Tetrahedron Vol. 46, No. 21, pp. 7557-7568, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

REGIOSELECTIVE REPLACEMENT OF NITRO OR SULFONYL GROUP IN CYCLIC α-(NITROALKYL)- OR α-(PHENYLSULFONYLALKYL)ENONES BY NUCLEOPHILES

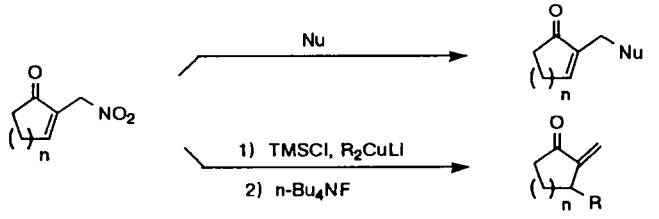
Rui Tamura,*[a] Hitoshi Katayama[a], Ken-ichiro Watabe[a] and Hitomi Suzuki[b]
[a]Department of Chemistry, Faculty of General Education, Ehime University, Matsuyama 790, and [b]Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606, Japan

(Received in USA 29 January 1990)

Summary: Cyclic α-(nitroalkyl)enones and α-(phenylsulfonylalkyl)enones undergo regioselective substitution of the nitro group by relatively soft sulfur, nitrogen and carbon nucleophiles.

Aliphatic nitro compounds are versatile components in organic synthesis due to the high electron-withdrawing property associated with the nitro group. This property permits them to play an important role in key organic reactions for carbon-carbon bond formation such as aldol, the Michael (both as acceptor and donor), and the Diels-Alder (as dienophile) reactions[1].

A new mode of their reactivity was demonstrated when certain nitro compounds were shown to undergo substitution of the nitro group by some nucleophiles via an electron transfer-chain process (the $S_{RN}1$ reaction)[2]. This mode of reactivity bears some resemblance to that of transition-metal-catalyzed substitution reactions[3,4b], and consequently we have aimed to develop a new and general substitution reaction of nitro compounds utilizing organotransition metal catalysts. Thus, we and another group have reported that in the presence of palladium(0)-phosphine complexes a variety of primary to tertiary allylic nitro compounds and even α-nitro olefins are subjected to replacement of the nitro group by nucleophiles such as stabilized carbanions[4], amines[5], phosphines[6], sulfinate ion[7], hydride ion[8], and enolate ions from ketones (albeit limited to tertiary nitro substrates)[9]. As an extension of this work we have recently revealed that cyclic α-(nitroalkyl)enones, activated allylic nitro compounds, undergo the regioselective replacement of the nitro group directly by soft nucleophiles[10] without the aid of a metal catalyst and indirectly by organocuprates[11] to give S_N2 and S_N2' type products, respectively, (eq 1 and 2)[12]. In



(1)

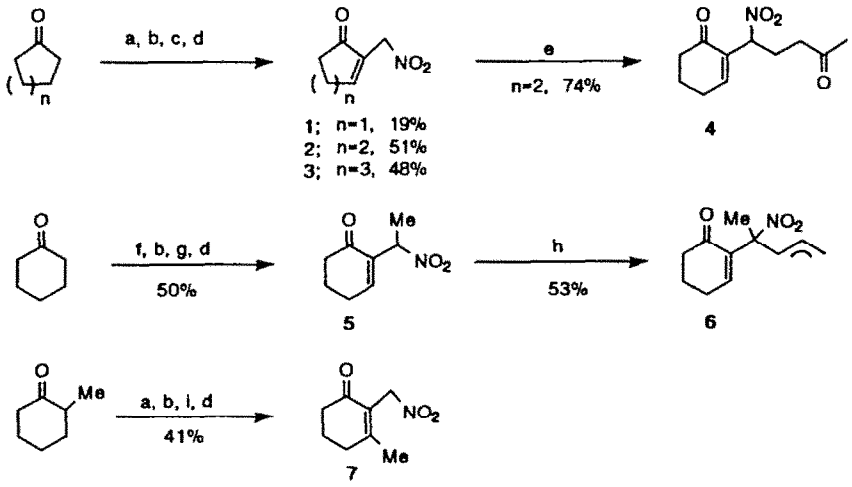
(2)

this paper we report the full experimental results of our further investigation on the former substitution reactions using various cyclic α-(nitroalkyl)enones and the sulfonyl analogues, which also enables us to evaluate the synthetic utility of these reactions.

Preparation of Cyclic α-(Nitroalkyl)enones

To study the substrate substituent effects, α-(nitromethyl)enones **1-3**, branched α-(nitroalkyl)enones **4-6**, and the β-methyl-α-(nitromethyl)enone **7** were prepared from the corresponding cyclic ketones and nitroalkanes[13,14]. Overall isolated yields are shown in Scheme 1. Unlike the simple allylic nitro compounds, the Michael reaction of **2** with activated olefins succeeded only in the case with methyl vinyl ketone to give **4** upon careful selection of solvent and base catalyst; the use of acrylic ester and acrylonitrile resulted in the recovery of **2**.

Scheme 1



a) CH_3NO_2, $H_2N(CH_2)_2NMe_2$, PhH (ref 13); b) MCPBA, CH_2Cl_2; c) Et_3N, CH_3CN; d) PCC, CH_2Cl_2; e) CH_2=$CHCOCH_3$, cat. t-BuOK, MeOH; f) $EtNO_2$, $H_2N(CH_2)_2NMe_2$, PhH; g) $H_2N(CH_2)_2NMe_2$, CH_3CN; h) CH_2=$CHCH_2OCOOCH_3$, $Pd(PPh_3)_4$, THF (ref 15); i) Et_3N, DMF

Reaction with Sulfur Nucleophiles

Regioselective conversiton of cyclic α-(nitroalkyl)enones to the corresponding α-(phenylsulfonylalkyl)enones was easily accomplished by exposure of the former enones to $PhSO_2Na \cdot 2H_2O$ in DMF at room temperature (eq 3 and Table 1). Alternatively, the five and six membered α-(phenylsulfonylmethyl)enones **8a** and **8b** could be obtained in good yields from the cycloalkenones by α-phenylthiomethylation[16] followed by oxidation with Oxone^R (eq 4).

