 2.8 mmol) followed by the normal procedure gave an off-white solid (0.70 g, 70%). The crude product was recrystallized from ethyl acetate/hexane (1:4) to give thin needles (0.46–0.51 g, 46–51%) with mp 80–85 °C dec: IR (KBr) cm^{-1} 1753 (COOR), 1730 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.45 (AB q, 4 H, J = 8.0 Hz, Ar C*H*), 5.27 (s, 1 H, C*H*), 2.33 (s, 3 H, $C(O)CH_3$), 1.44 (s, 9 H, $C(CH_3)_3$). Anal. Calcd for $C_{14}H_{17}NO_8S$: C, 46.79; H, 4.77; O, 3.9. Found: C, 46.49; H, 4.71; N, 3.75.

Ethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]-2-benzoylacetate (20) was prepared from ethyl 2-benzoylacetate (0.49 g, 2.5 mmol) and pNBSP (1.02 g, 2.5 mmol). The crude product was an off-white solid (0.82–90 g, 82–90%) that was recrystallized twice from ethyl acetate/hexane (1:5) to give small white prisms (0.62–65 g, 62–65%) with mp 106–108 °C: IR (KBr) cm^{-1} 1758 (COOR), 1685 (C=O), 1594 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.42 (AB q, 4 H, J = 9.0 Hz, Ar C*H*), 8.04 (d, J = 5.2 Hz, 2 H, *o*-C*H*), 7.65 (m, 3 H, Ar C*H*), 4.22 (q, 2 H, J = 7 Hz OCH_2), 1.86 (t, 3 H, J = 7 Hz, CH_3). Anal. Calcd for $C_{17}H_{15}NO_8S$: C, 51.90; H, 3.85; N, 3.56. Found: C, 51.33; H, 3.71; N, 3.89.

Ethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]-2-(4-nitrobenzoyl)acetate (21) was prepared from ethyl 2-(*p*-nitrobenzoyl)acetate (0.50 g, 2.1 mmol) and pNBSP (0.85 g, 2.1 mmol). The crude product was an off-white solid (1.00 g, 100%) that was recrystallized from ethyl acetate/hexane (1:5) to give off-white crystals (0.5–0.88 g, 70–89%) with mp 101–103 °C: IR (KBr) cm^{-1} 1743 (COOR), 1720 (C=O), 1653 (enol C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.44–7.27 (m, 8 H, Ar H), 6.14 (s, 0.66 H, C*H* (keto tautomer)), 4.24, 4.21 (overlapping q, J = 7.2 Hz, 2 H, OCH_2), 1.20 (t, J = 7.2 Hz, 3 H, CH_3); ^1H NMR (200 MHz, acetone-d_6) δ 8.40–7.70 (m, 8 H, Ar), 6.71 (s, 0.75 H, C*H*), 4.35 (q, J = 4.0 Hz, 0.5 H, OCH_2 (enol tautomer)), 4.18 (q, J = 4 Hz, 1.5 OCH_2 (keto tautomer)), 1.27 (t, J = 4.0 Hz, 1.5 H, CH_3 (keto tautomer)), 1.11 (t, J = 4.0 Hz, 0.5 H, CH_3 (enol tautomer)). Anal. Calcd for $C_{17}H_{14}NO_{10}S$: C, 46.57; H, 3.23; N, 6.39. Found: C, 46.29; H, 3.34; N, 6.19.

Ethyl 2-[[(p-nitrophenyl)sulfonyl]oxy]-2-methylacetoacetate (22) was prepared from ethyl 2-methylacetoacetate (0.42 g, 2.9 mmol) and pNBSP (1.17 g, 2.9 mmol). The crude product was an off-white solid (0.76 g, 76%) that was recrystallized from ethyl acetate/hexane (1:5) to give white flakes (0.43–0.57 g, 43–57%) with mp 55–58 °C: IR (KBr) cm^{-1} 1735 (COOR), 1723 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.3 (AB q, 4 H, J = 9.0 Hz, Ar H), 4.32 (overlapping q, J = 7.2 Hz, 2 H, OCH_2), 2.32 (s, 3 H, CH_3), 1.94 (s, 3 H, $C(O)CH_3$), 1.33 (t, J = 7.2 Hz, 3 H, CH_2CH_3). Anal. Calcd for $C_{13}H_{16}NO_8S$: C, 45.22; H, 4.28; N, 4.06. Found: C, 45.18; H, 4.37; O, 4.03.

