Rearrangements in the Reaction of β-Arylated Nitroparaffins with the Sodium Salt of Methanethiol

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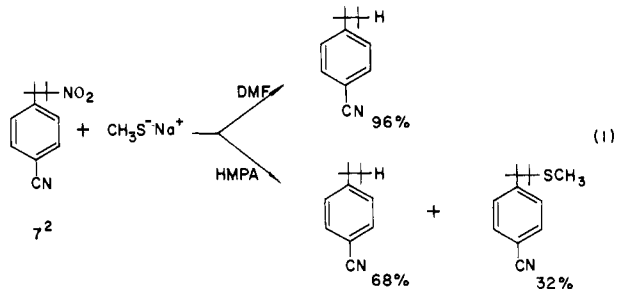
Abstract: Rearrangements occur when β-arylated nitroparaffins react with the sodium salt of methanethiol, a finding which provides support for the view that these reactions involve a spiro free radical intermediate.[1] By invoking spiro free radicals one can explain the striking solvent and substituent effects observed in the reactions of nitroparaffins with the sodium salt of methanethiol. A minor side reaction—fragmentation of radical anions derived from β-arylated nitroparaffins—is described.

The preceding paper[1] describes the reactions of tertiary nitroparaffins with the sodium salt of methyl mercaptan. Whereas the results obtained with purely aliphatic systems, and with α-nitrocumenes, are readily accounted for, it is not obvious how the transformations of β-arylated nitroparaffins can be rationalized; in particular, the fact that with β-arylated nitro compounds the reaction course depends on the solvent employed, and on the substitution in the aryl nucleus, requires explanation.

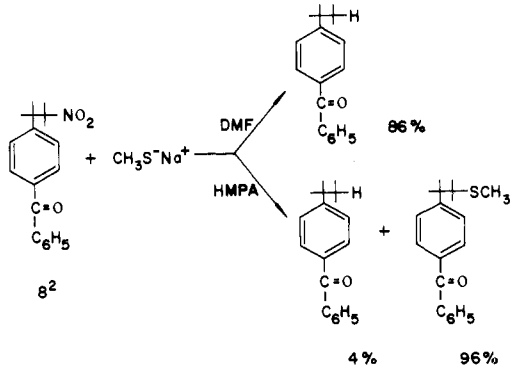
As shown in Table II of the accompanying paper,[1] treatment of a β-arylated nitro compound with the sodium salt of methyl mercaptan invariably brings about clean replacement of the nitro group by hydrogen—provided that the solvent is DMF. But if the reaction is carried out in HMPA replacement by hydrogen and by thiomethyl is observed, e.g., as in eq 1. Indeed,



(1)

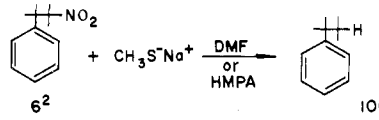
7[2]

with the *p*-benzoyl compound **8**[2] the thiomethyl ether comes close to being the sole product when the reaction is conducted in HMPA (eq 2). The behavior of the phenyl compound **6**[2] is at the other extreme; in contrast to all the other β-arylated nitro compounds replacement of the nitro group by hydrogen is the only process observed—even in HMPA (eq 3).



(2)

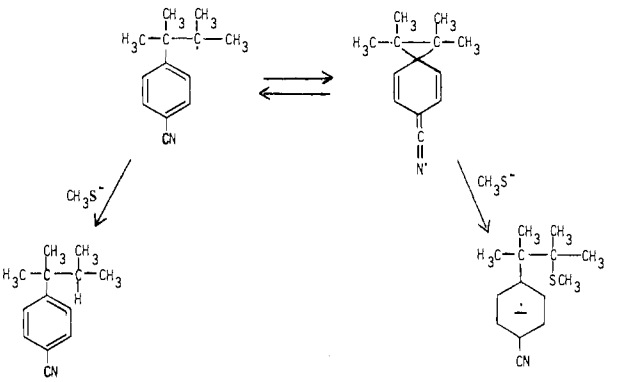
8[2]



(3)

6[2]

Scheme I



An explanation of these and the other facts in Table II of the accompanying paper has been proposed.[1] It is based on the idea that the radicals derived from β-arylated nitro compounds **7–10**[2] are differentiated from the other radicals by the ease with which they cyclize to spiro free radicals, and that thioethers are formed from the spiro free radicals as a consequence of a nucleophilic displacement by mercaptide ion on one of the carbons of the spirane ring (Scheme I). As shown in Scheme I, this displacement produces a relatively stable radical anion; the presumption is made that part of the driving force for displacement is provided by the relatively high stability of the radical anion which, of course, is manifested in the transition state. Furthermore, the proposed explanation requires that open-chain β-aryl radicals behave like the radicals derived from purely aliphatic nitro compounds; in other words, they abstract hydrogen from the methyl mercaptide ion (Scheme I). This seems an eminently reasonable assumption.

This not only provides a rationale for the behavior of the β-arylated nitro compounds (**7–10**)[2] but, in addition, offers a simple explanation for the fact that the unsubstituted β-aryl compound **6**[2] does not behave like the other β-arylated compounds. Cyclization of the unsubstituted radical **19**[2] will not

19[2]

be facilitated by delocalization such as is available to the substituted β-aryl radicals and, therefore, it should not occur as readily. Furthermore, any spiro free radicals which did form would be rather unlikely to undergo ring opening by the methyl mercaptide ion because the resulting unsubstituted radical anion would be of higher energy than radical anions containing electron-withdrawing substituents on the benzene ring. It is not surprising, then, that the unsubstituted radical **19**[2] exhibits the characteristics of a radical formed from a purely aliphatic nitro compound.

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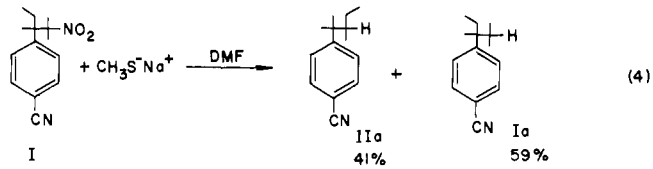
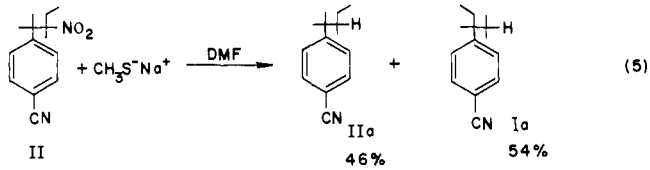
In the spiro radical of Scheme I the α and β carbons of the β-arylated nitro compound become equivalent. Thus, the mechanistic proposal embodied in Scheme I predicts that when β-arylated nitro compounds **7–10**[2] undergo replacement of nitro by thiomethyl, rearrangement will occur. And, while the prediction is less firm as regards replacement of nitro by hydrogen, it would be completely in accord with the proposed mechanism if rearrangement were also observed here. These predictions have now been tested.