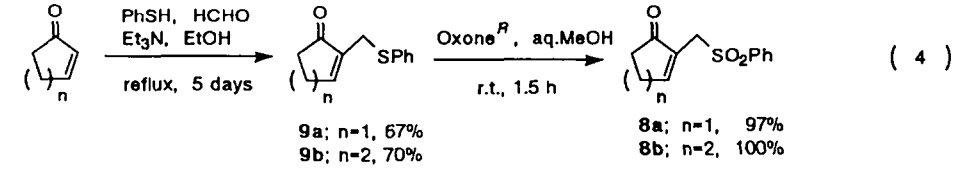
Replacement of the NO_2 group by PhS, or formal reduction of the $PhSO_2$ group to PhS in the activated enones was achieved regioselectively by subjecting these substrates to PhSNa in DMF at room temperature (eq 5 and Table 2). Thus, α-(phenylsulfonylalkyl)enones and

(3)

8a - f

Table 1. Denitro-Sulfonylation of 1-5 and 7

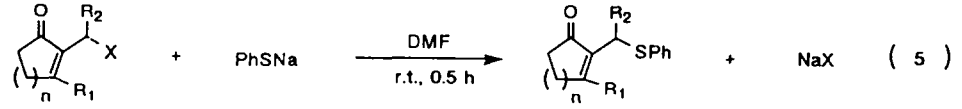
entry	enone	n	R_1	R_2	product	isolated yield(%)
1	**1**	1	H	H	**8a**	72
2	**2**	2	H	H	**8b**	75
3	**5**	2	H	Me	**8c**	75
4	**4**	2	H	CH_2CH_2COMe	**8d**	75
5	**7**	2	Me	H	**8e**	69
6	**3**	3	H	H	**8f**	83



(4)

9a; n=1, 67%
9b; n=2, 70%

8a; n=1, 97%
8b; n=2, 100%



(5)

9a - f

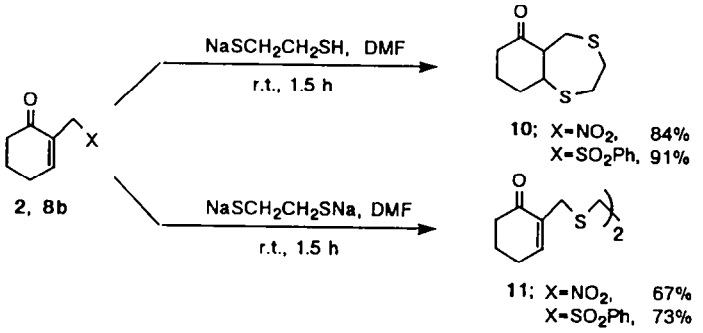
Table 2. Denitro- and Desulfonyl-Sulfenylation of 1-5, 7, 8a, 8b and 8f

entry	enone	n	R_1	R_2	X	product	isolated yield(%)
1	**1**	1	H	H	NO_2	**9a**	88
2	**2**	2	H	H	NO_2	**9b**	83
3	**5**	2	H	Me	NO_2	**9c**	94
4	**4**	2	H	CH_2CH_2COMe	NO_2	**9d**	83
5	**7**	2	Me	H	NO_2	**9e**	72
6	**3**	3	H	H	NO_2	**9f**	95
7	**8a**	1	H	H	SO_2Ph	**9a**	84
8	**8b**	2	H	H	SO_2Ph	**9b**	92
9	**8f**	3	H	H	SO_2Ph	**9f**	79

the corresponding α-(phenylthioalkyl)enones are easily interconvertible.

A further interesting aspect of these transformations is the control of the reaction site in the substitution with alkanedithiols. Typical examples are shown in eq 6 and 7. Subjection of **2** and **8b** to 1,2-ethanedithiol monosodium salt or disodium salt led to the selective formation of the cyclized product **10** via substitution followed by intramolecular 1,4-addition or the intermolecularly linked product **11** through the consecutive two substitutions, respectively. These results suggest the applicability of these reactions to

macrocycle synthesis[12e].

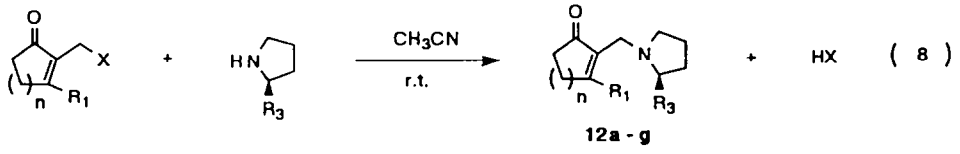


(6)

(7)

Reaction with Nitrogen Nucleophiles

Cyclic α-(dialkylaminomethyl)enones are interesting compounds in view of synthetic manipulation of cyclic enones[17]; e.g., the introduction of a chiral amino group would provide an asymmetric environment around the enone system[18]. Thus, we carried out denitro-amination and desulfonyl-amination using pyrrolidine and (S)-2-(methoxymethyl)pyrrolidine. The use of sulfonyl substrates often needed rather longer reaction time than that of nitro substrates, although yields of the desired products were comparable (eq 8 and Table 3).



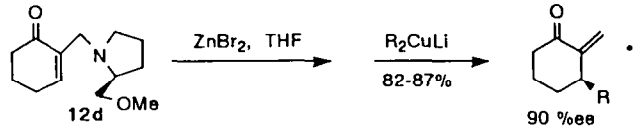
(8)

Table 3. Denitro- and Desulfonyl-Amination of **1-3**, **7**, **8a**, **8b** and **8f**

entry	enone	n	R_1	X	R_3	time(h)	product	isolated yield(%)
1	**1**	1	H	NO_2	H	1.0	**12a**	56
2	**8a**	1	H	SO_2Ph	H	2.0	**12a**	57
3	**1**	1	H	NO_2	CH_2OMe	1.0	**12b**	55
4	**8a**	1	H	SO_2Ph	CH_2OMe	48	**12b**	57
5	**2**	2	H	NO_2	H	1.0	**12c**	89
6	**8b**	2	H	SO_2Ph	H	7.0	**12c**	78
7	**2**	2	H	NO_2	CH_2OMe	1.0	**12d**	94
8	**7**	2	Me	NO_2	H	1.0	**12e**	67
9	**3**	3	H	NO_2	H	1.0	**12f**	94
10	**8f**	3	H	SO_2Ph	H	1.0	**12f**	93
11	**3**	3	H	NO_2	CH_2OMe	1.0	**12g**	95

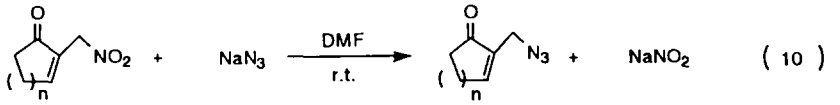
As expected addition of R_2CuLi in the presence of $ZnBr_2$ to (S)-α-[(2-methoxymethyl-1-pyrrolidinyl)methyl]enone **12d** produced the optically active 3-substituted 2-exo-

methylenecyclohexanones in good yield with high enantiomeric excess (90% ee) (eq 9)[18].