Methyl 2-[[(p-nitrophenyl)sulfonyl]oxy]-2-oxocyclopentanecarboxylate (23) was prepared from methyl 2-oxocyclopentanecarboxylate (0.41 g, 2.9 mmol) and pNBSP (1.18 g, 2.9 mmol). The crude product was an off-white solid (0.75–81 g, 75–81%) that was recrystallized from ethyl acetate/hexane (1:5) to give fine white needles (0.46–0.51 g, 46–51%) with mp 82–86 °C: IR (KBr) cm^{-1} 1765 (COOR), 1743 (C=O), 1605 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.31 (AB q, 4 H, J = 9.0 Hz, Ar H), 3.80 (s, 3 H, OCH_3), 2.77 (m, 2 H, CH_2), 2.55 (m, 2 H, CH_2), 2.12 (m, 2 H, CH_2). Anal. Calcd for $C_{13}H_{13}NO_8S$: C, 45.53; H, 3.81; N, 4.07. Found: C, 45.50; H, 3.77; N, 3.78.

2-[[(p-Nitrophenyl)sulfonyl]oxy]-2,4-pentanedione (24) was prepared from 2,4-pentanedione (0.33 g, 3.3 mmol) and pNBSP (1.34 g, 3.3 mmol). The crude product was an off-white solid (0.72–0.78 g, 72–78%) that was recrystallized from ethyl acetate/hexane (1:5) to give white plates (0.31–0.34 g, 31–34%). When the reaction was run in chloroform instead of methylene chloride the crude yield was 0.78–1.00 g (78–100%) and the recrystallized yield was 0.67–0.72 g (67–72%) with mp 83–85 °C: IR (KBr) cm^{-1} 1745 (C=O), 1728 (C=O), 1610 (Ar C=C); ^1H NMR (200 MHz, $CDCl_3$) δ 8.34 (AB q, 4 H, J = 6.8 Hz, Ar H), 2.05 (s, 6 H, $C(O)CH_3$). Anal. Calcd for $C_{11}H_{11}NO_7S$: C, 43.85; H, 3.68; N, 4.65. Found: C, 43.75; H, 3.57; N, 4.56.

***p*-[[(Nitrophenyl)sulfonyl]oxy]acetone (25).** Nosyl keto ester **19** (190 mg, 0.53 mmol) was suspended in dichloromethane (3 mL) and TFA (1 mL) was added. After being stirred at room temperature for 3 h, the mixture was concentrated by rotary evaporation. The residue was taken up in dichloromethane (20 mL), washed with water (20 mL), passed through a short pad of

(16) Still, C. W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(17) Dannley, R. L.; Gagen, J. E.; Stewart, O. J. *J. Org. Chem.* **1970**, *35*, 3076.

magnesium sulfate and silica gel, and concentrated to provide **25** (100 mg, 73%) as a white solid whose TLC behavior and ^1H NMR spectrum was identical with an authentic sample.[5a]