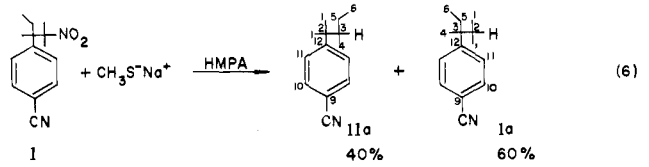
From the results of eq 4 and 5 it is apparent that with the isomeric β-arylated nitro compounds I and II replacement of

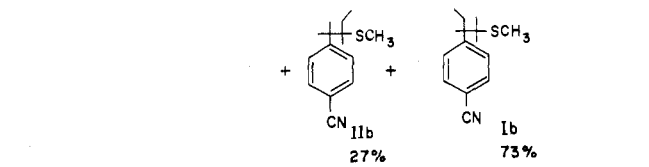


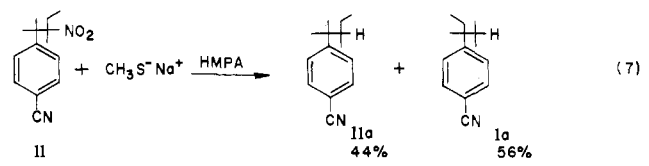


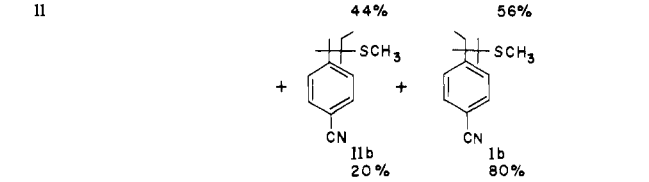
nitro by hydrogen involves a common intermediate, presumably a spiro radical analogous to that in Scheme I. Since, as pointed out earlier, replacement by hydrogen is believed to involve the open-chain radical, it follows that ring closure to the spiro structure must occur simultaneously with radical formation, or very soon thereafter. Furthermore, as shown in Scheme I, the spiro radical reverts to the open-chain radical and this must also be a rapid process.

As with the lower homologue, the reaction of I and II in HMPA results not only in substitution by hydrogen but, also, by thiomethyl (eq 6 and 7). In HMPA, as in DMF, replace-









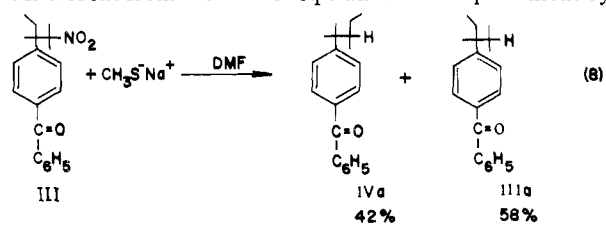
ment of the nitro group by hydrogen results in a mixture whose proportions are independent of the starting nitro compound; furthermore, the proportions from the reaction *in* HMPA are, within the experimental error, identical with those in DMF. As shown in eq 6 and 7, substitution by thiomethyl also occurs with rearrangement and the mixtures of thioethers obtained have, within the experimental error, the identical composition. Thus, as with hydrogen replacement, a common intermediate must be involved.

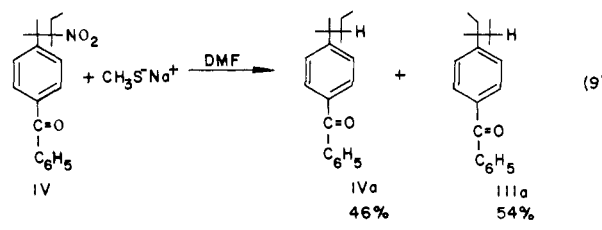
The mechanistic proposal of Scheme I does not provide a basis for predicting which of the two isomeric products resulting from hydrogen abstraction will preponderate. Reversion of the common spiro radical to an open-chain β-arylated radical should occur with a small preference for the more heavily substituted radical, i.e., the one with an ethyl group on the free-radical carbon. However, this radical has a larger steric requirement than the isomeric open-chain radical and, hence, its rate of hydrogen abstraction from thiomethoxide ion should be slower than with the less hindered radical. The data of eq 4–7 suggest that the second of these opposed factors may be more important but, in any event, the preference for hydrogen ending up on the less hindered position is not great.

In contrast, the postulate that thioether formation derives from a nucleophilic displacement by thiomethoxide ion on the spirane ring of the spiro radical leads to an unambiguous prediction: attack should occur preferentially at the less hindered carbon. As can be seen from eq 6 and 7 this is clearly the case.

The *p*-benzoylated systems III and IV on treatment with the sodium salt of methyl mercaptan in DMF, and in HMPA, gave the results shown in eq 8–11.

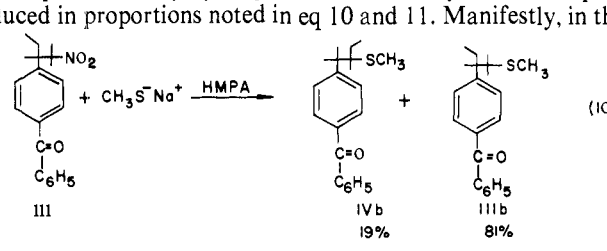
It is evident from the data of eq 8 and 9 that replacement by

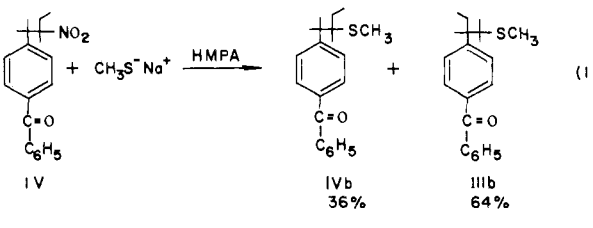




hydrogen is a process in which the α and β carbon atoms of the β-arylated nitro compounds III and IV become scrambled. Here, as with the *p*-cyano compounds of eq 4 and 5, both spiro ring closure and reversion to the open-chain radicals must occur rapidly. And, as in the *p*-cyano system, the preference for hydrogen being abstracted by the less hindered open-chain radical is not great.

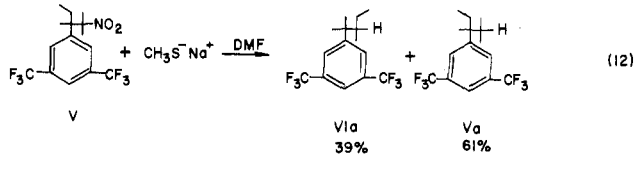
In HMPA nitro compounds III and IV undergo essentially no replacement by hydrogen;[3] the thiomethyl ethers are produced in proportions noted in eq 10 and 11. Manifestly, in the





course of undergoing substitution of nitro by thiomethyl the α and β carbon atoms of III and IV have not maintained their identity. In these experiments, especially that of eq 11, the purification of products is difficult because considerable fragmentation occurs (vide infra); it is easily possible that the differences in the proportions of isomeric thiomethyl ethers shown in eq 10 and 11 are not meaningful. However, there can be no doubt that regardless of whether one starts with III or IV the major product is the less hindered thiomethyl ether and this is consistent with the postulated nucleophilic displacement by methyl mercaptide ion on a common spiro radical.