(9)

Denitro-azidation also occurred smoothly to produce the α-(azidomethyl)enones **13a** and **13b** in good yields (eq 10).



(10)

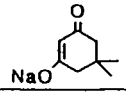
13a; n=1, 73%
13b; n=2, 79%

Reaction with Stabilized Carbanions

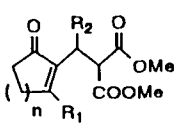
In a previous communication paper[10], we showed that rather poor results occurred upon denitro-alkylation of α-(nitroalkyl)enones. However, systematic studies using structurally different α-(nitroalkyl)enones as well as the phenylsulfonyl analogues with various carbanions (eq 11 and Table 4) demonstrated that this type of substitution reaction could indeed occur to generate the desired products. It would appear that the failure to denitro-alkylate α-(nitroalkyl)enones arose from the high acidity of α-nitro protons in substrates **1**, **2** and **3**. Carbanions abstract the acidic proton to generate the corresponding nitronate, which undergoes further undesired side reactions, probably initiated by intra- or inter-molecular conjugate addition of the nitronate oxygen atom to the enone moiety. Therefore, the use of the phenylsulfonyl analogues **8a**, **8b** and **8f** possessing less acidic α-sulfonyl protons resulted in successful substitution reaction to produce S_N2 type products regioselectively (entries 2, 4, 8, 16, 18 and 20 in Table 4). Noteworthy is the fact that the presence of a methyl group at the β position of the α-(nitromethyl)enone (**7**) effects the smooth substitution reaction with all carbanions employed (entries 5, 11, 14, 19 and 21). This substituent effect may be ascribed to steric suppression of the above described side reaction. The reaction of enones **2** and **8b** with the enolizable carbanions $NaCH(COCH_3)COOCH_3$ or $LiCH(CH_3)NO_2$ in DMF led to no detectable amount of substitution products **17a** or **18a** despite complete consumption of **2** and **8b** (entries 9, 10, 12 and 13), while the same carbanions reacted with the β-methylated enone **7** to give the desired products **17b** and **18b** in 76 and 61 % yields, respectively (entries 11 and 14). Interestingly, $LiC(CH_3)_2NO_2$ reacted with **8a** and **8b** as well as **7** to respectively afford the S_N2 type products **19a**, **19b** and **19c** in good yields (entries 16, 18 and 19). These results imply that the once formed S_N2 type products **17a** and **18a** bearing an acidic proton are likely to undergo further side reactions, probably intramolecular ones, although details are not understood yet. This drawback was surmounted by replacing DMF by methanol (entries 9, 10, 12 and 13).

(11)

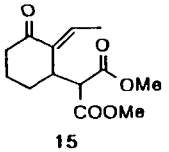
Table 4. Denitro- and Desulfonyl-Alkylation of 1-3, 5, 7, 8a, 8b and 8f

entry	Nu^-	enone	n	R^1	R^2	X	time (h)	product	yield (%)[a]
1	$NaCH(COOMe)_2$	1	1	H	H	NO_2	1.0	-	0
2		8a	1	H	H	SO_2Ph	1.0	**14a**	74
3		2	2	H	H	NO_2	2.0	**14b**	24
4		8b	2	H	H	SO_2Ph	2.0	**14b**	78
5		7	2	Me	H	NO_2	2.0	**14c**	82
6		5	2	H	Me	NO_2	1.5	**14d+15**(56:44)	73
7		3	3	H	H	NO_2	2.0	**14e+16**(80:20)	33
8		8f	3	H	H	SO_2Ph	2.0	**14e+16**(80:20)	91
9	NaCH(COMe)COOMe	2	2	H	H	NO_2	48	**17a**	0(10)[b]
10		8b	2	H	H	SO_2Ph	48	**17a**	0(32)[b]
11		7	2	Me	H	NO_2	2.0	**17b**	76
12	$LiCHMeNO_2$	2	2	H	H	NO_2	48	**18a**	0(60)[b]
13		8b	2	H	H	SO_2Ph	24	**18a**	0(70)[b]
14		7	2	Me	H	NO_2	2.5	**18b**	61
15	$LiCMe_2NO_2$	1	1	H	H	NO_2	2.0	**19a**	0
16		8a	1	H	H	SO_2Ph	2.0	**19a**	65
17		2	2	H	H	NO_2	2.0	**19b**	<10
18		8b	2	H	H	SO_2Ph	2.0	**19b**	74
19		7	2	Me	H	NO_2	2.5	**19c**	60
20		8b	2	H	H	SO_2Ph	2.5	**20**	59
21		7	2	Me	H	NO_2	2.5	**21+22**(60:40)	86

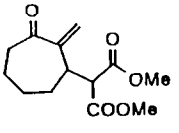
a) Isolated yield. b) Performed in MeOH.



