

Radical Reactions of Trimethylaluminium with a Sterically Hindered Chloro-nitroso-compound

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Trimethylaluminium does not methylate 1-chloro-1-nitroso-2,2,6,6-tetramethylcyclohexane (I), but functions as an electron donor and initiator of radical reactions that lead ultimately to products (II)–(V), oxime derivatives, and an imine as outlined in reaction (1). E.s.r. studies support the intermediacy of iminyl radical (VI) which can undergo ring opening to the cyano-substituted radical (VII). For a kinetic e.s.r. study of this isomerisation the iminyl radical (VI) was generated from the diphenylmethyl oxime ether (XI) by reaction with *t*-butoxyl radicals. Combination of radical (VII) with iminoxyl radicals gives rise to the oxime ether (IV). The same product can be obtained by photolysis of the oxalate (XIII) and this supports the radical nature of the process.

In recent papers¹ we have reported that organometallic reagents (containing Mg, Li, Cu, or Cd) can attack α -chloro-nitroso-compounds² either as alkylation agents or as (single) electron donors. The first type of reaction leads to a nitrene and the second *via* a hydroxyimino radical to an oxime as exemplified by the overall Grignard reactions in Scheme 1. The second type of reaction is particularly favoured when the chloro-nitroso-compound is sterically hindered as in 1-chloro-1-nitroso-2,2,6,6-tetramethylcyclohexane (I). In this case the group R from the Grignard reagent does no longer end up in a nitrene but in a (dimeric) hydrocarbon RR, while the oxime anion and chloride anion combine with $MgBr^+$.

Reaction of Trimethylaluminium with (I).—With trimethylaluminium as the organometallic reagent (THF complex in *n*-hexane), reaction with (I) gives no nitrene as expected for steric reasons, but somewhat unexpectedly no oxime ether. Instead, a variety of oxime derivatives (II)–(IV) in a total yield of 55% together with the imine (V) (40%) and methane (mass spectrometry) are formed. The structure of the isolated products suggests that the oxime ethers arise by combination of hydroxyimino radicals with various radicals X derived from the solvent and the substrate.³

The methyl radicals in Scheme 2 abstract hydrogen from THF and also from hexane, thus leading to the oxime derivative (II) (a kind of acetal) and (III) (a mixture of hex-2- and -3-yl ethers). Scheme 2 does not necessarily imply that *free* methyl radicals are generated: presumably the radicals remain incorporated in an aluminium complex in such a way that they cannot escape to form ethane for instance.

When cumene, with its easily abstractable tertiary hydrogen, is added as a co-solvent, the corresponding cumyl ether is isolated in >40% yield. This supports the radical nature of oxime ether formation.

In the presence as well as in the absence of cumene, the imine yield always ranges from 40 to 50%. Its formation is typical for aluminium alkyl reactions and so far, it has been found to be unimportant when other organometallic compounds react with (sterically hindered) chloro-nitroso-compounds.

The production of imine and particularly the formation of the cyano-derivative (IV) strongly suggests that iminyl radicals are involved, as explained below.

Iminyl Radicals.—Iminyl radicals have been studied in the past decade mainly by Symons⁴ at low temperature in a matrix and by Ingold *et al.*⁵ in solution. The latter authors generated iminyl radicals by hydrogen abstraction from ketimines and

found that these species readily undergo β -fission, thus leading to fragmentation products with a cyano-group.

A mechanistically similar process with the sterically hindered cyclic radical (VI) triggers ring opening and generates the tertiary radicals (VII) with a terminal cyano-group. Combination of this radical with a hydroxyimino radical makes formation of the oxime ether (IV) plausible. In this connection it is interesting to note that the unsubstituted cyclobutyliminyl radical also undergoes ring opening, but that the next higher (cyclopentyl) homologue does not.⁶ In fact the 4-cyanobutyl radical cyclises irreversibly to the cyclopentyliminyl radical.⁷ The influence of substituents has not been studied.

