Reactions of Benzocyclic β-Keto Esters with Sulfonyl Azides. 2.[1] Further Insight into the Influence of Azide Structure and Solvent on the Reaction Course

Luisa Benati,* Daniele Nanni, and Piero Spagnolo

Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy

Received January 27, 1999

The reactions of 2-ethoxycarbonyl-1-benzosuberone with 4-methoxybenzenesulfonyl, 2,4,6-triisopropylbenzenesulfonyl, methanesulfonyl, and trifluoromethanesulfonyl azide, in the presence of triethylamine, have been investigated in *N*,*N*-dimethylformamide, acetonitrile, or tetrahydrofuran with the intent of clarifying the influence of both the azide electrophile and solvent on the reaction course. The present findings, in addition to those previously obtained with tosyl and 4-nitrobenzenesulfonyl azide, indicate that both the electronic features of the sulfonyl azide and the solvent polarity greatly affect the possible occurrence of azidation and/or Favorskii-type ring contraction at the expense of deacylating diazo transfer. Azidation is promoted by the less electrophilic azides, while it is virtually avoided by the more electrophilic ones. Ring contraction occurs to a limited extent with the less electrophilic azides, but it becomes the main process with those more electrophilic. Moreover, azidation is virtually unaffected by the solvent polarity, while ring contraction can markedly be enhanced by a highly polar solvent. Firm evidence has additionally been obtained that, in contrast to a previous claim, trifluoromethanesulfonyl azide can normally perform diazotization of acyclic β-keto esters in preference to azidation.

Introduction

Sulfonyl azides are important intermediates widely used to accomplish diazo group transfer to the activated methylene of β-dicarbonyl compounds as well as to the poorly activated methylene of monocarbonyl compounds, in which cases prior activation by suitable acylation is normally required (deacylating diazo tranfer).[2] Toluene-4-sulfonyl (tosyl) azide (TsN_3) is often employed, but in recent years various studies have clearly revealed that the efficiency of the diazo transfer process can be markedly improved by a proper choice of sulfonyl diazo donors other than TsN_3.

Among several factors making a single azide not satisfactory for all uses, there is the fact that sulfonyl azides, to a varying and rather unpredictable extent, also have a tendency to transfer the azido group. For instance, 2,4,6-triisopropylbenzenesulfonyl (trisyl) azide, while proving superior to tosyl azide and 4-nitrobenzenesulfonyl azide (PNBSA) in the diazotization of cyclic ketones,[3] is instead inferior to those azides in the diazotization of acyclic imide and ester enolates owing to preferential azidation.[4] Furthermore, trifluoromethanesulfonyl (triflyl) azide seemingly behaves as a powerful diazo donor to amines[5,6] and enamino ketones,[7] but it is reported curiously to transfer the azido function to the methine and even methylene group of acyclic β-diketones and β-keto esters.[8]

In previous work we have studied sulfonyl azide reactions of monocyclic and benzocyclic β-keto esters.[1,9] In the presence of triethylamine (TEA), these dicarbonyl substrates can successfully be transformed by TsN_3 into synthetically appealing ring-opened *N*-tosylcarbamoyl-substituted α-diazo esters through a novel deacylating diazo transfer process. However, with those benzocyclic keto esters bearing a conjugated aryl ketone moiety, a competing α-azidation process occurs to an important or even exclusive extent.[1] Replacement of TsN_3 with more reactive PNBSA interestingly results in suppression of azidation, but the expected diazo transfer may be prevented by the preferential occurrence of Favorskii-type ring contraction.[1] These observations therefore revealed that, besides the structural features of the cyclic substrate, those of the azide reagent might greatly influence the course of our keto ester reactions.

To gain further useful information about the effect of sulfonyl azide structure, we were then prompted to consider the use of other arenesulfonyl and alkanesulfonyl azides of varying electrophilic power, including 4-methoxybenzenesulfonyl azide (PMBSA), trisyl azide, methanesulfonyl (mesyl) azide (MsN_3), and triflyl azide. 2-Ethoxycarbonyl-1-benzosuberone **1** was chosen as model substrate for this study in view of our earlier observation that this readily available benzocyclic keto ester can actually undergo azidation, diazotization, and ring contraction upon reaction with PNBSA and/or TsN_3. In the

(1) Part 1: Benati, L.; Calestani, G.; Nanni, D.; Spagnolo, P. *J. Org. Chem.* **1998**, *63*, 4679.
(2) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley-Interscience: New York, 1998, Chapter 1. Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. Regitz, M.; Maas, G. *Diazo Compounds*: *Properties and Synthesis*; Academic Press: New York, 1986; Chapter 13.
(3) Lombardo, L.; Mander, L. N. *Synthesis* **1980**, 368. Coates, R. M.; Kang, H.-Y *J. Org. Chem.* **1987**, *52*, 2065. Uyehara, T.; Takehara, N.; Ueno, M.; Sato, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2687.
(4) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 4011.
(5) Cavender, C. J.; Shiner, V. J., Jr. *J. Org. Chem.* **1972**, *37*, 3567.
(6) Zaloom, J.; Roberts, D. C. *J. Org. Chem.* **1981**, *46*, 5173.
(7) Norbeck, D. W.; Kramer, J. B. *J. Am. Chem. Soc.* **1988**, *110*, 7217.
(8) Hakimelahi, G. H.; Just, G. *Synth. Commun.* **1980**, *10*, 429.
(9) Benati, L.; Nanni, D.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 457.