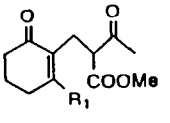
14



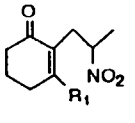
15



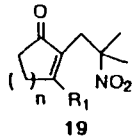
16



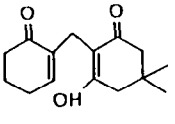
17



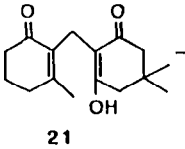
18



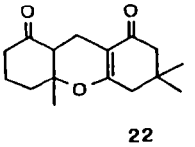
19



20



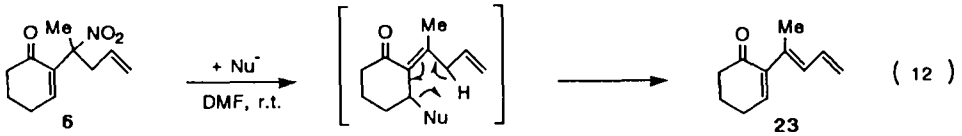
21



22

Mechanism

At the beginning of our studies, we postulated that most of the described substitution reactions of α-(nitroalkyl)enones might involve an electron-transfer process and proceed by a non-chain radical mechanism partly similar to the $S_{RN}1$ reaction, since the sterically congested carbanion $LiC(CH_3)_2NO_2$ and the methyl-substituted enone 7 participated in this substitution reaction. After several inhibition experiments with an excess amount of scavengers for free radical and anion radical, however, we noted that the radical mechanism should be a minor pathway if any, because so far no pronounced inhibition was observed in the reaction of 2 or 7 with $PhSO_2^-$, PhS^-, or $^-CH(COOMe)_2$. Moreover, the fact that tertiary nitro enone 6 failed to undergo the substitution reaction by $PhSO_2^-$, PhS^- and $^-CH(COOMe)_2$, instead giving the elimination product 23 (eq 12), supports the non-radical mechanism as a principal pathway.



6 23 (12)

$Nu^- = PhSO_2^-, PhS^-, {}^-CH(COOMe)_2$

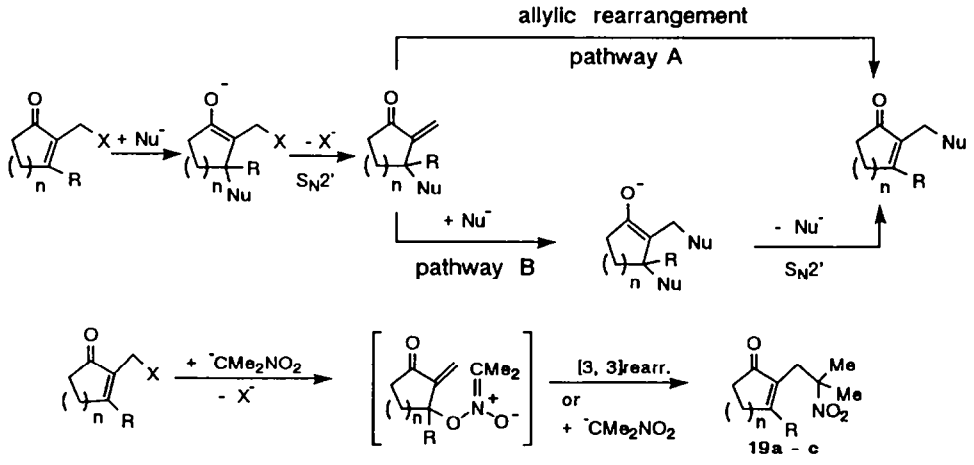
Two possible reaction mechanism compatible with these results involves either A) an S_N2'-allylic rearrangement process or B) a S_N2'-S_N2' reaction, depending on the type of nucleophiles (Scheme 2). It is more likely that the substitution reaction with enolizable carbanions is initiated by conjugate addition of the enolate oxygen atom to the β position of enones and subsequent elimination of the leaving group X followed by either [3,3]rearrangement or additional S_N2' process[12b]. This explanation convinces us of the observed smooth reactions of 8a, 8b and 7 with the hindered carbanion $LiC(CH_3)_2NO_2$ (entries 16, 18 and 19 in Table 4 and Scheme 2). The simultaneous formation of the S_N2 and S_N2' type products from $NaCH(COOMe)_2$ and 5, 3, or 8f (entries 6, 7 and 8 in Table 4) seems to reflect the competition between initial O-attack and C-attack of $^-CH(COOMe)_2$, since rearrangement of the separated S_N2' product 15 into the S_N2 one 14d upon treatment with $NaCH(COOMe)_2$ occurs quite slowly. As to the other heteroatom nucleophiles employed, both pathways A and B should be considered.

Conclusion

Studies on reaction of cyclic α-(nitroalkyl)- and α-(phenylsulfonylalkyl)-enones with various soft nucleophiles reveal that (i) these enones undergo the regioselective replacement of NO_2 and SO_2Ph groups by SPh, NR_2 groups and stablized carbanions to give the S_N2 type products, (ii) α-(phenylsulfonylalkyl)- and the corresponding α-(phenylthioalkyl)enones are interconvertible, (iii) optically active α-(pyrrolidinylmethyl)enones are obtained, (iv) α-(phenylsulfonylalkyl)enones are the more suitable substrate than the nitro analogues with respect to substitution by stabilized carbanions, while unexceptionally the β-methyl-α-(nitromethyl)enone 7 effects smooth substitution reaction with all carbanions

Scheme 2

S_N2'- allylic rearrangement (pathway A)
S_N2'- S_N2' process (pathway B)



employed to afford the S_N2 type products, and (v) this type of substitution reaction may proceed through S_N2' reaction followed by either allylic rearrangement or additional S_N2' reaction (Scheme 2).

Experimental Section

General procedure for the Preparation of α-(Nitroalkyl)enones (Scheme 1). The β,γ Epoxynitro compound (20 mmol), prepared by epoxydation of the corresponding allylic nitro compound[13,14], was dissolved in CH_3CN (60 mL) [DMF for **7**], and Et_3N (2 mmol) [$H_2N(CH_2)_2NMe_2$ (2mmol) for **5**] was added. The resulting orange to red solution was heated at 80°C for 2h [48 h for **5** and **7**; r.t., 24 h for **1**] and then poured into aq. 2N HCl (100 ml). The aqueous mixture was extracted with ether (3 X 40 mL). The ether extracts were washed with water (40 mL) [brine (3 X 40 mL) and water (40 mL) for **7**], dried over $MgSO_4$, and concentrated *in vacuo*. The crude hydroxy allylic nitro compound was dissolved in CH_2Cl_2 (50 mL) and added to a mixture of pyridinium chlorochromate (PCC, 25-30 mmol) and neutral alumina (25 g) in CH_2Cl_2 (250 mL). After approximately 2 h, the mixture was filtered through celite. The filtrate was concentrated and then subjected to column chromatography on silica gel (CH_2Cl_2) to give the pure α-(nitroalkyl)enones.

Allylation of **5** was carried out according to published procedure[15]. Compound **4** was prepared by stirring a mixture of **2** (20 mmol), methyl vinyl ketone (24 mmol) and t-BuOK (2 mmol) in MeOH (80 mL) overnight at r.t. followed by concentration and purification by column chromatography on silica gel (1:1 hexane-EtOAc).