The results obtained on treating bis(trifluoromethyl) compounds V and VI with the sodium salt of methyl mercaptan, superficially considered, appear to be at variance with the mechanistic proposal of this paper; in actuality, they fit very well. Consider first the reactions in DMF (eq 12 and 13). As



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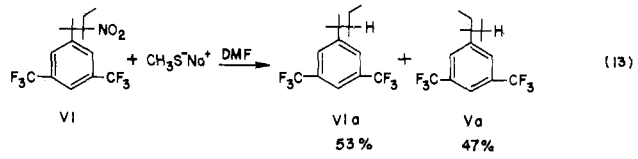
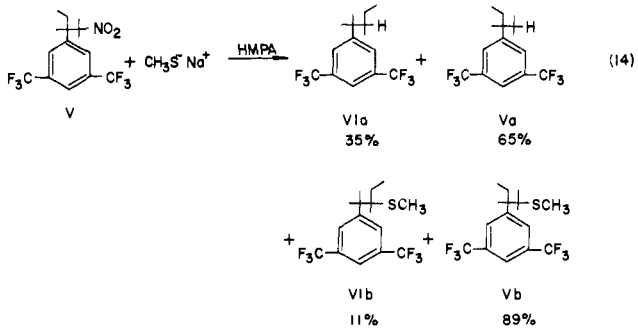


(13)

before, replacement of a nitro group by hydrogen proceeds with scrambling of the α and β carbon atoms; but now, for the first time, a preference is observed for hydrogen going to the more hindered radical (eq 13). To be sure, the preference is small, but the result of eq 13, taken in conjunction with that of eq 12, suggests that with the fluorinated compounds there is a memory effect. This rather marginal effect becomes more apparent in HMPA as can be seen from eq 14 and 15. Of



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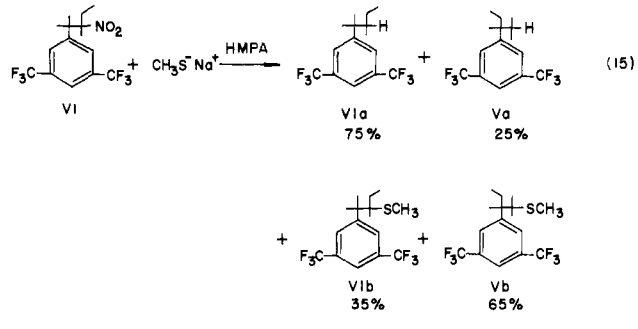


(15)

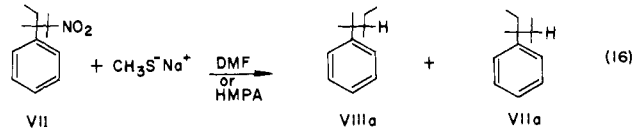
special interest is the fact that in one case (eq 15) replacement of nitro by hydrogen occurs with the formation of the more hindered isomer as 75% of the total.

It is clear from eq 12–15 that replacement of a nitro group by hydrogen occurs with scrambling of the α and β carbons, but this scrambling is, manifestly, incomplete. For while the disparity in the results of eq 12 and 13 is quite small this is certainly not the case with the processes of eq 14 and 15. In the reaction of eq 14 replacement of nitro by hydrogen results in the formation of the less hindered product as 65% of the total whereas in the reaction of eq 15 this product is but 25% of the total. Thus, complete scrambling of the α and β carbons does not accompany replacement of nitro by hydrogen.

These observations make sense if one accepts the idea that in the bis(trifluoromethyl) system the spiro radical analogous to that of Scheme I is not as well stabilized as a spiro radical which has a cyano group, or a benzoyl group, in the para position. Hence, the driving force for cyclization is smaller and, as a consequence, in the bis(trifluoromethyl) system cyclization of the open-chain radical to the spiro radical occurs relatively slowly. This longer life of the open-chain radical increases the probability that a significant fraction of the open-chain radicals initially produced from nitro compounds V and VI will, before they ever cyclize to spiro radicals, abstract a hydrogen atom from the methyl mercaptide ion, thereby maintaining the integrity of the α and β carbon atoms. In other words, the product distribution observed on replacing a nitro group by hydrogen is easy to understand on the basis that in the bis(trifluoromethyl) system cyclization prior to hydrogen abstraction is incomplete.

Turning now to the replacement of nitro by thiomethoxy it is seen (eq 14 and 15) that the product distribution bears no relationship to that observed when nitro is replaced by hydrogen; the less hindered thioether is the preferred product regardless of which nitro compound is employed. This is accommodated by the proposed mechanism which postulates that thiomethyl ethers arise from an S_N2 displacement by thiomethoxide ion on the spiro radical (Scheme I). Thus, thioether formation is not subject to a "memory effect" because it involves an intermediate in which the α and β carbons of the β-arylated nitro compound become equivalent. Here the product ratio is determined by the steric requirements of the two carbon atoms of the spiro ring and, not surprisingly, the less hindered position is more susceptible to attack by the thiomethoxide ion.[4]

Finally we consider β-arylated nitro compounds in which the aryl ring is phenyl. The studies of the accompanying paper[1] establish that the β-phenyl nitro compound **6**[2] differs from all the other β-arylated nitro compounds in that treatment with the sodium salt of methyl mercaptan produces no thioether—even in HMPA. Since thioethers are taken to arise from a nucleophilic displacement by methyl mercaptide ion on the spiro radical, failure to observe thioether formation with **6**[2] may well mean that here little or no cyclization to the spiro radical occurs.[16] That this is indeed the case is shown by experiments employing nitro compounds VII and VIII; very little scrambling of the α and β carbons of these compounds occurs when they are treated with the sodium salt of methyl mercaptan (eq 16 and 17).



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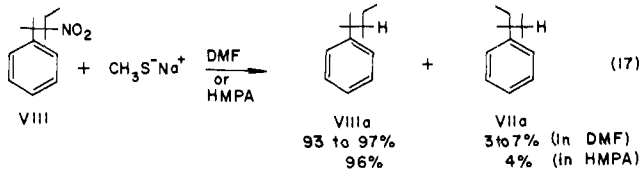
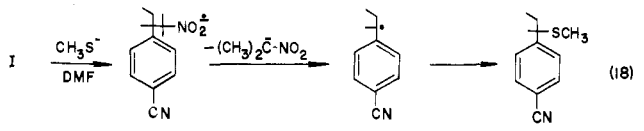


(17)

We see then that the reactions of β-arylated nitro compounds with the sodium salt of methyl mercaptan vary continuously between the extremes of complete rearrangement of the α and β carbons to almost no rearrangement. The mechanistic proposals of this, and the accompanying paper,[1] provide a simple explanation for what would otherwise be a most mysterious set of facts.