10.1021/jo9901541 CCC: $18.00
Published on Web 06/17/1999

Table 1. Yields (%)[a] of Azido-Transfer, Ring-Contraction, and Diazo-Transfer Products from the Reactions of Benzosuberone 1 with Sulfonyl Azides[b]

entry	sulfonyl azide	solvent	time	azido-transfer product **2** (%)	ring-contraction product (%)	diazo-transfer product(s) (%)
1	PMBSA	THF	6 d	31	**3a** (34)	**5a** (14)
2	MsN_3	THF	3 d	24	**3b** (30)	**5b** (28)
3	MsN_3	AN	15 h	19	**3b** (60)	**5b** (8)
4	trisyl azide	THF	10 d	72		
5	trisyl azide	AN	4 d	80		
6	triflyl azide[c]	CH_2Cl_2	1 h		**3c** (71)	**5c** (15)
7	PNBSA[d]	THF	4 h		**3e** (75)	
8	TsN_3	THF	5 d	31	**3d** (25)	**4d** (20), **5d** (13)
9	TsN_3	AN	1 d	20	**3d** (56)	**4d** (18)
10	TsN_3	DMF	10 h	32	**3d** (30)	**5d** (10)

[a] Yields isolated by column chromatography. [b] Reactions were normally carried out at room temperature in the presence of TEA. [c] Reaction carried out at 0 °C. [d] See ref 1.

course of this work we happened to discover that triflyl azide performed no azidation of compound **1**. This fact also led us to explore the reactivity of triflyl azide with further keto-ester substrates and thence to prove that this azide can by no means behave as a special azido transfer agent.

Results and Discussion

Following our previous procedure, PMBSA was treated with the benzosuberone **1** in dry tetrahydrofuran (THF), in the presence of TEA, for ca. 6 days, until TLC showed essential absence of the initial reactants. After aqueous acid workup, chromatographic separation gave the azide **2** and the ring-contracted tetralin derivative **3a** along with minor amounts of the pentenoate **5a,** which was the formal β-hydride-elimination carbene product of the unstable diazo pentanoate **4a** (Figure 1 and Table 1, entry 1).

Under analogous conditions mesyl azide similarly furnished comparable amounts of **2** and the respective ring-contraction and carbene products **3b** and **5b** (Table 1, entry 2). Trisyl azide, instead, reacted even more slowly and eventually yielded the azide **2** as the exclusive product (Table 1, entry 4). By contrast, highly hazardous triflyl azide, which was produced as a dichloromethane solution from triflic anhydride and sodium azide through a documented method,[5,6] displayed a very fast reaction with the keto ester **1** and furnished no azidation. This sulfonyl azide furnished mainly the tetralin **3c** and, to a little extent, the pentenoate **5c** (Table 1, entry 6).

The behavior of PNBSA was previously found to resemble that of triflyl azide. In the presence of the benzosuberone **1**, in fact, PNBSA rapidly yielded the ring-contracted compound **3e**, while it totally failed to afford any azidation product (Table 1, entry 7). On the other hand, tosyl azide had been found to exhibit a behavior closely similar to that of PMBSA and MsN_3. Indeed, our earlier reaction of TsN_3 with compound **1** had proved comparably slow and, additionally, had resulted in analogous occurrence of both azidation and diazo transfer, although no parallel occurrence of ring contraction had been revealed at the time. However, a present reinvestigation led us to establish that the reaction actually results in ring contraction to an extent comparable to both azidation and diazo transfer (Table 1, entry 8).

The general evidence provided by the benzosuberone **1** reactions clearly suggests that the electronic features of the sulfonyl azide reagent can profoundly influence the

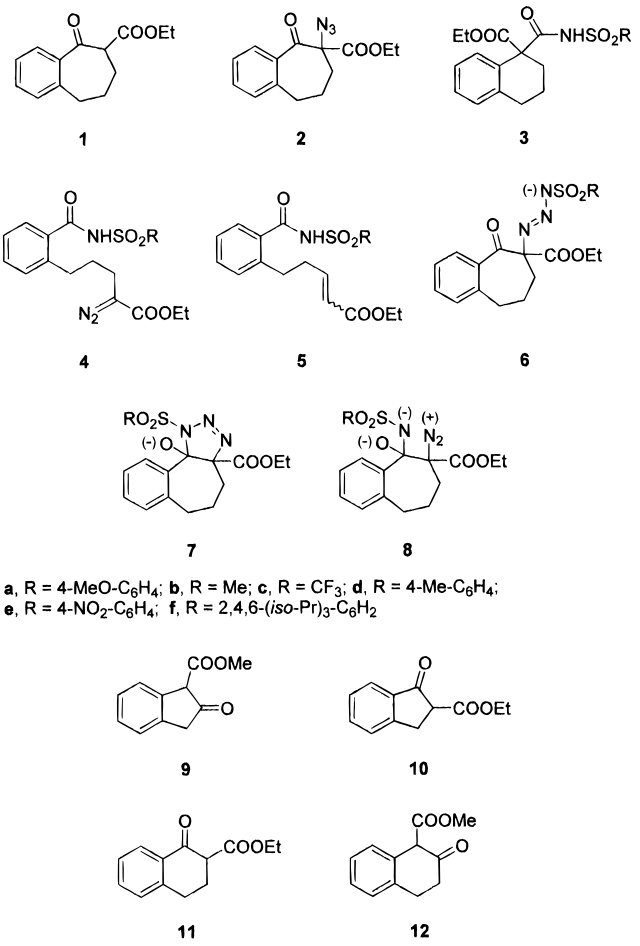


Figure 1.

distribution of resulting azidation, diazo-transfer, and ring-contraction products. Poorly electrophilic TsN_3, PMBSA, MsN_3, and, particularly, trisyl azide show a common propensity to perform significant azidation at the expense of diazo transfer and ring contraction, whereas highly electrophilic triflyl azide and PNBSA avoid azidation essentially in favor of ring contraction.

The observed findings can readily be explained on the basis of the mechanism previously invoked to explain our reactions of cyclic keto esters with sulfonyl azides.[1,9] This would primarily involve the triazenyl anion **6** in the production of azide **2** and the cyclized triazoline **7** in the formation of both ring-contraction and diazo-transfer products **3** and **4**. PMBSA, TsN_3, MsN_3, and trisyl azide normally react with benzosuberone enolate to give ini-

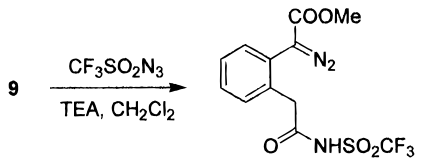
tially the respective triazenyl anions **6a,b,d,f**. The intermediates **6a,b,d**, owing to the limited reactivity of the aromatic ketone moiety,[1] are discouraged from cyclizing to the corresponding triazolines **7a,b,d** and thence somewhat entitled to furnish the azide **2**. The intermediate **6f**, whose cyclization to triazoline **7f** is further discouraged by the steric hindrance afforded by the *o*-isopropyl groups, yields only **2**. By contrast, triflyl azide and PNBSA fail to give the corresponding triazenyl anions **6c,e**, which in principle might have led to the azide **2** more readily than their congeners **6a,b,d**. Presumably, those highly reactive azides react with the benzosuberone enolate to give directly triazoline adducts **7c,e** via a concerted 1,3-dipolar cycloaddition process.