General Procedure for Denitro-Sulfonylation, Denito-Sulfenylation, Desulfonyl-Sulfenylation and Denitro-Azidation (eq 3,5,6,7,10 and Table 1,2). A mixture of the enone (5 mmol) and $PhSO_2Na \cdot 2H_2O$ (7.5 mmol), PhSNa (7.5 mmol), or NaN_3 (7.5 mmol) in DMF (10 mL) was stirred at r.t. for 0.5 h under argon. The reaction mixture was partitioned between ether (50 mL) and water (50 mL), and the aqueous phase was extracted with ether (2 X 30 mL). The ether extracts were washed with brine (3 X 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (4:1 hexane-EtOAc). Compounds **10** and **11** were prepared by stirring a mixture of **2** or **8b** (1 mmol) and $NaSCH_2CH_2SH$ (1mmol) or $NaSCH_2CH_2SNa$ (1 mmol) in DMF (5 mL) at r.t. for 1.5 h followed by the above workup procedure.

General Procedure for Denitro-Amination and Desulfonyl-Amination (eq 8 and Table 3). A mixture of the enone (5 mmol) and the amine (10 mmol) in CH_3CN (10 mL) was stirred at r.t. for the stated period of time. The solvent was evaporated *in vacuo* and the residue was dissolved in ether (100 mL). The ether solution was washed with water (30 mL). The aqueous phase was extracted with ether (3 X 30 mL). The combined organic phase was dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was in a high state of purity and if necessary may be purified by column chromatography on neutral alumina.

General Procedure for Denitro-Alkylation and Desulfonyl-Alkylation (eq 11 and Table 4). Solid $LiCHMeNO_2$ or $LiCMe_2NO_2$ was prepared by stirring a mixture of MeOLi (1 equiv) and $EtNO_2$ or Me_2CHNO_2 (1.05 equiv) in MeOH at r.t. for 24 h under argon, respectively, followed by concentration, washing with pentane, and drying in vacuo. Other carbanions were prepared by adding the active methylene compound (1 equiv) to a slurry of pentane-washed NaH (1 equiv) in DMF and stirring until homogeneous.

To the carbanion (1.05 mmol) in DMF (2 mL) was added a DMF (2 mL) solution of the enone (1.0 mmol) at r.t. The reaction mixture was stirred for the stated period of time and then partitioned between ether (30 mL) and water (30 mL), and the aqueous phase was extracted with ether (3 X 30 mL). The ether extracts were washed with brine (3 X 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude product could be purified by column chromatography on silica gel (4:1 hexane-EtOAc).

Table 5. Spectroscopic data of compounds **1-20, 22** and **23**[a]

compound	^{1}H NMR spectra[b]	^{13}C NMR spectra[b]	I.R.[c]
1[14c]	7.88(br,1H),5.14(s,2H),2.75-2.55(m,2H) 2.50-2.45(m,2H)	206.2,165.5,135.5, 69.0,34.0,27.3	1710,1642,1555, 1375
2[14c]	7.20(t,J=3.9Hz,1H),5.04(s,3H),2.72-2.38 (m,4H),2.32-1.90(m,2H)	196.8,153.9,130.5, 73.5,37.5,26.2,22.5	1680,1555,1380
3[14c]	6.89(t,J=6.1Hz,1H),5.10(s,2H),2.84-2.38 (m,4H),2.04-1.68(m,4H)	201.9,150.6,133.8, 77.2,42.4,28.5,25.0, 21.2	1667,1553,1377
4	7.19(t,J=3.9Hz,1H),5.48(m,1H),2.68-2.32 (m,8H),2.32-1.83(m,2H),2.16(s,3H)	206.2,196.1,149.5, 134.6,82.6,39.6,37.8, 30.0,26.4,26.1,22.2	1708,1690,1548, 1370
5	7.19(t,J=4.0Hz,1H),5.66(q,J=7.0Hz,1H), 2.82-2.35(m,4H),2.35-1.93(m,2H),1.75 (d,J=7.0Hz,3H)	d	1680,1550,1385
6[e]	6.96(t,J=4.3Hz,1H),5.51(dddd,J=7.3,7.3, 10.3,16.2Hz,1H),5.11(dd,J=10.3,3.2Hz, 1H),5.09(dd,J=16.2,3.2Hz,1H),3.00(dd, J=7.3,13.7Hz,1H),2.87(dd,J=7.3,13.7Hz, 1H),2.57-2.42(m,4H),2.15-1.94(m,2H), 1.68(s,3H)	196.5,147.4,138.0, 131.3,120.2,89.3, 41.5,38.6,26.1,24.0, 22.1	1682,1545,1343, 995,925
7	5.28(s,2H),2.46-2.55(m,4H),2.07(s,3H), 2.04(m,2H)	196.3,165.0,126.3, 68.9,36.7,32.9,21.6, 21.5	1670,1630,1550, 1380
8a[f]	7.98-7.40(m,5H),4.02(s,2H),2.86-2.53 (m,2H),2.52-2.20(m,2H)	d	1709,1448,1320, 1310,1155
8b[f]	7.98-7.36(m,5H),7.23(t,J=4.4Hz,1H), 4.07(s,3H),2.61-2.18(m,4H),2.12-1.90 (m,2H)	195.7,153.3,138.8, 133.7,128.9,128.6, 128.2,54.2,37.4,26.5, 22.5	1675,1445,1318, 1307,1128,1082
8c[f]	8.06-7.33(m,5H),7.30(t,J=4.2Hz,1H), 4.81(q,J=7.6Hz,1H),2.66-2.15(m,4H), 2.15-1.75(m,2H),1.50(d,J=7.0Hz,3H)	d	1680,1635,1583, 1443,1380,1300, 1150
8d	7.84-7.47(m,5H),7.29(t,J=4.2Hz,1H), 4.64(dd,J=10.3,4.6Hz,1H),2.60-2.24 (m,6H),2.22-1.92(m,4H),2.09(s,3H)	206.6,196.0,151.0, 138.0,133.7,132.3, 129.1,128.8,58.5, 40.5,37.3,29.9,26.4, 22.4,22.2	1713,1672,1580, 1480,1438,1170