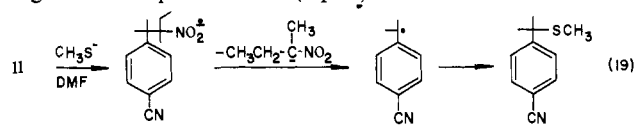
Fragmentation. In the preceding paper[1] brief notice is taken of the fragmentation process observed on treating β-arylated nitro compounds with the sodium salt of methyl mercaptan. Fragmentation accounts for only 2–3% of the product with nitro compounds **7–10**,[2] but when there is a nitro group in the para position of the aryl nucleus it becomes the major process (eq 24 of ref 1). At the other extreme, when the aryl nucleus is unsubstituted fragmentation is not detected.

A significant amount of fragmentation occurs with β-arylated nitro compounds I–VI and, therefore, the data of eq 4–15 are product ratios and not yields. Thus, the combined yield of the products shown in eq 4 is 72% but, in addition, an 11% yield of the fragmentation product X is isolated; i.e., extrusion of the 2-nitropropyl anion from the radical anion IX occurs as a minor process (eq 18). With the isomeric *p*-cyano compound



IX X

II fragmentation is more important; along with the two products of eq 5 (52% yield) there is obtained a 27% yield of the fragmentation product XII (eq 19).



XI XII

Fragmentation is also observed in HMPA. The reaction of eq 6 gives the compounds shown (in 65% yield) and, in addition, a 5% yield of XIII. Rather more striking is the 29% yield of fragmentation product XIV produced in the reaction of eq 7.

XIII XIV

It is noteworthy that each isomer gives but a single fragmentation product; from the reaction of eq 7 only *p*-cyanocumene (XIV) is found while in the reaction of eq 6 only XIII is isolated and there is no evidence of XIV. InMF the fragmentation product is a thioether and each isomer gives only a single thioether. Thus, the reaction of eq 18 gives none of thioether XII and the reaction of eq 19 gives none of X. Clearly, fragmentation occurs prior to rearrangement, i.e., prior to the formation of a spiro radical analogous to that of Scheme I.

It is also clear that fragmentation is enhanced by steric strain—a not very surprising result. Thus, with compounds **7–10**[2] of the accompanying paper fragmentation is a trivial side reaction but it becomes a significant competitor when the higher homologues I–VI are employed; indeed, in one instance it is the major process (vide infra). Furthermore, it will be seen that in each pair of isomers of the group I–VI the compound in which the nitro group is on the more heavily substituted carbon, i.e., is more strained sterically, is the one which undergoes more fragmentation.[5]

These results illustrate two general characteristics of the fragmentation process which are even more readily discerned in the reactions of the *p*-benzoylated nitro compounds III and IV. In DMF, as shown in eq 8, the nitro group of III is replaced by hydrogen (62% yield); in addition, the fragmentation product XV is produced (11% yield). In contrast, the reaction employing compound IV (eq 9) gives no less than a 43% yield of the cumyl sulfide XVI. And, in HMPA the reaction of III

XV XVI

with methyl mercaptide ion produces, in addition to the compounds of eq 10, an 11% yield of the fragmentation product XVII whereas that of eq 11 gives the products shown there in

XVII XVIII

a total yield of only 37% with fragmentation accounting for 55% of the starting nitro compound IV.[6]

With the bis(trifluoromethyl) compounds (V and VI) the same pattern is again followed: fragmentation occurs prior to rearrangement; and the more sterically strained nitro compound (VI) undergoes more fragmentation.

Finally, it is striking that the β-phenylated nitro compounds, VII and VIII, on treatment with the sodium salt of methyl mercaptan react cleanly according to eq 16 and 17; fragmentation is not observed. This, in conjunction with the results obtained with compounds I–VI, highlights the importance of resonance stabilization of the cumyl radical as a factor facilitating fragmentation.

Experimental Section

Caution: HMPA should be handled with great care since it has recently been found to cause cancer in laboratory animals.[15]

General Procedures. The reactions of tertiary nitro compounds with sodium thiomethoxide were carried out as described in the accompanying paper[1] with the exception that the system was purged of air by evacuating and then bleeding in argon. This process was repeated three times and then the solvent was frozen by liquid nitrogen. The system was evacuated to ca. 1 mm and the frozen solvent was allowed to thaw. This freeze–pump–thaw procedure was repeated two more times and then argon at 1 atm pressure was bled in. Reactions were allowed to proceed in the light bank[7] for as long as indicated in the individual cases. Workup involved pouring the reaction mixture into a tenfold excess of water and extracting with pentane, benzene, or ethyl ether. In some instances extraction with two of these solvents was employed. The combined extracts were dried ($MgSO_4$ or Na_2SO_4) and then the solvents were removed under reduced pressure. The resulting residual material is referred to as the crude product. With some of the hydrocarbon fractions NMR spectroscopy revealed the presence of small amounts of olefins; they were removed by permanganate oxidation. For each mmol of starting nitro compound 0.4 g of $KMnO_4$, 0.9 g of $MgSO_4$, 20 mL of acetone, and 4 mL of H_2O were used to treat the hydrocarbon fraction. The mixture was stirred at 25 °C for 16 h after which it was poured into saturated aqueous $NaHSO_3$, extracted with benzene, dried, and concentrated under reduced pressure.

NMR Spectroscopy. The ^1H NMR spectra were recorded on Varian A-60 and Perkin-Elmer R-32, 90 MHz spectrometers. The ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer. Wide-band proton decoupling and a spectral width of 4000 Hz were used. In most spectra the acquisition parameters follow: acquisition time, 1.024 s; pulse delay; 3 s; pulse width, 7–9 μs (90° pulse width = 14 μs); 8K data points.

Table V. Ratio IIa:Ia Produced in the Reaction of Equation 6 as Determined by ^{13}C NMR

carbon atom[a]	IIa:Ia	carbon atom[a]	IIa:Ia
1	41:59	6	33:67
2:3	47:53	10	40:60
3:2	41:59	11	41:59
4	39:61	12	39:61
5	33:67	av	40:60 ± 7

[a] See eq 6 for carbon numbering.

The structures of the starting nitro compounds I–VIII were established by unambiguous syntheses and, in each case, the NMR spectra were fully consistent with the structural assignments. The identity of the methyl groups used in the ratio determinations by ^1H NMR was made on the basis of their multiplicities. ^{13}C NMR assignments are shown in Tables I and II.[17] These assignments were made by comparison with chemical shifts predicted according to the equations of Lindeman and Adams[12] (see Tables III and IV).[17]

The ratios of the isomers Ia to IIa, IIIa to IVa, Va to VIa, and VIIa to VIIIa were determined in two ways: ^1H NMR and ^{13}C NMR spectroscopy. With ^1H NMR the expanded spectrum was recorded and the integrated singlets between 1.1 and 1.3 ppm due to the methyl groups on the quaternary carbon atom were used.

With ^{13}C NMR the isomer ratio was determined by comparison of the intensities of the corresponding carbon atoms. The tentative assignment given in Tables I and II was used and intensities were the computer-derived peak heights. As an example, all the ratios of intensities of the isomers IIa and Ia in the reaction of eq 6 are given in Table V. The averages of the ratios of all pairs are given in Table V as well as the largest deviation of a single value from the average.