The ensuing triazolines **7a,b,d** show a comparable propensity for causing ring contraction and diazo transfer, whereas the analogues **7c,e**, bearing a more strongly electron-attracting sulfonyl substituent, largely favor ring contraction. This observation interestingly suggests that those intermediates **7** can decompose through two distinctly different modes. Single-step [3 + 2] cycloreversion would result in deacylating diazo transfer, whereas heterolytic ring opening would lead to a diazonium zwitterion **8** and thence to ring contraction with nitrogen loss. This possibility is actually substantiated by the findings that we obtained by reacting the keto ester **1** with TsN_3 and MsN_3 in acetonitrile (AN) or *N*,*N*-dimethylformamide (DMF). In fact, in such highly polar solvents, both reactions, besides proceeding much more quickly, could result in a marked enhancement of the proportion of ring contraction relative to diazo transfer (Table 1, entries 2, 3, and 8−10). Under these circumstances, the extent of the azidation process remained instead roughly constant. This fact indicates that the possible fragmentation of triazenyl anion **6** to azide **2**, with respect to its cyclization to triazoline **7**, is hardly affected by the solvent polarity. Accordingly, exclusive formation of azide **2** still occurred, although in a shorter time, when trisyl azide was reacted with the benzosuberone **1** using AN in place of THF (Table 1, entries 4 and 5).

The total failure of triflyl azide to perform azidation of the compound **1**, although being consistent with the reactivity trend displayed by all of our azides, seemed rather surprising in view of the mentioned report that triflyl azide transfers the azido group to *β*-dicarbonyl compounds, at least the acyclic ones.[8] We were then led to study further reactions of that azide with the five- and six-membered 1- and 2-benzocycloalkanones **9**−**12** (Figure 1), which we had already investigated with both TsN_3 and PNBSA.[1]

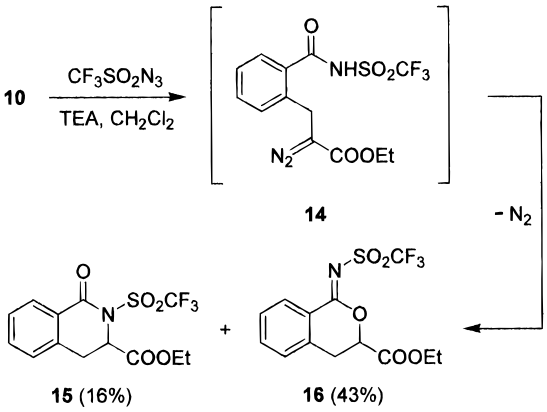
In the usual solvent dichloromethane, triflyl azide rapidly reacted with the indanones **9** and **10** to afford exclusively the diazo amido esters **13** and **14**, respectively. The diazo ester **13** was obtained in virtually quantitative yield as its triethylammonium salt (Scheme 1). The diazo ester **14** was decomposed under the reaction conditions to give an isomeric mixture of the ring-expanded compounds **15** and **16**, which were formally produced through intramolecular attack of a transient carbene at the nitrogen and oxygen atom of the carbamoyl moiety (Scheme 2).[1,9] With the tetralone homologue **11**, under analogous conditions, triflyl azide furnished the indan derivative **17**, but in moderate yield, and provided no evidence for any production of azide (Scheme 3). Moreover, with the isomeric tetralone **12**, triflyl azide

Scheme 1



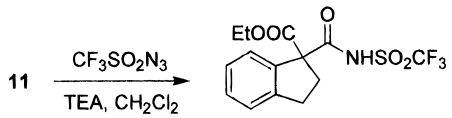
13 (96%)

Scheme 2



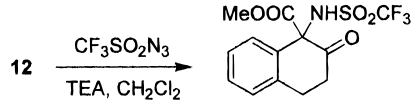
15 (16%) **16** (43%)

Scheme 3



17 (50%)

Scheme 4



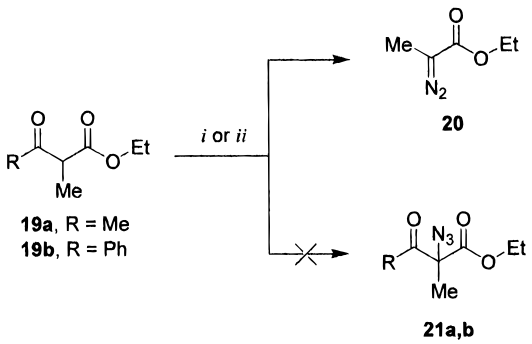
18 (89%)

yielded only the aminated derivative **18**, which actually was the expected product of an intermediate triazoline suffering a peculiar decomposition mode (Scheme 4).[1]

The above findings clearly support our initial observation with the benzosuberone **1**, that the highly reactive triflyl azide can display a chemical behavior closely resembling that of PNBSA. Indeed, consistent with our earlier results encountered with PNBSA,[1] triflyl azide proved generally reluctant to perform azidation, but it was fairly prone to effect diazotization of the indanones **9,10**, ring contraction of the 1-tetralone **11**, and, additionally, amination of the 2-tetralone **12**. Incidentally, it is worth noting that TsN_3, while similarly performing diazo transfer to both indanones **9** and **10**, exhibits only azido transfer with the tetralone **11**.[1]