Conversion of Nosylate 16 to Quinoxaline 27. Nosylate **16** (322 mg, 1 mmol) was dissolved in a mixture of benzene (80 mL) and triethylamine (1 mL) and stirred overnight at room temperature. (Attempts to isolate tricarbonyl **26** by flash chromatography led to extensive decomposition during chromatography and low (20-30%) yield of product.) To the reaction mixture were added *o*-phenylenediamine (200 mg, 1.85 mmol) and *p*-toluenesulfonic acid (50 mL, 0.3 mmol). A Dean-Stark apparatus was fitted to the reaction flask and the mixture was refluxed for 1 h. The reaction mixture was concentrated by rotary evaporation, and the residue was taken up in ethyl acetate (50 mL), washed with HCl (1 N, 50 mL) and then saturated sodium bicarbonate (50 mL), passed through a short pad of magnesium sulfate and silica gel, and concentrated to give **27** as a yellow oil. The crude product showed only traces of other components. Flash chromatography (hexane/ethyl acetate, 9:1) yielded **27** as a pale pink solid (160 mg, 74%) with mp 65-66 °C: IR (KBr) cm^{-1} 3040, 2970 (CH), 1720 (C=O), 1500 (C=N); ^1H NMR (200 MHz, $CDCl_3$) δ 1.50 (t, 3 H, OCH_2CH_3), 2.96 (s, 3 H, CH_3), 4.57 (q, 2 H, OCH_2CH_3), 7.75-8.3 (m, 4 H, Ar CH). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.67; H, 5.56; N, 12.96. Found: C, 66.29; H, 5.55; N, 12.74.

Reduction of Nosylate 17 to Nosyl Alcohol 28. A stirred solution of 3-keto-2-nosyl ester **17** (360 mg, 1 mmol) in ethanol (10 mL) was cooled to 0 °C and sodium borohydride (40 mg, 1 mmol) was added in one portion. After stirring this mixture at 0 °C for 1 h, 1 N hydrochloric acid (5 mL) was added slowly. Most of the ethanol was removed from the reaction mixture by rotary evaporation, the aqueous residue was mixed with ethyl acetate (50 mL), and the layers were separated. The organic extract was washed with brine (50 mL), passed through a short pad of magnesium sulfate and silica gel, and evaporated to 3-hydroxy-2-nosyl ester **28** as a yellow oil. The crude product was purified by flash chromatography (hexane/ethyl acetate 4:1) to give pure **28** (260 mg, 72%) with mp 101-102 °C: IR (CH_2Cl_2 solution) cm^{-1} 3550 (OH), 3100, 2960 (CH), 1725 (C=O), 1530 (NO_2); ^1H NMR (200 MHz, $CDCl_3$) δ 0.97, 1.04 (d's, 6 H, J = 7 Hz, $CH(CH_3)_2$), 1.23 (t, 3 H, J = 6.6 Hz, OCH_2CH_3), 1.83 (m, 1 H, $CH(CH_3)_2$), 2.30 (br s, 1 H, OH), 3.70 (dd, 1 H, J = 2.8, 2.6 Hz, CHOH), 4.17 (q, 2 H, J = 6.6 Hz, OCH_2CH_3), 5.19 (d, 1 H, J = 2.8 Hz, CHONs), 8.19-8.39 (AB q, 4 H, Ar H). Anal. Calcd for $C_{14}H_{17}NO_8S$: C, 46.54; H, 5.26; N, 3.88. Found: C, 46.64; H, 5.52; N, 3.68.

On the basis of the relatively small coupling constant (J = 2.8 Hz) of the doublet at δ 5.19, the product was assigned as the syn isomer **28s**.[18] A very small doublet was observed at δ 5.09 with J = 4.8 Hz, which was assigned to the anti isomer **28a**. From the relative intensities of these two signals, the syn stereoselectivity is 97:3.

Acknowledgment. This work was supported by the National Science Foundation (87-09853). We also thank Prof. Gerald Koser for communicating his unpublished results and for helpful discussions.

Registry No. **3**, 6209-72-9; **5**, 105-45-3; **6**, 141-97-9; **7**, 7152-15-0; **8**, 22502-03-0; **9**, 1694-31-1; **10**, 94-02-0; **11**, 838-57-3; **12**, 609-14-3; **13**, 10472-24-9; **14**, 123-54-6; **15**, 124716-78-5; **16**, 124716-79-6; **17**, 124716-80-9; **18**, 124716-81-0; **19**, 124716-82-1; **20**, 124716-83-2; **21**, 124716-84-3; **22**, 124716-85-4; **23**, 124716-86-5; **24**, 124716-87-6; **25**, 98990-66-0; **26**, 1723-25-7; **27**, 3885-38-9; **28a**, 124716-77-4; **28s**, 124716-76-3; *o*-$NH_2C_6H_4NH_2$, 95-54-5.