Reaction of 3-*p*-Cyanophenyl-2,3-dimethyl-2-nitropentane (I) with Sodium Thiomethoxide. A. In DMF. Nitro compound I[8] (984 mg, 4 mmol) was allowed to react with 840 mg (12 mmol) of sodium thiomethoxide in 40 mL of DMF for 40 h according to the general procedure. The crude product (793 mg) was chromatographed through silica gel using hexane–benzene mixtures. The first fractions after distillation in a Kugelrohr apparatus at 100 °C and 1 mm consisted of a mixture of pure Ia and IIa (347 mg, 1.76 mmol): NMR ($CDCl_3$) δ 0.4–1.0 (m, 8.4 H), 1.18 (s, 1.91 H), 1.23 (s, 2.89 H), 1.4–2.3 (m, 2.5 H), 7.2–7.75 (m, 4 H). The ratio of the isomers was determined by NMR: IIa:Ia = 46:54. By ^{13}C NMR the ratio is IIa:Ia = 41:59 ± 4.

Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.69; H, 9.31; N, 6.77.

This was followed by a mixture of Ia and IIa contaminated with a little olefin (268 mg, 1.48 mmol). Finally, a fraction was obtained which, on Kugelrohr distillation at 80 °C and 1 mm, weighed 51 mg (0.25 mmol); this is the pure fragmentation product X, a thiomethyl ether.

Anal. Calcd for $C_{12}H_{15}NS$: C, 70.19; H, 7.37; N, 6.82. Found: C, 70.13; H, 7.52; N, 7.10.

IR (5% in $CHCl_3$): 3.33 (s), 4.46 (s), 6.29 (m) μ.

NMR (in $CDCl_3$): 0.83 (t, J = 7 Hz, 3 H), 1.68 (s), 1.73 (s), 1.6–2.4 (m, total of last 3 signal groups, 8 H), 7.61 ppm (s, 4 H).

B. In HMPA. Nitro compound I (984 mg, 4 mmol) was treated with sodium thiomethoxide (840 mg, 12 mmol) in 40 mL of HMPA for 2 h in the usual way. The crude product (839 mg) was chromatographed on silica gel using hexane–benzene and, then, benzene–ether mixtures. The first fractions were NMR-pure mixtures of Ia and IIa (391 mg, 1.95 mmol).

Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.45; H, 9.75; N, 6.94.

By NMR the ratio of the isomers is IIa:Ia = 41:59. ^{13}C NMR shows the ratio to be IIa:Ia = 40:60 ± 7.

This was followed by a mixture (96 mg) which by NMR was 68% Ia + IIa and 32% of the fragmentation product XIII. The next fraction was NMR-pure XIII (24 mg, 0.15 mmol). The next material to come off the column was NMR-pure IIb (33 mg, 0.13 mmol) and the final fraction was impure Ib (74 mg, 0.29 mmol).

Reaction of 2-*p*-Cyanophenyl-2,3-dimethyl-3-nitropentane (II) with Sodium Thiomethoxide. A. In DMF. Nitro compound II[8] (615 mg, 2.5 mmol) and sodium thiomethoxide (526 mg, 7.5 mmol) were allowed to react in 25 ml of DMF for 24 h following the general procedure. The crude product was chromatographed through silica gel with cyclohexane–ethyl acetate (50:1). The first fraction was a mixture of the two isomeric hydrocarbons Ia and IIa contaminated by a trace of olefinic impurities. Oxidation with $KMnO_4$ (vide supra) followed by Kugelrohr distillation at 100 °C and 1 mm gave a mixture consisting only of Ia and IIa (260 mg, 1.3 mmol). The NMR spectrum showed the ratio IIa:Ia to be 46:54. In a duplicate experiment the NMR ratio IIa:Ia = 41:59 and ^{13}C NMR gave IIa:Ia = 46:54 ± 4.

Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.81; H, 9.71; N, 6.77.

This was followed by a second fraction (130 mg, 0.68 mmol) which was identified by its NMR spectrum as pure *p*-cyanocumyl thiomethyl ether (XII).[1]

B. In HMPA. The nitro compound II[8] (663 mg, 2.7 mmol) was treated in the usual way with 630 mg (9 mmol) of sodium thiomethoxide in 30 mL of HMPA for 4 h. The crude product (548 mg) was chromatographed on silica gel using hexane–benzene mixtures and, then, benzene–ether mixtures. This gave, as the first fraction, a mixture (196 mg) of *p*-cyanocumene (XIV) and Ia and IIa. Preparative VPC effected the separation of XIV from Ia and IIa after which 57 mg (0.41 mmol) of pure *p*-cyanocumene (XIV)[1] was obtained by Kugelrohr distillation at 50 °C and 1 mm. The mixture of Ia and IIa was treated with permanganate (vide supra) to remove an olefinic impurity and, then, a benzene solution of the crude oxidation product was passed through silica gel. This gave pure Ia and IIa (90 mg, 0.43 mmol).

Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.40; H, 9.40; N, 6.71.

From the NMR spectrum the ratio IIa:Ia = 43:57 and by ^{13}C NMR the ratio IIa:Ia = 44:56 ± 6. In a duplicate experiment the NMR spectrum gave a ratio IIa:Ia = 47:53.

The second fraction to come off the silica gel column was the impure thiomethyl ether IIb which, after preparative VPC followed by Kugelrohr distillation at 1 mm, gave 17 mg (0.08 mmol) of pure IIb.

Anal. Calcd for $C_{15}H_{21}NS$: C, 72.84; H, 8.56; N, 5.66; S, 12.94. Found: C, 72.67; H, 8.71; N, 5.88; S, 13.11.

IR (neat): 3.34, 4.48, 6.25, 6.67, 11.98 μm.

NMR ($CDCl_3$): 0.93 (t, J = 7 Hz, 3 H), 1.12 (s, 3 H), 1.48 (s, 6 H), 1.53 (s, 3 H), 1.50 (q, J = 7 Hz, 2 H), 7.45–7.75 ppm (m, 4 H).

The third fraction (125 mg) was, by NMR analysis, 95% Ib and 5% IIb. This was followed by a fourth fraction (94 mg) consisting of the impure thiomethyl ether (Ib) which after preparative VPC and Kugelrohr distillation at 115 °C and 1 mm yielded 57 mg (0.24 mmol) of pure Ib.

Anal. Calcd for $C_{15}H_{21}NS$: C, 72.84; H, 8.56; N, 5.66; S, 12.94. Found: C, 72.70; H, 8.43; N, 5.50; S, 13.21.

Ir (neat): 3.34, 4.46, 6.21, 6.62, 15.50 μm.

NMR ($CDCl_3$): 0.66 (t, J = 7 Hz, 3 H), 1.24 (s, 6 H), 1.48 (s, 3 H), 1.77 (s, 3 H), 1.5–2.7 (m, 2 H), 7.57 ppm (s, 4 H).