In the light of the conclusive evidence obtained with the cyclic keto esters **1** and **9**−**12**, we subsequently turned to examine the acylated propionates **19a,b** (Scheme 5). We aimed to ascertain the possible reasons why triflyl azide might act as a peculiar azido group donor toward the acyclic counterparts. Dicarbonyl analogues of **19a,b** have recently been shown by Taber and co-workers to undergo deacylating diazo transfer smoothly with PNBSA or MsN_3 and DBU.[10] Nevertheless, compound **19a** itself and other acyclic congeners were originally reported

Scheme 5[a]



[a] Reagents: *i*, triflyl azide, TEA, CH_2Cl_2; *ii*, TsN_3 or PNBSA, DBU, CH_2Cl_2.

to undergo azidation with triflyl azide, which was believed to form cleanly in situ in DMF upon treatment of triflyl chloride with sodium azide.[8] However, both keto esters **19a,b**, when usually reacted in dichloromethane with triflyl azide, furnished the deacylated diazo compound **20** in moderate yields (40−50%). In either case there was no occurrence at all of any possible azido-transfer product, **21a** or **21b**, as clearly proven by spectral comparison of the crude mixtures with authentic azides **21a,b**, produced through bromination of **19a,b** and subsequent displacement of halide with azide ion. In full agreement with Taber's findings, the diazo compound **20** was also exclusively formed, but in higher yields (75−85%), from further reactions of **19a,b** with PNBSA and TsN_3 using DBU as the base (Scheme 5).[10,11]

Our overall observations therefore lead to the conclusion that triflyl azide can normally act with β-keto esters and, presumably, β-diketones as a reactive diazo group donor. Consequently, the reported azidations were not due to claimed azido-transfer reactions of triflyl azide, but they must have been caused by other unclear reactions which could occur under those circumstances as a presumable result of improper choice of triflyl chloride[8,12] for the in situ production of the azide target in DMF. It is hoped that future studies will succeed in explaining such intriguing results.

Conclusions

Present and previous findings from our cyclic keto ester reactions with sulfonyl azides have clearly shown that, at least in the case of the 1-benzocycloalkanone derivatives, both the azide electrophile structure and the solvent polarity can greatly affect the outcome of azidation and/or ring contraction at the expense of deacylating diazo transfer. Azidation is especially promoted by slightly electrophilic (and sterically hindered) sulfonyl azides, owing to a limited proneness of derived triazenyl anions to cyclize to triazolines. Conversely, azidation is almost avoided by the highly electrophilic azides able to give directly the triazoline cycloadducts. However, with such highly reactive azides, ring contraction may become the most preferred process as a likely result of a special preference of ensuing triazolines to suffer heterolytic fragmentation to diazonium zwitterions over concerted cycloreversion to deacylated diazo componds. Azidation is hardly affected by the solvent polarity, but ring contraction can be markedly enhanced by the use of a highly polar solvent. Furthermore, our present findings have also revealed that, in contrast with a previous claim, highly reactive triflyl azide can normally be envisaged as a diazo-transfer agent rather than an azido-transfer one.

Experimental Section

General Procedures. The starting keto esters **1** and **9**−**12**, as well as tosyl and 4-nitrobenzenesulfonyl azide (PNBSA), were prepared by the known methods cited in part 1.[1] Ethyl 2-methyl-3-oxobutanoate (**19a)** was commercially available; ethyl 2-methyl-3-oxo-3-phenylpropanoate (**19b**) was prepared from commercially available ethyl benzoyl acetate according to the procedure used by Taber[10c] for 1,3-diketones and was authenticated by spectral comparison with the literature.[13] 4-Methoxybenzenesulfonyl azide (PMBSA),[14] mesyl azide,[15] and trisyl azide[16] were obtained by literature methods. Triflyl azide was prepared by the protocol of Cavender and Shiner[5] by treating triflic anhydride in dichloromethane with aqueous sodium azide. The resulting dichloromethane solution of triflyl azide was washed with aqueous NaOH,[6] dried with magnesium sulfate, and then directly used. [**Caution**: All the employed sulfonyl azides are potentially explosive; these compounds have recently been subjected to risk evaluation.[17] Explosions may be expected to result in situations involving neat triflyl azide,[5] and although we experienced no problems in handling dichloromethane solutions of the azide (even stored at −14 °C for several weeks), we feel that for safety's sake the solutions should under no circumstances be allowed to evaporate.] Common reaction products such as the azide **2**[1] and the diazopropanoate **20**[18] were normally identified by spectral comparison with authentic samples.

All solvents were distilled before use. THF was distilled from sodium benzophenone and dichloromethane from calcium hydride. Anhydrous acetonitrile (AN) and dimethylformamide (DMF) were available from Aldrich. All melting points (Kofler melting point apparatus) are uncorrected. ^1H and ^{13}C NMR spectra were normally carried out in $CDCl_3$ solutions, using tetramethylsilane as the internal standard. Mass spectra were determined by the electron impact method (70 eV). IR spectra were recorded in chloroform solutions, unless otherwise stated. Column chromatography was performed on ICN silica gel (63−200, 60 Å) by gradual elution with light petroleum (bp = 40−70 °C)/diethyl ether mixtures and final elution with ethyl acetate and acetone.

(10) Taber, D. F.; You, K.; Song, Y. *J. Org. Chem.* **1995**, *60*, 1093. (b) Taber, D. F.; Herr, R. J.; Pack, S. K.; Geremia, J. M. *J. Org. Chem.* **1996**, *61*, 2908. (c) For related deacylating diazo transfer reactions of β-diketones with PNBSA, see: Taber, D. F.; Gleave, D. M.; Herr, R. J.; Moody, K.; Hennessy, M. J. *J. Org. Chem.* **1995**, *60*, 2283.

(11) It is noteworthy that acyclic β-keto esters, contrary to our cyclic counterparts, normally undergo deacylating diazo transfer in preference to azidation and/or Favorskii-type rearrangement, irrespective of the aromatic or aliphatic ketone moiety and the sulfonyl azide reagent. This fact probably arises from comparatively easier production of monocyclic triazolines as well as from higher propensity of such monocyclic intermediates to suffer ring-cleavage fragmentations to diazo compounds.

(12) Hakimelahi, G. H.; Just, G. *Tetrahedron Lett.* **1979**, *38*, 3643.