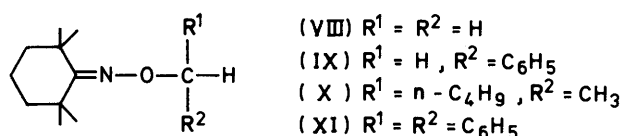
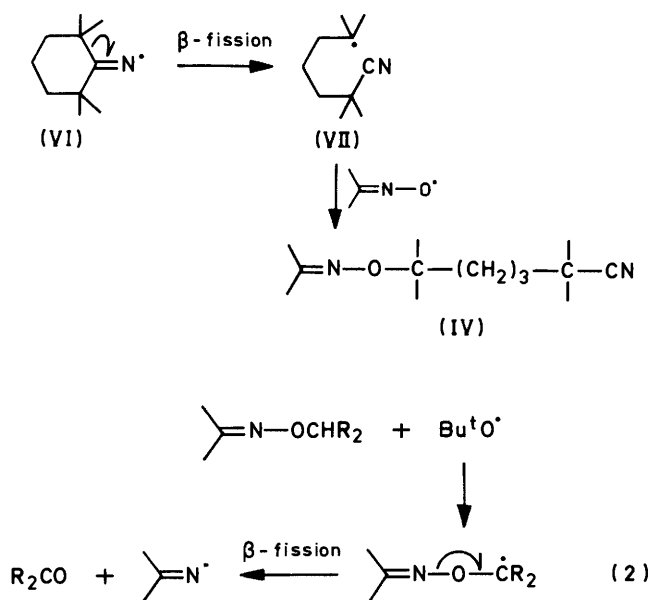
Forrester *et al.*⁸ have recently shown that iminyl radicals can also be generated from oxime ethers by reaction with *t*-butoxyl radicals [reaction (2)]. Considering that oxime ethers are important products in our reaction of trimethylaluminium with sterically hindered α -chloro-nitroso-compounds, we investigated the behaviour of a variety of such ethers derived from 2,2,6,6-tetramethylcyclohexanone oxime towards *t*-butoxyl radicals. Reactions were carried out by photolysing the oxime ethers (VIII)–(XI) in the presence of di-*t*-butyl peroxide in the cavity of an e.s.r. spectrometer. In all cases a transient signal was detected with a_N 10.4, a_H 0.6 G (6 H), and g 2.0031. Hyperfine coupling with only six hydrogens indicates that in the 2,2,6,6-tetramethylcyclohexyliminyl radical the four methyl groups are not equivalent. Models suggest that the two equatorial methyl groups are responsible for the observed coupling. These a_N and g values closely resemble those reported by Ingold *et al.*⁵ for the radical obtained by photolysing di-*t*-butyl peroxide in the presence of di-*t*-butyl ketimine, a_N 1.31 G, a_H 1.0 G (18 H), and g 2.0032.

Somewhat surprisingly in a similar reaction with 2,2,6,6-tetramethylcyclohexylimine we could not detect the corresponding iminyl radical. Apparently the imine hydrogen in our cyclic ketimine is less easily accessible to *t*-butoxyl radicals than in di-*t*-butyl or diadamantyl ketimine.⁵

In the oxime ethers (VIII)–(XI) the abstractable hydrogen is further removed from the highly substituted ring and this makes these compounds more suitable than the ketimine as precursors for iminyl radicals.

It should be pointed out that e.s.r. spectra of iminyl radicals can only be obtained when solutions are thoroughly oxygen-free.⁹ Upon admission of oxygen, rapid oxidation takes place to the corresponding hydroxyimino radicals, characterised by their three times higher a_N values.¹⁰ In the absence of oxygen, iminyl radicals decay slowly because of β -fission.