2-(*p*-Benzoylphenyl)-2-nitrobutane. The lithium salt of 2-nitrobutane[9] (21.80 g, 200 mmol), 4-nitrobenzophenone (9.08 g, 40 mmol), 200 mL of HMPA, and a reaction time of 24 h were employed.[10] On workup 10.9 g of an orange oil was obtained; it was chromatographed through a short column of alumina using benzene as eluent. The resulting yellow oil (10.4 g) when Kugelrohr distilled at 0.006 mm and 120 °C gave 9.34 g of yellow oil which was essentially pure except for a small amount of an olefin produced during distillation. The olefin was destroyed by treatment with permanganate (vide supra) after which a benzene solution of the crude product was passed through a short alumina column. Removal of solvent gave 8.72 g (77% yield) of a colorless oil: NMR ($CDCl_3$) δ 0.90 (t, 3 H), 1.92 (s, 3 H), 2.10–2.70 (m, 2 H), and 7.20–8.00 (m, 9 H); IR (neat) μ 6.08 (C=O), 6.48 and 7.46 (NO_2).

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05; N, 4.94. Found: C, 72.34; H, 6.24; N, 4.90.

3-*p*-Benzoylphenyl-2,3-dimethyl-2-nitropentane (III). The lithium salt of 2-nitropropane[9] (4.75 g, 50 mmol), 2-(*p*-benzoylphenyl)-2-nitrobutane (4.75 g, 50 mmol), and 100 mL of HMPA were employed. The reaction was conducted in the light bank for 64 h. Workup yielded 3.46 g of an orange oil which was Kugelrohr distilled at 120 °C and 0.006 mm to give 2.63 g of a yellow oil. This 2.63 g contained a large amount of newly formed olefin. Crystallization from hexane gave 1.283 g (41% yield) of the pale yellow β-aryl nitro compound III: mp 92.5–94 °C; NMR ($CDCl_3$) δ 0.83 (t, 3 H), 1.50 (s, 6 H), 1.57 (s, 3 H), 1.50–2.50 (m, 2 H), 7.30–7.95 (m, 9 H).

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 74.01; H, 7.06; N, 4.31.

Reaction of 3-*p*-Benzoylphenyl-2,3-dimethyl-2-nitropentane (III) with Sodium Thiomethoxide. A. In DMF. Nitro compound III (325 mg, 1 mmol) and sodium thiomethoxide (210 mg, 3 mmol) were allowed to react in 10 mL of DMF for 18 h according to the general procedure. The crude product was chromatographed on silica gel using cyclohexane–ethyl acetate (50:1). The first fraction consisted of a mixture of IIIa and IVa contaminated with olefin. After $KMnO_4$ oxidation (vide supra) the pure mixture of IIIa and IVa was obtained (110 mg, 0.39 mmol). The ratio of IVa:IIIa = 42:58 as determined by NMR.

Anal. Calcd for $C_{20}H_{24}O$: C, 85.66; H, 8.63. Found: C, 86.04; H, 8.72.

The second fraction (52 mg) was a mixture of IIIa, IVa, and the thiomethyl ether XV and by NMR was shown to consist of ca. 0.06 mmol of XV and ca. 0.12 mmol of IIIa and IVa. The third fraction was essentially pure XV (12 mg, 0.04 mmol) and had two characteristic NMR singlets, one δ 1.71 and the other δ 1.78. These are presumably due to the methyl on the quaternary carbon atom and to the $-SCH_3$.

B. In HMPA. Nitro compound III (325 mg, 1 mmol) and sodium thiomethoxide (210 mg, 3 mmol) were allowed to react in 10 mL of HMPA for 30 min according to the general procedure. The crude product was chromatographed on silica gel with cyclohexane–ethyl acetate (50:1). Based on its NMR spectrum the first fraction (26 mg) consisted of slightly impure 2-*p*-benzoylphenylbutane (XVII). The second fraction (80 mg) was shown by NMR to be a mixture of XVII (ca. 0.17 mmol) and the thiomethyl ether IVb (ca. 0.12 mmol). The third fraction (120 mg) was impure thiomethyl ether IIIb and by NMR was judged to contain ca. 0.23 mmol of IIIb. The fourth fraction was pure IIIb (91 mg, 0.28 mmol). For analysis it was Kugelrohr distilled at 100 °C and 0.01 mm.

Anal. Calcd for $C_{21}H_{26}OS$: C, 77.25; H, 8.03; S, 9.82. Found: C, 76.93; H, 7.55; S, 10.06.

Reaction of 2-*p*-Benzoylphenyl-2,3-dimethyl-3-nitropentane (IV) with Sodium Thiomethoxide. A. In DMF. The nitro compound IV[8] (325 mg, 1 mmol) and sodium thiomethoxide (210 mg, 3 mmol) were allowed to react in 10 mL of DMF for 18 h according to the general procedure. The crude product was chromatographed through silica gel with cyclohexane–ethyl acetate (50:1). The first fraction was a mixture of IIIa and IVa contaminated with a little olefinic material. Permanganate oxidation (vide supra) gave the pure mixture of IIIa and IVa (75 mg, 0.27 mmol). By NMR, IVa:IIIa = 46:54.

Anal. Calcd for $C_{20}H_{24}O$: C, 85.66; H, 8.63. Found: C, 85.67; H, 8.62.

IR (4% in $CHCl_3$): 3.38 (s), 6.10 (s), 6.27 (m), 7.87 (s) μ.

NMR ($CDCl_3$): 0.45–1.05 (complex), 1.21 and 1.26 (s each, α-methyl groups of the two isomers), 1.55–2.15 (complex, total 15 H), 7.25–7.95 ppm (complex, 9 H). The NMR spectrum revealed that the second fraction (45 mg) consisted of ca. 10 mmol of IIIa and IVa and ca. 0.06 mmol of *p*-benzoyl-α-thiomethoxycumene (XVI). The third fraction was the pure thioether XVI[1] (100 mg, 0.37 mmol).

B. In HMPA. Nitro compound IV (325 mg, 1 mmol) and sodium thiomethoxide (210 mg, 3 mmol) were allowed to react in 10 mL of HMPA for 30 min according to the general procedure. The crude product was chromatographed on silica gel with cyclohexane–ethyl acetate (100:1). The first fraction consisted of pure *p*-benzoylcumene XVIII (50 mg, 0.22 mmol), the NMR spectrum of which was identical with that of an authentic sample.[1] By NMR the second fraction (38 mg) consisted of the cumene XVIII (ca. 0.07 mmol), *p*-benzoyl-α-methylstyrene (ca. 0.03 mmol), IVb (ca. 0.045 mmol), and a trace of IIIb. The third fraction (180 mg) was a three-component mixture which on being rechromatographed gave two mixtures. The first of these (70 mg) consisted of IVb (ca. 0.085 mmol) and the *p*-benzoyl cumyl thiomethyl ether XVI (ca. 0.16 mmol). The second (95 mg) consisted of IIIb (ca. 0.23 mmol) and XVI (ca. 0.07 mmol).