(13) Newman, M. S.; Stalick, W. M. *J. Org. Chem.* **1973**, *38*, 3386.

(14) Reagan, M. T.; Nickon, A. *J. Am. Chem. Soc.* **1968**, *90*, 4096.

(15) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959.

(16) Harmon, R. E.; Wellman, G.; Gupta, S. K. *J. Org. Chem.* **1973**, *38*, 11.

(17) Bollinger, F. W.; Tuma, L. D. *Synlett* **1996**, 407.

(18) Regitz, M.; Menz, F. *Chem. Ber.* **1968**, *101*, 2622.

Synthesis of Ethyl 2-Azido-2-methyl-3-oxobutanoate (21a) and Ethyl 2-Azido-2-methyl-3-oxo-3-phenylpropanoate (21b). Ketoester **19a** (9 mmol) was treated with *N*-bromosuccinimide (9 mmol) in tetrachloromethane (50 mL) in the presence of catalytic amounts of dibenzoyl peroxide, and the resulting solution was refluxed for 10 h. After cooling, succinimide was filtered off and the filtrate was concentrated under vacuum to give ethyl 2-bromo-2-methyl-3-oxobutanoate in almost quantitative yield. Without any further purification, the bromide was dissolved in dimethyl sulfoxide (7 mL) and treated with sodium azide (9 mmol). The mixture was stirred at room temperature for 2 h, and then it was poured into water and extracted with diethyl ether. The organic phase was dried, the solvent was evaporated, and the residue was chromatographed on a silica gel column eluting with light petroleum/diethyl ether 95:5 v/v. Azide **21a** was obtained in 50% yield as an oil:[19] IR ν_{max} (cm^{-1}, CH_2Cl_2) 2100 (N_3), 1740 (CO), 1720 (CO); ^1H NMR (200 MHz) δ 1.32 (3H, t, $J = 7$ Hz), 1.58 (3H, s), 2.24 (3H, s), 4.28 (2H, q, $J = 7$ Hz); ^{13}C NMR (50 MHz) δ 14.44, 19.65, 25.78, 63.30, 73.46 (q), 168.91 (q), 200.85 (q). Following the same procedure, azide **21b** was obtained in 45% yield as an oil: IR ν_{max} (cm^{-1}) 2120 (N_3), 1740 (CO), and 1690 (CO); ^1H NMR (200 MHz) δ 1.11 (3H, t, $J = 6.4$ Hz), 1.82 (3H, s), 4.13−4.29 (2H, 2 overlapped quartets, $J = 6.4$ Hz), 7.37−7.64 (3H, m), 7.91−8.04 (2H, m); ^{13}C NMR (50 MHz) δ 14.26, 20.65, 63.24, 71.51 (q), 129.09, 129.84, 134.04 (q), 134.14, 170.22 (q), 191.48 (q).

Reactions of Sulfonyl Azides with Keto Esters 1, 9−12, and 19a,b. General Procedure. The reactions of PMBSA, MsN_3, TsN_3, and trisyl azide (3 mmol) with the benzosuberone **1** (3 mmol) in the presence of triethylamine (TEA) (3 mmol) were properly carried out in 5 mL of THF, AN, or DMF by following the same general procedure as described in part 1[1] for corresponding reactions of TsN_3 and PNBSA with benzocyclic keto esters. With all of the above azides, every reaction mixture was normally quenched by addition of water (20 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic extract was dried and concentrated, and the residue (crude A) was chromatographed. The aqueous layer was acidified with concentrated HCl and extracted with diethyl ether (3 × 10 mL). Evaporation of the solvent eventually gave a residue (crude B) that was chromatographed.

The triflyl azide reactions with the keto esters **1** and **9−12** were performed at 0 °C by adding dropwise TEA (3 mmol) to a solution of the appropriate keto ester (3 mmol) in 20 mL of a 0.15 M solution of triflyl azide in dichloromethane. The resulting mixture was kept at 0 °C for 15−60 min and then at room temperature for 4−5 h. After IR analysis of the crude, to verify the absence of any azidation product, the mixture was generally poured into water, acidified, and extracted with dichloromethane. The organic phase was dried and the solvent evaporated to give a residue that was usually chromatographed.

Approximate times and isolated yields of the azido-transfer, diazo-transfer, and ring-contraction products for the reactions of the benzosuberone **1** with the sulfonyl azides are given in Table 1. The yields of the compounds obtained from the reactions of the keto esters **9−12** with triflyl azide are shown in Schemes 1−4.

The reactions of TsN_3 and PNBSA with the acyclic compounds **19a,b** were performed by treating with DBU (2 equiv)[10] a dichloromethane solution of the starting reagents. The resulting mixture was kept at 0 °C for 1 h and then at room temperature overnight. The triflyl azide reactions with the keto esters **19a,b** were performed at 0 °C by adding dropwise triethylamine (3 mmol) to a solution of the appropriate keto ester (3 mmol) in 20 mL of a 0.15 M solution of triflyl azide in dichloromethane. The resulting mixture was kept at 0 °C for 1 h and then at room temperature for 5 h. In all cases, the reaction mixtures were carefully concentrated under atmospheric pressure at ca. 40 °C to give a yellow oily residue. This was preliminarily shown by IR and ^1H NMR analysis to contain the diazopropanoate **20** with no accompanying azide **21a** or **21b**. The mixture was then quickly chromatographed, under a slight nitrogen pressure, on a very short silica gel (230−400, 60 Å) column eluting with pentane. The yellow-colored fractions were evaporated under atmospheric pressure at ca. 40 °C to give the diazopropanoate **20**.