Returning to the reaction of trimethylaluminium with



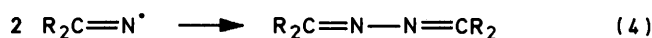
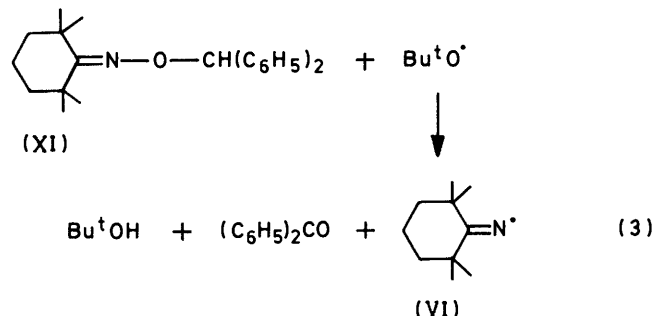
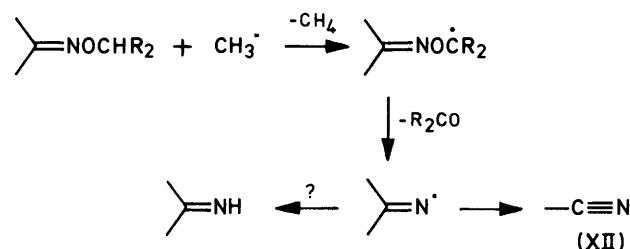
complexes leading to amines. A similar reaction with α -chloro-nitroso-compounds could trivially lead to an α -chloro-amine, *i.e.* formally the HCl adduct of a ketimine.

Kinetics of Iminyl Radical Decay.—The diphenylmethyl oxime ether (XI) is a particularly suitable source for generating the iminyl radical (VI) for kinetic studies of its decay [reaction (3)]. The by-product benzophenone does not interfere with the t-butoxy radicals. Thus direct photolysis in the cavity of the e.s.r. spectrometer of di-t-butyl peroxide and the oxime ether (XI) dissolved in rigorously oxygen-free toluene in the temperature range -55 to $+10^\circ\text{C}$, provides the typical e.s.r. spectrum of the iminyl radical (VI). When irradiation is stopped its decay can simply be determined by following the signal decrease.

At temperatures below -55°C we find a second-order decay. This may be due to dimerisation as suggested by Ingold *et al.*⁵ for the decay of the sterically hindered di-t-butyl ketimine at low temperatures [reaction (4)]. At higher temperatures (up to 10°C) the decay becomes first order. This must be attributed to β -splitting [(VI) \rightarrow (VII)] also found earlier for di-t-butyl ketimine.⁵ The Arrhenius parameters for the ring opening (VI) \rightarrow (VII) are represented by $\ln(k/s^{-1}) = 16.4 \pm 2 - (8.2 \pm 2.0 \text{ kcal mol}^{-1})/RT$. This equation implies a half-life of *ca.* 0.2 s at 0°C . This means that decomposition is of the same order as that of di-t-butyl ketimine (half-life at 0°C *ca.* 0.1 s).

With the benzyl ether (IX) as the iminyl radical source, essentially the same results were obtained. Although benzaldehyde is now formed, which can give benzoyl radicals by reaction with $\text{Bu}^t\text{O}^\bullet$, this does not interfere with the iminyl radical decay.

Decay Product Analysis.—For product studies we employed as a thermal source for t-butoxy radicals di-t-butyl peroxalate (TBPO) instead of di-t-butyl peroxide. In this way we avoid the danger of photolysing some of the products arising from



reaction (2). TBPO decomposes in benzene at 30° and in the presence of the diphenylmethyl oxime ether (XI), the following products can be isolated after 10% conversion: $\text{HC}(\text{CO}_3)_2\text{-CH}_2\text{CH}_2\text{CH}_2(\text{CH}_3)_2\text{CN}$ (4%), $\text{CH}_2=\text{C}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{-}(\text{CH}_3)_2\text{CN} + (\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{C}(\text{CH}_3)_2\text{CN}$ (total olefin yield 5.7%), together with benzophenone (10%) and t-butyl alcohol. The cyano-substituted products arise obviously from disproportionation of iminyl radicals (VII).