8e[f]	7.87-7.49(m,5H),4.28(s,2H),2.44(m,2H), 2.23(m,2H),2.10(s,3H),1.89(m,2H)	195.4,164.3,138.8, 133.5,128.5,128.2,123.9 51.7,36.4,33.0,22.5,21.3	1665,1620,1440, 1380,1310,1140, 1080,730,690
8f[f]	7.88-7.50(m,5H),6.84(t,J=6.3Hz,1H), 4.13(s,2H),2.48(m,4H),1.73(m,4H)	d	1665,1448,1388, 1305,1140,1090,
9a	7.38(m,1H),7.33-7.14(m,5H),3.67(brs,2H), 2.58-2.50(m,2H),2.46-2.38(m,2H)	d	1700,1635,1582, 1480,1440
9b	7.28(m,5H),6.77(t,J=4.9Hz,1H),3.70(brs, 2H),2.60-2.13(m,4H),2.13-1.80(m,2H)	198.1,147.4,136.3, 135.3,130.4,128.8, 126.5,38.4,32.7,26.1, 23.0	1670,1585,1482, 1438,1370,1255, 1172
9c	7.66-7.10(m,5H),6.86(t,J=4.0Hz,1H), 4.48(q,J=7.2Hz,1H),2.65-2.17(m,4H), 2.17-1.60(m,2H),1.40(d,J=7.2Hz,3H)	d	1680,1440,1380, 1025
9d	7.37(brm,5H),6.89(t,J=4.0Hz,1H),4.34 (t,J=7.0Hz,1H),2.70-2.23(m,6H),2.10 (s,3H),2.00-1.75(m,4H)	d	1712,1672,1582, 1480,1483,1170
9e	7.41-7.19(m,5H),3.85(s,2H),2.42-2.32 (m,4H),1.92(m,2H),1.85(s,3H)	197.0,159.3,136.5, 131.3,131.0,128.6,126.5, 37.4,32.8,28.9,21.9,21.3	1665,1625,1440, 1380,740,690
9f	7.34-7.15(m,5H),6.47(t,J=6.3Hz,1H), 3.74(s,2H),2.58(m,2H),2.31(m,2H), 1.61-1.78(m,4H)	203.5,143.6,138.7, 135.9,130.6,128.7, 126.4,42.6,36.4,27.4, 24.8,21.1	1665,1480,1440, 740,690
10[f,g]	4.26-2.71(m,8H),2.48-1.67(m,6H)	209.1,207.9,60.4, 55.4,50.2,50.0,41.9, 40.6,39.4,39.3,37.5, 37.0,33.4,33.3,32.9, 31.3,25.4,23.0	1710,1410,1305, 1280,1170,1020
11	6.94(t,J=4.0Hz,2H),3.33(s,4H),2.67 (s,4H),2.44(m,8H),2.02(m,4H)	198.0,147.1,136.1, 38.2,31.7,29.9,25.9, 22.8	1675,1420,1370, 1260,1175,1135, 1100,1070
12a	7.60(m,1H),3.28(brs,2H),2.72-2.40 (m,8H),1.83-1.58(m,4H)	d	1700,1632,1422
12b[h]	7.57(m,1H),3.63(d,J=15.1Hz,1H),3.43 (dd,J=5.0,9.5Hz,1H),3.35(s,3H),3.32 (dd,J=3.8,9.5Hz,1H),3.12(d,J=15.1Hz, 1H),3.03(m,1H),2.73-2.53(m,2H),2.42 (m,3H),2.22(m,1H),1.95-1.53(m,4H)	209.4,160.5,143.7, 76.0,63.1,59.1,54.7, 48.8,34.7,28.2,26.6, 22.8	1700,1440,1120 735
12c	6.97(t,J=4.0Hz,1H),3.26(brs,2H),2.83- 2.25(m,8H),2.22-1.58(m,6H)	d	1670,900,725
12d[h]	6.98(t,J=4.0Hz,1H),3.63(d,J=14.0Hz,1H), 3.46(dd,J=4.6,9.5Hz,1H),3.36(s,3H),3.29 (dd,J=6.4,9.5Hz,1H),3.08(d,J=14.0Hz,1H), 2.99(m,1H),2.66(m,1H),2.48-2.34(m,4H), 2.16(m,1H),2.05-1.82(m,3H),1.76-1.56(m,3H)	199.1,147.4,137.1, 76.0,63.2,59.0,54.6, 52.7,38.4,28.3,25.9, 22.9,22.8	1675,1120,735
12e	3.36(s,2H),2.37-2.52(m,8H),2.07(s,3H), 1.95(m,2H),1.73(m,4H)	198.2,159.5,132.6, 53.8,48.1,37.6,32.9, 23.2,21.9,21.4	1665,1620,1380
12f	6.66(t,J=1.2Hz,1H),3.27(s,2H),2.50- 2.38(m,8H),1.84-1.72(m,8H)	204.8,142.8,140.8, 57.2,54.0,42.6,27.5, 25.0,23.3.21.6	1665,1460,1130
12g[h]	6.64(t,J=6.1Hz,1H),3.74(d,J=13.4Hz,1H), 3.43(dd,J=4.2,9.4Hz,1H),3.35(s,3H),3.23 (dd,J=6.4,9.4Hz,1H),3.02(d,J=13.4Hz,1H), 2.95(brm,1H),2.60(brm,3H),2.40(brm,2H), 2.12(m,1H),1.95-1.50(m,8H)	204.7,142.7,141.0, 75.9,62.9,58.9,56.3, 54.4,42.6,28.4.27.6, 25.0,22.7,21.7	1670,1450,1120
13a	7.66(brm,1H),4.04(brs,2H),2.80-2.24(m,4H)	d	2100,1700
13b	7.00(t,J=3.9Hz,1H),3.97(s,2H),2.62-2.32	198.1,148.4,134.4,	2100,1670