Reaction of PMBSA with the Benzosuberone 1 in THF. Column chromatography of crude A gave **2**. Chromatography of crude B afforded ethyl 1-({[(4-methoxyphenyl)sulfonyl]amino}carbonyl)-1,2,3,4-tetrahydro-1-naphthalenecarboxylate (**3a**) as a white solid, mp = 145−146 °C (from 2-propanol) [IR ν_{max} (cm^{-1}) 3380 (NH), 1730 (CO), 1710 (CO); MS *m/z* 417 (M^+, 3), 204 (100), 129 (82); ^1H NMR (200 MHz) δ 1.14 (3H, t, $J = 6.9$ Hz), 1.58−1.92 (2H, m), 2.20−2.49 (2H, m), 2.78 (2H, t, $J = 6.7$ Hz), 3.84 (3H, s), 4.11 (2H, q, $J = 6.9$ Hz), 6.93 (2H, d, $J = 9.4$ Hz), 7.02−7.29 (4H, m), 7.91 (2H, d, $J = 9.4$ Hz), 8.44 (1H, bs); ^{13}C NMR (50 MHz) δ 14.31, 19.80, 29.44, 31.93, 56.20, 60.85 (q), 62.79, 114.50, 127.31, 129.06, 129.31, 129.82 (q), 130.99, 131.40, 138.50 (q), 164.47 (q), 170.10 (q), 171.79 (q). Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42; H, 5.55; N, 3.36; S, 7.68. Found: C, 60.68; H, 5.54; N, 3.37; S, 7.65.], and a 1:1 *E*/*Z* mixture of ethyl 5-[2-({[(4-methoxyphenyl)-sulfonyl]amino}carbonyl)phenyl]-2-pentenoate (**5a**) [*E*-isomer: ^1H NMR (200 MHz) δ 1.23 (3H, t, $J = 6.9$ Hz), 2.22−2.40 (2H, m), 2.82 (2H, bt, $J = 8$ Hz), 3.93 (3H, s), 4.22 (2H, q, $J = 6.9$ Hz), 5.73 (1H, d, $J = 15.5$ Hz), 6.86 (1H, dt, $J_d = 15.5$ Hz, $J_t = 6.6$ Hz), 7.08 (2H, d, $J = 9.7$ Hz), 7.26−7.32 (2H, m), 7.42−7.55 (2H, m), 8.13 (2H, d, $J = 9.7$ Hz). *Z*-isomer: ^1H NMR (200 MHz) δ 1.20 (3H, t, $J = 6.9$ Hz), 2.89−3.02 (2H, m), 3.38−3.49 (2H, m), 3.89 (3H, s), 4.04 (2H, q, $J = 6.9$ Hz), 5.69 (1H, d, $J = 11.1$ Hz), 6.07 (1H, dt, $J_d = 11.1$ Hz, $J_t = 6.9$ Hz), 6.97−7.98 (8H, m). Anal. Calcd for $C_{21}H_{23}NO_6S$: C, 60.42; H, 5.55; N, 3.36; S, 7.68. Found: C, 60.65; H, 5.53; N, 3.35; S, 7.64.]. This reaction also yielded 4-methoxybenzenesulfonamide (0.3 mmol).[20]

Reactions of MsN_3 with the Benzosuberone 1 in THF or AN. Column chromatography of crude A gave **2**. Chromatography of crude B afforded ethyl 1-{[(methylsulfonyl)amino]carbonyl}-1,2,3,4-tetrahydro-1-naphthalenecarboxylate (**3b**) as a solid, mp = 168−170 °C [IR ν_{max} (cm^{-1}) 3340 (NH), 1740 (CO), 1720 (CO); MS *m/z* 325 (M^+, 21), 204 (65), 129 (100); ^1H NMR (200 MHz) δ 1.23 (3H, t, $J = 6.9$ Hz), 1.64−1.98 (2H, m), 2.31−2.55 (2H, m), 2.82 (2H, t, $J = 6.2$ Hz), 3.25 (3H, s), 4.20 (2H, q, $J = 6.9$ Hz), 7.11−7.31 (4H, m), 8.31 (1H, bs); ^{13}C NMR (50 MHz) δ 14.40, 19.88, 29.44, 31.84, 41.57, 61.04 (q), 63.00, 127.42, 128.84, 129.42, 131.11, 131.27 (q), 138.59

(19) Azide **21a** had been previously reported, but no spectral data were available: Forster, M. O.; Müller, R. *J. Chem. Soc.* **1910**, *97*, 126.

(20) Commercially available (Lancaster).

(q), 171.48 (q), 172.02 (q). Anal. Calcd for $C_{15}H_{19}NO_5S$: C, 55.37; H, 5.89; N, 4.30; S, 9.85. Found: C, 55.52; H, 5.86; N, 4.32; S, 9.90.], and a 1.5:1 *E*/*Z* mixture of ethyl 5-(2-{[(methylsulfonyl)amino]carbonyl}phenyl)-2-pentenoate (**5b**) [*E*-isomer: ^{1}H NMR (200 MHz) δ 1.19 (3H, t, J = 6.9 Hz), 2.36−2.52 (2H, m), 2.90 (2H, bt, J = 8 Hz), 3.31 (3H, s), 4.05 (2H, q, J = 6.9 Hz), 5.69 (1H, d, J = 16.0 Hz), 6.83 (1H, dt, J_d = 16.0 Hz, J_t = 6.8 Hz), 7.09−7.48 (4H, m), 9.00 (1H, bs). *Z*-isomer: ^{1}H NMR (200 MHz) δ 1.15 (3H, t, J = 6.9 Hz), 2.72−3.02 (2H, m), 3.23−3.50 (2H, m), 3.29 (3H, s), 4.04 (2H, q, J = 6.9 Hz), 5.78 (1H, d, J = 12.0 Hz), 6.17 (1H, dt, J_d = 12.0 Hz, J_t = 7.6 Hz), 7.09−7.48 (4H, m), 9.00 (1H, bs). Anal. Calcd for $C_{15}H_{19}NO_5S$: C, 55.37; H, 5.89; N, 4.30; S, 9.85. Found: C, 55.54; H, 5.85; N, 4.32; S, 9.91.].

Reactions of Trisyl Azide with the Benzosuberone 1 in THF or AN. In THF, without aqueous workup, column chromatography of the crude product obtained by evaporation of the solvent gave the azide **2**; the two starting materials were recovered in ca. 25% yield. By replacing THF with AN, we observed complete conversion of the starting azide and 67% conversion of the starting keto ester; azide **2** was obtained in 80% yield together with an hitherto unidentified white solid, which was also obtained in a control experiment performed with trisyl azide and triethylamine in AN in the absence of keto ester **1**.