(18) (a) Guanti, G.; Banfi, L.; Narisano, E.; Thea, S. *Chem. Lett.* **1989**, 1686. (b) Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1980**, 1641.

Intramolecular Diels-Alder Reactions of Sulfur-Substituted Dienes via 3-Sulfolenes

Shang-Shing P. Chou* and Shiow-Jyi Wey

Department of Chemistry, Fu Jen University, Taipei, Taiwan 24205, Republic of China

Received July 27, 1989

Sulfur-substituted dienes containing an unsaturated alkyl chain were readily prepared from 3-sulfolenes. The intramolecular Diels-Alder (IMDA) reaction of these derivatives was studied for the first time. A sulfonyl group on the diene was found to facilitate the IMDA reaction. Hexahydroindenes were produced in good yield and with high stereoselectivity. Octahydronaphthalenes were also obtained, but the stereoselectivity was low and the IMDA reaction was more sensitive to steric hindrance.

The Diels-Alder reaction is one of the most useful methods in organic synthesis.[1] The intramolecular version of this reaction (IMDA) has also been widely used in the construction of polycyclic ring systems with different levels of stereocontrol.[2] The problem of using the IMDA reaction is often the efficient and selective synthesis of the required diene and dienophile within the same molecule.

It is well established that 3-sulfolenes are useful precursors to 1,3-dienes[3] and have been often used in the IMDA reaction.[4] We have been interested in the synthesis and reactions of sulfur-substituted dienes via 3-sulfolenes.[5] Although there are many examples of sulfur-substituted dienes in the intermolecular Diels-Alder reaction,[6] they

(1) Carruthers, W. *Some Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: Cambridge, 1986; Chapter 3, and references therein.

(2) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (c) Taber, D. F. *Intramolecular Diels-Alder Reactions and Alder Ene Reactions*; Springer Verlag: New York, 1984. (d) Ciganek, E. *Org. React.* **1984**, *32*, 1. (e) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 238.

(3) Chou, T. S.; Hung, S. C. *J. Org. Chem.* **1988**, *53*, 3020, and references therein.

(4) (a) Nicolaou, K. C.; Barnette, W. E.; Ma, P. *J. Org. Chem.* **1980**, *45*, 1463. (b) Schmitthenner, H. F.; Weinreb, S. M. *J. Org. Chem.* **1980**, *45*, 3372. (c) Martin, S. F.; Tu, C.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634. (d) Nomoto, T.; Takayama, H. *Heterocycles* **1985**, *23*, 2913. (e) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Chem. Commun.* **1985**, 236. (f) Tso, H. H.; Chang, L. J.; Lin, C. L.; Chou, T. S. *J. Chin. Chem. Soc.* **1985**, *32*, 333. (g) Lee, S. J.; Chou, T. S. *J. Chem. Soc., Chem. Commun.* **1988**, 1188.

(5) (a) Chou, S. S. P.; Liou, S. Y.; Tsai, C. Y.; Wang, A. J. *J. Org. Chem.* **1987**, *52*, 4468. (b) Chou, T. S.; Lee, S. J.; Peng, M. L.; Sun, D. J.; Chou, S. S. P. *J. Org. Chem.* **1988**, *53*, 3027. (c) Chou, S. S. P.; Sun, D. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1176. (d) Chou, S. S. P.; Liou, S. Y.; Tsai, C. Y. *J. Chin. Chem. Soc.* **1988**, *35*, 379. (e) Chou, S. S. P.; Tsai, C. Y. *J. Org. Chem.* **1988**, *53*, 5305. (f) Chou, S. S. P.; Sun, D. J. *J. Chin. Chem. Soc.* **1988**, *35*, 437. (g) Chou, S. S. P.; Tsai, C. Y.; Sun, C. M. *J. Chim. Chem. Soc.* **1989**, *36*, 149. (h) Chou, S. S. P.; Tsai, C. Y.; Sun, C. M. *J. Chin. Chem. Soc.* **1989**, *36*, 227.

0022-3263/90/1955-1270$02.50/0