Reaction of 3-*m,m'*-Bis(trifluoromethyl)phenyl-2,3-dimethyl-2-nitropentane (V) with Sodium Thiomethoxide. A. In DMF. Nitro compound V[8] (425 mg, 1.19 mmol) and sodium thiomethoxide (500 mg, 7.14 mmol) were allowed to react in 12 mL of DMF for 24 h according to the general procedure. The crude product was chromatographed on silica gel with cyclohexane. The first fraction (300 mg) consisted of Va and VIa and a relatively large amount of an olefin which, from its GLC characteristics, did not appear to be a fragmentation product. From the NMR spectrum it appeared that this first fraction contained ca. 0.35 mmol of the olefin(s) and ca. 0.61 mmol of Va and VIa. The olefin was removed by the permanganate oxidation procedure (vide supra) and this gave 180 mg (0.58 mmol) of pure Va and VIa. By NMR the ratio of VIa:Va = 39:61.

Anal. Calcd for $C_{15}H_{18}F_6$: C, 57.68; H, 5.81. Found: C, 57.83; H, 5.92.

A second fraction (18 mg) was obtained. This was 0.07 mmol of the fragmentation product, 2-*m,m'*-bis(trifluoromethyl)phenyl-2-thiomethylbutane.

B. In HMPA. Nitro compound V[8] (714 mg, 2 mmol) was allowed to react with sodium thiomethoxide (420 mg, 6 mmol) in 20 mL of HMPA for 3 h according to the general procedure. GLC analysis of the crude product revealed the presence of a ca. 5% yield of the fragmentation product 2-*m,m'*-bis(trifluoromethyl)phenylbutane. The crude product was chromatographed on silica gel using cyclohexane. The first fraction (260 mg) was a mixture of Va and VIa and an olefin. By NMR the ratio of VIa:Va = 35:65.

By NMR the second fraction (100 mg) was found to consist of ca. 0.10 mmol of VIb and ca. 0.18 mmol of Vb. The third fraction was Kugelrohr distilled at 80 °C and 1 mm; the resulting 240 mg was the pure thioether Vb (0.67 mmol).

Anal. Calcd for $C_{16}H_{20}SF_6$: C, 53.61; H, 5.63; S, 8.95. Found: C, 53.66; H, 5.77; S, 9.00.

IR (5% in $CHCl_3$): 3.37 (s), 6.21 (w), 6.87 (m), 7.35 (s) μ.

NMR ($CDCl_3$): 0.70 (t, 3 H), 1.22 and 1.26 (s, each, total 6 H), 1.53 (s, 3 H), 1.71 (s, 3 H), 1.7–2.7 (c, 2 H), 7.78 (broad s, 1 H), 7.90 ppm (broad s, 2 H).

Reaction of 2-*m,m'*-Bis(trifluoromethyl)phenyl-2,3-dimethyl-3-nitropentane (VI) with Sodium Thiomethoxide. A. In DMF. The nitro compound VI[8] (357 mg, 1 mmol) and sodium thiomethoxide (420 mg, 6 mmol) were allowed to react in 10 mL of DMF for 24 h according to the general procedure. The crude product was chromatographed on silica gel with cyclohexane. The first fraction consisted of Va, VIa, and an olefinic impurity. The latter was removed by treatment with $KMnO_4$ (vide supra) and the resulting oil was Kugelrohr distilled at 90 °C and 12 mm. This gave 210 mg (0.67 mmol) of Va and VIa. By NMR the ratio VIa:Va = 53.47.

Anal. Calcd for $C_{15}H_{18}F_6$: C, 57.67; H, 5.81. Found: C, 57.55; H, 5.95.

IR (5% in $CHCl_3$): 3.37 (s); 6.17 (w); 6.85 (m); 7.33 (s) μ. NMR ($CDCl_3$): δ 0.45–1.05 (c), 1.27 (s), 1.30 (s), 1.55–2.2 (c) (total of preceding signals 15 H), 7.65–7.9 (c, 3 H).

The second chromatographic fraction consisted of 35 mg (0.136 mmol) of 3,5-bis(trifluoromethyl)-α-thiomethoxycumene.[1]

B. In HMPA. Nitro compound VI[8] (714 mg, 2 mmol) and sodium thiomethoxide (420 mg, 6 mmol) were allowed to react in 20 mL of HMPA for 3 h according to the general procedure. The crude product was chromatographed on silica gel with hexane. The first fraction (390 mg) was a mixture of Va, VIa, and 3,5-bis(trifluoromethyl)cumene.[1] By NMR it was found that ca. 0.33 mmol of the cumene was present along with ca. 0.90 mmol of a mixture of Va and VIa. The ratio of VIa:Va was 75:25.

Using a hexane–benzene mixture (3:2) as the eluent a second fraction was obtained; this, when Kugelrohr distilled at 80 °C and 1 mm, gave 60 mg (0.17 mmol) of the pure thiomethyl ether VIb.

Anal. Calcd for $C_{16}H_{20}SF_6$: C, 53.61; H, 5.63; S, 8.95. Found: C, 53.45; H, 6.07; S, 9.01.

IR (5% in $CHCl_3$): 3.33 (s), 6.17 (w), 6.80 (s), 7.30 (s) μ.

NMR ($CDCl_3$): 0.95 (t, 3 H), 1.3–1.8 (complex, with two singlets at 1.50 and 1.54 ppm, total 14 H), 7.75 (broad s, 1 H), 8.00 ppm (broad s, 2 H).

Fraction 3 (180 mg) was found by NMR to consist of the thioether VIb (ca. 0.10 mmol) and its isomer Vb (ca. 0.40 mmol). The fourth fraction (40 mg) was slightly impure Vb (0.11 mmol).

3-*p*-Aminophenyl-2,3-dimethyl-2-nitropentane. 3-*p*-Nitrophenyl-2,3-dimethyl-2-nitropentane[8] (9.0 g, 33.8 mmol) was dissolved in 70 mL of absolute ethanol and 70 mL of ethyl acetate and hydrogenated over 0.19 g of platinum oxide at ca. 50 lb pressure until 101 mmol of hydrogen was taken up. After the catalyst and the solvent were removed a small portion of the amine was recrystallized for analysis from cyclohexane as pale yellow needles, mp 78.5–80 °C.

Anal. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.83. Found: C, 65.85; H, 8.60; N, 11.99.

IR ($CDCl_3$): 2.86–2.99 (NH_2), 3.33 (CH), 6.17 and 6.58 (NO_2) μm.

NMR ($CDCl_3$): δ 0.68 (t, 3 H), 1.37, 1.42, 1.50 (s each, total 9 H), 1.6–2.6 (m, 2 H), 3.67 (br s, 2 H), 6.58 and 7.03 (AA'BB' system, J_{AB} = 8.5 Hz, 4 H).