Reaction of Triflyl Azide with the Benzosuberone 1 in CH_2Cl_2. Without column chromatography, the oily residue was treated with diethyl ether to give a precipitate of ethyl 1-({[(trifluoromethyl)sulfonyl]amino}carbonyl)-1,2,3,4-tetrahydro-1-naphthalene-carboxylate (**3c**), white solid: mp = 128−130 °C; IR ν_{max} (cm^{-1}) 3320 (NH), 1750 (b, CO); MS *m*/*z* 379 (M$^+$, 11), 204 (59), 158 (32), 129 (100); ^{1}H NMR (200 MHz) δ 1.25 (3H, t, J = 7.1 Hz), 1.75−2.02 (2H, m), 2.39−2.54 (2H, m), 2.86 (2H, t, J = 6.5 Hz), 4.25 (2H, q, J = 7.1 Hz), 7.12−7.36 (4H, m); ^{13}C NMR (50 MHz) δ 14.29, 19.76, 29.31, 32.43, 61.02 (q), 63.54, 119.67 (q, CF_3), 127.52, 128.84, 129.59, 131.12, 138.62 (q), 142.17 (q), 169.42 (q), 172.48 (q). Anal. Calcd for $C_{15}H_{16}F_3NO_5S$: C, 47.49; H, 4.25; N, 3.69; S, 8.45. Found: C, 47.61; H, 4.23; N, 3.68; S, 8.50.

The filtrate contained small amounts of **3c** and ethyl (*E*)-5-[2-({[(trifluoromethyl)sulfonyl]amino}carbonyl)-phenyl]-2-pentenoate (**5c**), contaminated with trace amounts of the *Z*-isomer: ^{1}H NMR (200 MHz) δ 1.19 (3H, t, J = 7.1 Hz), 2.36−2.52 (2H, m), 2.90−3.05 (2H, m), 4.18 (2H, q, J = 7.1 Hz), 5.79 (1H, d, J = 16 Hz), 6.89 (1H, dt, J_d = 16 Hz, J_t = 6.8 Hz), 7.20−7.62 (4H, m).

Reactions of TsN_3 with the Benzosuberone 1 in THF, AN, and DMF. In THF, without aqueous workup, column chromatography of the crude product obtained by evaporation of the solvent gave, eluting with light petroleum/diethyl ether 95:5 v/v, azide **2**. Further elution with diethyl ether afforded ethyl 2-diazo-5-[2-({[(4-methylphenyl)sulfonyl]amino}carbonyl)phenyl]pentanoate (**4d**) [^{1}H NMR (200 MHz) δ 1.24 (3H, t, J = 7.2 Hz), 1.49−1.71 (2H, m), 2.10−2.22 (2H, m), 2.44 (3H, s), 2.69 (2H, bt), 4.13 (2H, q, J = 7.2 Hz), 7.09−7.47 (6H, m), 8.02 (2H, d, J = 8.3 Hz), 8.93 (1H, bs)] and **5d**.[1] Final elution with acetone yielded an oily residue that was suspended in water, acidified, and extracted with diethyl ether to give small amounts of **4d** together with ethyl 1-({[(4-methylphenyl)sulfonyl]amino}carbonyl)-1,2,3,4-tetrahydro-1-naphthalenecarboxylate (**3d**): mp = 121−122 °C; IR ν_{max} (cm^{-1}) 3360 (NH), 1740 (CO), 1720 (CO); MS *m*/*z* 401 (M$^+$, 4), 204 (100), 129 (82), 91 (44); ^{1}H NMR (200 MHz) δ 1.14 (3H, t, J = 7.1 Hz), 1.52−1.93 (2H, m), 2.22−2.43 (2H, m), 2.48 (3H, s), 2.83 (2H, t, J = 6.5 Hz), 4.19 (2H, q, J = 7.1 Hz), 7.17−8.38 (4H, m), 7.43 (2H, d, J = 8.3 Hz), 7.99 (2H, d, J = 8.3 Hz), 8.57 (1H, bs); ^{13}C NMR (50 MHz) δ 14.27, 19.79, 20.20, 29.43, 31.91, 60.85 (q), 62.79, 127.31, 129.03, 129.32, 129.97, 130.99, 131.43 (q), 131.51 (q), 138.52 (q), 145.62 (q), 170.08 (q), 171.78 (q). Anal. Calcd for $C_{21}H_{23}NO_5S$: C, 62.83; H, 5.77; N, 3.49; S, 7.99. Found: C, 63.02; H, 5.80; N, 3.48; S, 8.04.

In AN or DMF, crude A gave **2** and **5d** and crude B afforded **3d**. In THF and DMF 0.23 mmol of tosyl amide was also recovered.

Reaction of Triflyl Azide with the Indanone 9 in CH_2Cl_2. Evaporation of the solvent gave the triethylammonium salt of methyl 2-diazo-2-[2-(2-oxo-2-{[(trifluoromethyl)sulfonyl]amino}ethyl)phenyl]acetate (**13**) as a yellow solid: IR ν_{max} (cm^{-1}) 2080 (C=N$_2$); ^{1}H NMR (200 MHz) δ 1.21 (9H, t, J = 6.9 Hz), 3.06 (6H, q, J = 6.9 Hz), 3.78 (2H, s), 3.83 (3H, s), 7.28−7.46 (4H, m).