	(m,4H),2.22-1.92(m,2H)	49.7,38.1,26.0,22.8	
14a	7.41(t,J=2.7Hz,1H),3.73(t,J=7.6Hz,1H), 3.73(s,6H),2.81(d,J=7.6Hz,2H),2.58(m,2H)	208.9,169.0,159.9, 142.0,52.5,49.6,34.2,	1740,1700,1440, 1235,1155,1130
14b	6.83(t,J=4.1Hz,1H),3.72(t,J=7.9Hz,1H), 3.71(s,6H),2.77(d,J=7.9Hz,2H),2.45-2.32 (m,4H),1.97(m,2H)	198.7,169.3,148.2, 135.5,52.3,50.3,38.2, 29.8,26.0,22.8	1740,1670,1435, 1235,1155,1030
14c	3.71(t,J=7.9Hz,1H),3.70(s,6H),2.88(d, J=7.9Hz,2H),2.37(m,4H),1.98(s,3H),1.92 (m,2H)	198.1,169.3,158.2, 130.9,52.0,49.9,37.3, 32.7,24.9,21.7,21.0	1730,1640,1430, 1235,1150,1040
14d	6.78(t,J=4.3Hz,1H),3.83(d,J=9.2Hz,1H), 3.65(s,6H),2.45-2.30(m,4H),2.00-1.75 (m,3H),1.17(d,J=7.0Hz,3H)	d	1740,1650,1430, 1235,1150,1035
15	6.52(q,J=7.3Hz,1H),3.75(s,6H),3.58 (d,J=9.1Hz,1H),2.60-2.25(m,3H),2.00-1.83(m,4H),1.79(d,J=7.3Hz,3H)	d	d
14e	6.64(t,J=6.4Hz,1H),3.72(t,J=7.9Hz,1H), 3.71(s,6H),2.81(d,J=7.9Hz,2H),2.58(m,2H), 2.39(m,2H),1.97-1.69(m,4H)	203.8,169.3,145.4, 139.2,52.2,50.7,42.3, 32.9,27.4,24.7,21.0	1740,1660,1440, 1235,1150,1020
16	5.99(brs,1H),5.28(brs,1H)		
17a	6.84(t,J=4.3Hz,1H),3.80(dd,J=8.5,6.4Hz, 1H),3.71(s,3H),2.77(dd,J=13.7,6.4Hz,1H), 2.63(dd,J=13.7,8.5Hz,1H),2.44-2.30(m,4H), 2.24(s,3H),1.98(m,2H)	202.5,199.0,169.6, 148.6,135.8,57.9, 52.2,38.2,29.3,28.9, 26.0,22.8	1745,1710,1670, 1435,1360,1240, 1155
17b	3.79(t,J=7.5Hz,1H),3.69(s,3H),2.80(d, J=7.5Hz,2H)2.37(m,4H),2.24(s,3H),1.99 (s,3H),1.93(m,2H)	203.0,198.6,169.9 158.6,131.3,57.7, 52.1,37.6,32.9,29.2, 24.4,21.9,21.3	1740,1715,1660, 1430,1360,1150
18a	6.79(t,J=4.0Hz,1H),4.83-4.75(m,1H),2.77 (m,J=13.9Hz,1H),2.56(dd,J=13.9,9.9Hz,1H), 2.47-2.30(m,4H),1.98(m,2H),1.53(d,J= 6.4Hz,3H)	198.7,149.3,134.2, 82.6,38.1,36.3,26.0, 22.7,19.3	1670,1545,1385, 1110
18b	4.76(m,1H),2.89(dd,J=9.1,14.0Hz,1H), 2.76(dd,J=5.0,14.0Hz,1H),2.39(m,4H), 1.94(s,3H),1.88-1.98(m,2H),1.54(d,J= 6.7Hz,3H)	198.4,159.8,130.0, 82.4,37.5,33.0,31.8, 21.9,21.3,19.2	1660,1625,1545, 1380,1360
19a[f]	7.39(t,J=2.8Hz,1H),2.84(s,2H),2.60 (m,2H),2.41(m,2H),1.56(s,6H)	208.9,162.0,140.3, 88.4,34.6,33.8,26.8, 25.8	1700,1540,1345
19b	6.73(t,J=4.1Hz,1H),2.84(s,2H),2.47-2.33(m,4H),1.98(m,2H),1.51(s,6H)	198.5,150.5,134.3, 89.1,38.3,38.1,26.3, 25.7,22.7	1675,1535,1380, 1345,1130
19c	3.02(s,2H),2.39(m,4H),1.94(m,2H), 1.87(s,3H),1.53(s,6H)	198.2,160.7,130.2, 88.3,37.5,35.3,33.2, 25.9,21.7,21.6	1665,1540,1380, 1350,1135
20	10.20(s,1H),7.31(t,J=4.3Hz,1H),3.09 (s,2H),2.35-2.50(m,4H),2.31(s,2H), 2.17(s,2H),1.96(m,2H),1.02(s,6H)	204.5,198.0,171.3, 152.1,137.6,112.2, 50.6,43.0,37.6,31.4, 28.3,27.1,26.1,22.7, 22.3	1665,1615,1385, 1370,1240,1160, 1105,1080,1040, 735
22[f]	2.98(d,J=16.8Hz,1H),2.64(d,J=6.4Hz,1H), 2.48-2.02(m,5H),2.23(s,2H),2.15(brm,2H), 1.95(brm,2H),1.35(s,3H),1.04(s,3H),1.00 (s,3H)	207.1,197.5,167.4, 108.0,81.4,50.5,50.1, 42.4,40.3,36.6,32.2, 29.1,27.2,25.3,21.4,14.9	1720,1620,1390, 1295,1210,1140, 1115,1070,735
23	6.82(t,J=4.3Hz,1H),6.63(ddd,J=9.9,10.9, 16.9Hz,1H),6.09(d,J=10.9Hz,1H),5.21(d, J=16.9Hz,1H),5.12(d,J=10.9Hz,1H),2.51-2.37(m,4H),2.10-1.87(m,2H)	198.6,145.4,143.7, 135.5,133.0,129.4, 117.4,39.2,26.2,22.9, 16.5	1680,990,905

(a) Satisfactory microanalyses are obtained. (b) All spectra are recorded in $CDCl_3$ using TMS as internal standard. (c) As film (neat) for liquids, or KBr plates for solids. (d) Not

recorded. (e) Referred to the terminal olefinic isomer. (f) M.p.(°C): 150.0-151.0 (**8a**); 128.5-130.0(**8b**); 120.0-122.0 (**8c**); 99.0-101.0 (**8e**); 73.5-75.0 (**8f**); 70.0 (**10**); 64.0-65.5 (**19a**); 113.0-120.0 (**22**) (g) A mixture of cis and trans isomers. (h) $[\alpha]_D^{25}(CHCl_3)$: -77.0°(c 1.26, **12b**); -60.6° (c 1.34, **12d**); -53.9° (c 1.14, **12g**).