3-Phenyl-2,3-dimethyl-2-nitropentane (VII). The major portion (8 g) of the crude *p*-amino compound obtained in the preceding experi-

ment was diazotized and treated with hypophosphorous acid.[11] This gave, after distillation at 120 °C and 1 mm, 6.15 g (90% yield) of VII, a pale yellow oil.

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.66; N, 6.33. Found: C, 70.50; H, 8.69; N, 6.22.

IR ($CHCl_3$): 3.33 (CH), 6.55 (NO_2), 7.46 (NO_2) μm.

NMR ($CDCl_3$): δ 0.67 (t, 3 H), 1.42 and 1.51 (s each, total 9 H), 1.6–2.6 (m, 2 H), 7.26 (s, 5 H).

Reaction of 3-Phenyl-2,3-dimethyl-2-nitropentane (VII) with Sodium Thiomethoxide. A. In DMF. The nitro compound VII (876 mg, 4 mmol) and sodium thiomethoxide (840 mg, 12 mmol) were allowed to react in 40 mL of DMF for 48 h following the general procedure. The crude product was chromatographed on silica gel with pentane and then Kugelrohr distilled at 50 °C and 1 mm. In this way 605 mg (87% yield) of 3-phenyl-2,3-dimethylpentane (VIIa) was obtained.

Anal. Calcd for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.58; H, 11.46.

NMR ($CDCl_3$): δ 0.59 (t, J = 7 Hz, 3 H), 0.61 (d, J = 7 Hz, 3 H), 0.89 (d, J = 7 Hz, 3 H), 1.16 (s, 3 H), 1.35–2.2 (m, 3 H), 7.05–7.45 (m, 5 H).

By ^{13}C NMR it was found that this product was actually 7% VIIIa and 93% VIIa ± 2. A duplicate experiment gave VIIIa:VIIa = 1:99 ± 2.

B. In HMPA. The nitro compound VII (876 mg, 4 mmol) and sodium thiomethoxide (840 mg, 12 mmol) were allowed to react in 40 mL of HMPA for 22 h in the usual way. The crude product was chromatographed through silica gel using pentane. This gave an oil which was contaminated with ca. 2% olefin. After the olefin was removed by treating with $KMnO_4$ (vide supra) and Kugelrohr distillation at 50 °C and 1 mm, 521 mg (74% yield) of a colorless liquid was obtained.

Anal. Calcd for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.68; H, 11.41.

^{13}C NMR showed that this product was 7% VIIIa and 93% VIIa ± 2. A duplicate experiment gave a product with the identical product ratio.

2-Phenyl-2,3-dimethyl-3-nitropentane (VIII). 2-*p*-Nitrophenyl-2,3-dimethyl-3-nitropentane[8] (6.65 g, 25 mmol) in 100 mL of absolute ethanol was hydrogenated over 0.15 g of platinum oxide at ca. 50 lb pressure. After 15 min 75 mmol of hydrogen was consumed. Removal of the platinum and ethanol gave 6.50 g of an oil which was dissolved in benzene and extracted with 0.3 N hydrochloric acid. The extract was rendered alkaline and the crude amine (6.15 g) was deaminated by diazotization and treatment with H_3PO_2.[11] The crude product (5.17 g) was Kugelrohr distilled at 100 °C and 1 mm and, then, chromatographed on silica gel using hexane–ether (19:1). This gave 4.66 g (84% yield) of pure 2-phenyl-2,3-dimethyl-3-nitropentane (VIII) as a white solid, mp 49–50 °C.

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.35; H, 8.75; N, 6.56.

NMR ($CDCl_3$): δ 0.75 (t, 3 H), 1.37 (s, 3 H), 1.49 (s, 6 H), 1.53 (m, 1 H), 2.50 (m, 1 H), and 7.15–7.50 (m, 5 H). IR: cm^{-1} 1520 and 1345 (NO_2).

Reaction of 2-Phenyl-2,3-dimethyl-3-nitropentane (VIII) with Sodium Thiomethoxide. A. In DMF. The nitro compound VIII (876 mg, 4 mmol) and sodium thiomethoxide (840 mg, 12 mmol) were allowed to react in 40 mL of DMF for 48 h following the general procedure. The crude product was chromatographed through silica gel using pentane and then Kugelrohr distilled at 50 °C and 1 mm. This gave 614 mg (88% yield) of a colorless oil.

Anal. Calcd for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.53; H, 11.48.

NMR ($CDCl_3$): δ 0.55–1.10 (m, 7 H), 1.21 (s, 6 H), 1.10–1.90 (m, 2 H), 7.0–7.5 (m, 5 H).

^{13}C NMR showed that the product was 93% VIIIa and 7% VIIa ± 2. A duplicate experiment gave a product with the ratio VIIIa:VIIa = 97:3 ± 2.

B. In HMPA. The nitro compound VIII (876 mg, 4 mmol) and sodium thiomethoxide (840 mg, 12 mmol) were allowed to react in 40 mL of HMPA for 16 h according to the general procedure. Chromatography of the crude on silica gel with pentane, followed by Kugelrohr distillation at 50 °C and 1 mm, gave 612 mg (87% yield) of a colorless oil.

Anal. Calcd for $C_{13}H_{20}$: C, 88.57; H, 11.43. Found: C, 88.68; H, 11.59.

^{13}C NMR showed that the product was 96% VIIIa and 4% VIIa ± 2.

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Supplementary Material Available: ^{13}C NMR chemical shifts for Ia, IIa, V, Vb, VI, VIb, VIIa, and VIIIa (Tables I–IV) (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Part 21 in the series "Substitution Reactions Which Proceed via Radical Anion Intermediates". For the preceding paper see N. Kornblum, S. C. Carlson, and R. G. Smith, *J. Am. Chem. Soc.*, preceding paper in this issue.
(2) The numbering of this compound corresponds to that employed in the preceding paper.
(3) This is not a surprising result when it is recalled that the lower homologue **8**[2] gives only a trace of the product in which nitro is replaced by hydrogen (cf. Table II of ref 1).
(4) The difference in proportions of thioethers produced in eq 14 and 15 is, in our opinion, more likely to prove apparent rather than real, for the experiments of eq 14 and 15, in contrast to most of the others, were only done once. But regardless of the explanation for the discrepancy there can be no doubt about the essential point which is that here, too, scrambling occurs.
(5) The fact that the radical anion of *tert*-nitrooctane expels a nitrite ion about 250 times faster than the radical anion of *tert*-nitrobutane was reported by A. K. Hoffmann, W. G. Hodgson, D. L. Maricle, and W. H. Jura, *J. Am. Chem. Soc.*, **86**, 636 (1964), in their classical study of cleavage reactions of aliphatic tertiary nitro radical anions. And these authors clearly recognized that the greater instability of the *tert*-nitrooctane radical anion derives from greater steric strain at the tertiary center.
(6) The fragmentation products in this case consist of XVIII (29%), the thiomethyl ether XVI (23%), and *p*-benzoyl-α-methylstyrene (3%).
(7) The light bank consists of two ordinary 20-W fluorescent lights.
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