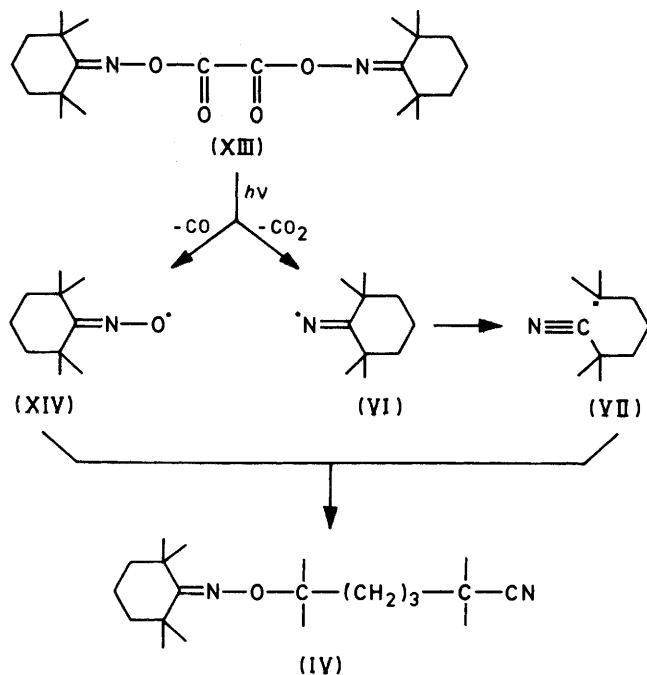
The same products were found when the benzyl ether (IX) instead of the diphenylmethyl ether (XI) was employed. Instead of benzophenone only traces of benzaldehyde could be detected, as might have been expected in view of its reactivity towards t-butoxy radicals.

Earlier we showed that one of the products from the reaction of trimethylaluminium with the chloro-nitroso-compound (I) is the cyano-substituted oxime ether (IV) [*cf.* reaction (1)].

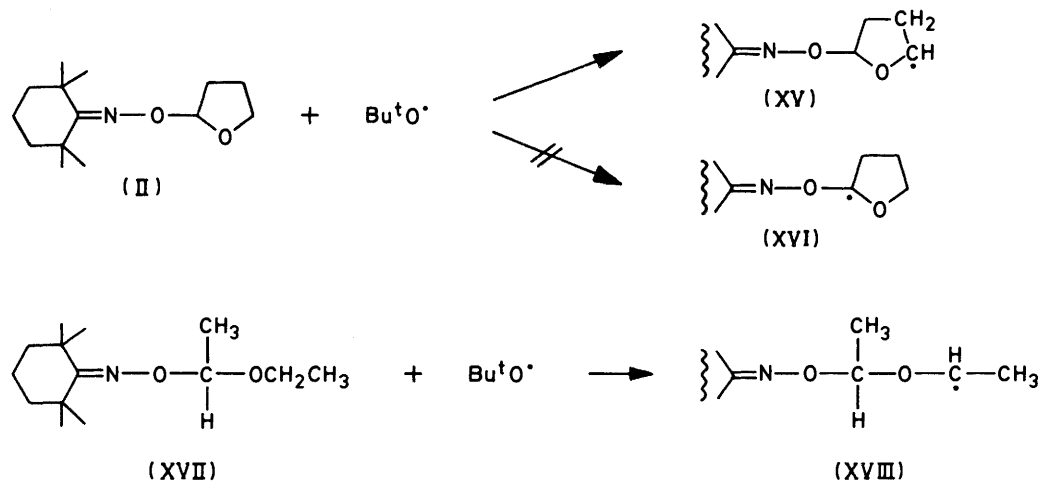
In the absence of trialkylaluminium the same oxime ether can be obtained by photolysis of the oxalate (XIII) in benzene. When the oxalate loses CO and CO_2 the iminoxyl and iminyl radicals (XIV) and (XV) are left. Ring opening of (VI) to the cyano-substituted radical (VII) and combination with (XIV), in 60% yield, leads directly to the oxime ether (IV), identical with the product obtained earlier from reaction (1). When the solvent benzene is replaced by THF, photolysis of (XIII) leads to a product mixture containing the ether (acetal) (II), earlier found among the products of reaction (1) with $\text{Al}(\text{CH}_3)_3\cdot\text{THF}$.