Reaction of Triflyl Azide with the Indanone 10 in CH_2Cl_2. After usual workup, column chromatography afforded ethyl 1-oxo-2-[(trifluoromethyl)sulfonyl]-1,2,3,4-tetrahydro-3-isoquinolinecarboxylate (**15**), mp = 86−87 °C [IR ν_{max} (cm^{-1}) 1740 (CO), 1720 (CO); MS *m*/*z* 351 (M$^+$ − 73, 1), 278 (100), 128 (39); ^{1}H NMR (200 MHz) δ 1.14 (3H, t, J = 7.1 Hz), 3.58 (1H, dd, J_1 = 2.8 Hz, J_2 = 16.6 Hz), 3.69 (1H, dd, J_1 = 5.3 Hz, J_2 = 16.6 Hz), 4.22 (2H, q, J = 7.1 Hz), 5.44 (1H, dd, J_1 = 2.8 Hz, J_2 = 5.3 Hz), 7.44 (1H, bd, J = 6.6 Hz), 7.59 (1H, dd, J_1 = 6.6 Hz, J_2 = 7.3 Hz), 7.75 (1H, dd, J_1 = 6.6 Hz, J_2 = 7.3 Hz), 8.31 (1H, bd, J = 6.6 Hz); ^{13}C NMR (50 MHz) δ 14.26, 32.32, 59.19, 63.32, 119.20 (q, CF_3), 127.39 (q), 128.51, 128.92, 130.19, 135.32, 136.13 (q), 162.29 (q), 168.77 (q). Anal. Calcd for $C_{13}H_{12}F_3NO_5S$: C, 44.45; H, 3.44; N, 3.99; S, 9.13. Found: C, 44.55; H, 3.45; N, 3.97; S, 9.16.], and ethyl 1-{[(trifluoromethyl)sulfonyl]imino}-3,4-dihydro-1*H*-isochromene-3-carboxylate (**16**), mp = 118−120 °C [IR ν_{max} (cm^{-1}) 1740 (CO), 1620 (C=N); MS *m*/*z* 351 (M$^+$, 10), 282 (74), 278 (100); HRMS calcd for $C_{13}H_{12}F_3NO_5S$ 351.0388, found 351.0375; ^{1}H NMR (300 MHz) δ 1.20 (3H, t, J = 7.2 Hz), 3.40 (1H, dd, J_1 = 3.5 Hz, J_2 = 17.0 Hz), 3.64 (1H, dd, J_1 = 6.2 Hz, J_2 = 17.0 Hz), 4.22 (2H, q, J = 7.2 Hz), 5.42 (1H, dd, J_1 = 3.5 Hz, J_2 = 6.2 Hz), 7.35 (1H, bd, J = 6.6 Hz), 7.51 (1H, dd, J_1 = 6.6 Hz, J_2 = 7.3 Hz), 7.69 (1H, dd, J_1 = 6.6 Hz, J_2 = 7.3 Hz), 8.17 (1H, bd, J = 6.6 Hz); ^{13}C NMR (75 MHz) δ 13.69, 29.33, 62.68, 76.35, 118.80 (q, CF_3), 123.42 (q), 128.12, 128.58, 129.98, 134.81 (q), 135.82, 165.64 (q), 167.23 (q)].

Reaction of Triflyl Azide with the Tetralone 11 in CH_2Cl_2. After usual workup, column chromatography afforded ethyl 1-({[(trifluoromethyl)sulfonyl]amino}-carbonyl)-1-indanecarboxylate (**17**): mp = 98−100 °C; IR ν_{max} (cm^{-1}) 3340 (NH), 1750 (CO), 1700 (CO); MS *m*/*z* 365 (M$^+$, 6), 190 (92), 115 (100); ^{1}H NMR (200 MHz) δ 1.26 (3H, t, J = 6.7 Hz), 2.79−2.97 (2H, m), 3.15−3.26 (2H, m), 4.32 (2H, 2 overlapped quartets, J = 6.7 Hz), 7.35−7.56 (4H, m), 10.44 (1H, bs); ^{13}C NMR (50 MHz) δ 13.81, 31.42, 32.97, 63.54, 66.73 (q), 119.00 (q, CF_3), 123.68, 125.92, 127.65, 129.97, 138.27 (q), 144.74 (q), 166.92 (q), 171.93 (q). Anal. Calcd for $C_{14}H_{14}F_3NO_5S$: C, 46.03; H, 3.86; N, 3.83; S, 8.78. Found: C, 46.12; H, 3.85; N, 3.85; S, 8.82.

Reaction of Triflyl Azide with the Tetralone 12 in CH_2Cl_2. After usual workup, column chromatography gave methyl 2-oxo-1-{[(trifluoromethyl)sulfonyl]amino}-

1,2,3,4-tetrahydro-1-naphthalenecarboxylate (**18**): mp = 143−144 °C; IR ν_{max} (cm^{-1}) 3310 (NH), 1750 (CO), 1730 (CO); MS *m*/*z* 351 (M^+, 2), 218 (85), 175 (54), 130 (100); ^1H NMR (200 MHz) δ 2.90−3.44 (4H, m), 3.76 (3H, s), 6.82 (1H, bs), 7.26−7.44 (4H, m); ^{13}C NMR (50 MHz) δ 27.91, 38.68, 54.88, 69.97 (q), 118.40 (q, CF_3), 127.49, 127.63, 128.84, 129.52, 133.04 (q), 137.24 (q), 167.55 (q), 201.95 (q). Anal. Calcd for $C_{13}H_{12}F_3NO_5S$: C, 44.45; H, 3.44; N, 3.99; S, 9.13. Found: C, 44.52; H, 3.43; N, 4.01; S, 9.16.

Reactions of Triflyl Azide with the Keto Esters 19a and 19b in CH_2Cl_2. Following the general procedure described above, the keto esters **19a,b** afforded ethyl 2-diazopropanoate (**20**), as a yellow oil, in 51% and 36% yield, respectively: IR ν_{max} (cm^{-1}) 2080 (CN_2), 1670 (CO); ^1H NMR (200 MHz) δ 1.26 (3H, t, J = 7.0 Hz), 1.97 (3H, s), 4.23 (2H, q, J = 7.0 Hz).

Reactions of PNBSA with the Keto Esters 19a and 19b in CH_2Cl_2. Following the general procedure described above, the keto esters **19a,b** afforded **20** in 80% and 85% yield, respectively.

Reactions of TsN_3 with the Keto Esters 19a and 19b in CH_2Cl_2. Following the general procedure described above, the keto esters **19a,b** afforded **20** in 78% and 76% yield, respectively.

Acknowledgment. We gratefully acknowledge financial support from MURST, CNR, and the University of Bologna (1997−1999 Funds for selected research topics).

JO9901541