References and Notes

1. For reviews, see:(a) Seebach,D.; Colvin,E.W.; Lehr,F.; Weller,T. **Chimica 1979**, 33, 1. (b) Yoshikoshi,A.; Miyashita,M. **Acc. Chem. Res. 1985**,18,284. (c) Barret,A.G.M.; Graboski, G.G.; **Chem. Rev. 1986**, 86, 751. (d) Varma,R.S.; Kabalka,G.W. **Heterocycle 1986**, 24,2645. (e) Kabalka,G.W., Varma,R.S. **Org. Prep. Proced. Int. 1987**, 19, 283. (f) Fischer,R.H.; Weitz,H.M. **Synthesis 1980**, 261. (g) Ono,N.; Kaji,A. **Synthesis 1986**, 693. (h) Rosini,G.; Ballini,R. **Synthesis 1988**, 833.
2. For reviews, see: (a) Kornblum,N. **Angew. Chem., Int. Ed. Engl. 1975**, 14, 734. (b) Kornblum,N. In **Supplement F: The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives**; Patai,S., Ed.; Wiley: New York, **1982**; Part 1, pp 361-393.
3. Collman,J.P.; Hegedus,L.S.; Norton,J.R.; Finke, R.G. **Principles and Applications of Organotransition Metal Chemistry**;University Science Books: California, **1987**; pp 279-353.
4. (a) Tamura,R.; Hegedus,L.S. **J. Am. Chem. Soc. 1982**, 104, 3727. (b) Tamura,R.; Kai,Y.; Kakihana,M.; Hayashi,K.; Tsuji,M.; Nakamura,T.; Oda,D. **J. Org. Chem. 1986**, 51, 4375. (c) Ono,N.; Hamamoto,I.; Kaji,A. **J. Chem. Soc., Chem. Commun. 1982**, 821. (d) Ono,N.; Hamamoto,I.; Kaji,A. **J. Chem. Soc., Perkin Trans. 1 1986**, 1439.
5. Tamura,R.; Hayashi,K.; Kai,Y.; Oda,D. **Tetrahedron Lett. 1984**, 25, 4437. Also see ref 4b.
6. Tamura,R.; Kato,M.; Saegusa,K.;Kakihana,M.;Oda,D. **J. Org. Chem. 1987**, 52, 4121.
7. (a) Tamura,R.; Hayashi,K.; Kakihana,M.; Tsuji,M.; Oda,D. **Tetrahedron Lett. 1985**, 26, 851. (b) Tamura,R.; Hayashi,K.; Kakihana,M.; Tsuji,M.; Oda,D. **Chem. Lett. 1985**, 229. (c) Ono,N.; Hamamoto,I.; Yanai,T.; Kaji,A. **J. Chem. Soc., Chem. Commun. 1985**, 523. (d) Ono,N.; Hamamoto,I.; Kawai,T.; Kaji,A.; Tamura,R.; Kakihana,M. **Bull. Chem. Soc. Jpn. 1986**, 59, 405. Also see ref 4b.
8. Ono,N.; Hamamoto,I.; Kamimura,A.; Kaji,A. **J. Org. Chem. 1986**, 51, 3734.
9. Ono,N.; Hamamoto,I.; Kaji,A. **Bull. Chem. Soc. Jpn. 1985**, 58, 1863.
10. Tamura,R.; Tamai,S.; Suzuki,H. **Tetrahedron Lett. 1989**, 30, 2413.
11. Tamura,R.; Tamai,S.; Katayama,H.; Suzuki,H. **Tetrahedron Lett. 1989**, 30, 3685.
12. For reactions of various activated allylic compounds with nucleophiles,see: (a) Smith,A.B.III; Wexler,B.A.; Slade,J.S. **Tetrahedron Lett. 1980**, 21, 3237. (b) Takahashi, T.; Hori,K.; Tsuji,J. **Tetrahedron Lett. 1981**, 22, 119. (c) Takahashi,T.; Hori,K.; Tsuji,J. **Chem. Lett. 1981**, 1189. (d) Nelson,R.P.; McEuen,J.M.; Lawton,R.G. **J. Org. Chem. 1969**, 34, 1225. (e) Brocchini,S.J.; Eberle,M.; Lawton,R.G. **J. Am. Chem. Soc. 1988**, 110, 5211. (f) Seebach,D.; Knochel,P. **Helv. Chim. Acta 1984**, 67, 261. (g) Seebach,D.; Calderari,G.; Knochel,P. **Tetrahedron 1985**, 41, 4861. (h) Auvray,P.; Knochel,P.; Normant,J.F. **Tetrahedron 1988**, 44, 4495; 4509; 6095. Also see ref 17.
13. (a) Tamura,R.; Sato,M.; Oda,D. **J. Org. Chem. 1986**, 51, 4368. (b) Barton,D.H.R.; Fernandez,I.; Richard,C.S.; Zard,S.Z. **Tetrahedron 1987**, 43, 551.
14. (a) Tamura,R.; Kato,M.; Saegusa,K.; Oda,D.; Egawa,T.; Yamamoto,T. **J. Org, Chem. 1987**, 52, 1640. (b) Tamura,R.; Kusama,Y.; Oda,D. **J. Org. Chem. 1990**, 55, 595. (c) Sakakibara,T.; Manandhar,M.; Ohkita,N.; Ishido,Y. **Bull. Chem. Soc. Jpn. 1987**, 60, 3425.
15. Tsuji,J.; Shimizu,I.; Minami,I.; Ohashi,Y.; Sugiura,T.;Takahashi,K. **J. Org. Chem. 1985**, 50, 1523.
16. Cohen,T.; Kosarych,Z.; Suzuki,K.; Yu,L-C. **J. Org. Chem. 1985**, 50, 2965.
17. (a) Okamoto,S.; Kobayashi,Y.; Kato,H.; Hori,K.;Takahashi,T.; Tsuji,J.; Sato, F. **J. Org. Chem. 1988**, 53, 5590. (b) Okamoto,S.; Kobayashi,Y.; Sato,F. **Tetrahedron Lett. 1989**, 30, 4379.
18. Tamura,R.; Watabe,K.; Katayama,H.; Suzuki,H.; Yamamoto,Y. **J. Org. Chem. 1990**, 55, 408.