Apparently an α -hydrogen atom is abstracted from THF and the resulting radical combines with the hydroxyiminyl radical (XIV). Because the resulting ether (acetal) (II) seems to contain particularly labile hydrogen a separate study was made of its behaviour towards t-butoxy radicals.

Anomalous Radicals derived from Oxime Ethers.—When the oxime derivative (II) is made to react with t-butoxy radicals, generated by photolysis of di-t-butyl peroxide, the somewhat unexpected hydrogen abstraction in Scheme 4 prevails. The hyperfine spin coupling of H_α is 14.7 G and of the non-equivalent β -hydrogens 36.2 and 23.6 G, the larger value



Scheme 3.



Scheme 4.

corresponding to an axial β -hydrogen with a very small dihedral angle between the C-H bond and the p -type orbital containing the electron.¹⁴ These values are close to the corresponding values for radicals derived from tetrahydrofuran and 1,3-dioxolan.¹⁵ Considering our earlier observations on hydrogen abstraction from oxime ethers by *t*-butoxyl radicals [cf. reaction (2)], it is surprising that radical (XVI) does not seem to be formed nor its ring-opened isomer with an ester function.

Similar results were found for the somewhat related oxime derivative (XVII) (obtainable by replacing THF by diethyl ether), which gives the radical (XVIII) with g 2.0029, a_{H_2} (1 H) 15.1 G and $a_{\text{H}\beta}$ (3 H) 22.1 G rather than the isomer resulting from abstraction of the acetal hydrogen. This hydrogen is relatively close to the congested ring, and this seems to make it less vulnerable to attack by *t*-butoxyl radicals. However, we cannot discount the possibility that some abstraction of acetal hydrogen does take place, which is followed by pro-

cesses which escape detection by e.s.r. So far we have found no indication for fragmentation to iminyl radicals [cf. reaction (2)] when (II) and (XVII) react with *t*-butoxyl radicals.

Experimental

Instruments and Materials.—I.r. spectra refer to CHCl_3 solutions and were recorded on a Perkin-Elmer 257 spectrophotometer. N.m.r. spectra were obtained with Varian A60D, HA 100, or Bruker WM 250 instruments and were taken in CDCl_3 solution using tetramethylsilane as internal standard. E.s.r. spectra were recorded on a Bruker ER 200D instrument. Trimethylaluminium in hexane was obtained from Alfa Inorganics and all operations were performed under argon (Aga N50) purified through a Chrompack column, resulting in <0.1 p.p.m. H_2O and O_2 . 2,2,6,6-Tetramethylcyclohexanone¹⁶ and the chlorination procedure of its oxime has been described previously.¹⁷

E.s.r. Measurements.—Samples were dissolved in benzene or toluene containing di-*t*-butyl peroxide as a radical source. Oxygen was excluded from the e.s.r. cavity by flushing thoroughly with purified argon. Photolyses were performed with a 200 W medium pressure mercury lamp at temperatures ranging from -40 to $+10$ °C. In kinetic experiments a Princeton Applied Research signal averager model 4202 was employed.

Preparation of Oxime Ethers (VIII), (IX), and (XI).—2,2,6,6-Tetramethylcyclohexanone oxime (2.9 g, 0.02 mol) was converted into the anion with sodium hydride in THF solution. After addition of 1 mol. equiv. of the appropriate halide, the solution was refluxed for 4 h (methyl iodide, benzyl bromide) or 72 h (diphenylmethyl bromide). Diethyl ether was added and the solution was washed with concentrated aqueous ammonium chloride and with water. After drying (MgSO_4) and evaporation of the solvents, the resulting viscous liquid was purified by chromatography (hexane-silica gel). Yields were ca. 60% in each case. 2,2,6,6-Tetramethylcyclohexanone oxime methyl ether (VIII) was a viscous liquid, δ (60 MHz) 1.15 [s, $(\text{CH}_3)_2\text{C}$, 6 H], 1.25 [s, $(\text{CH}_3)_2\text{C}$, 6 H], 1.52 [m, $(\text{CH}_2)_3$, 6 H], 3.75 (s, CH_3O , 3 H). 2,2,6,6-Tetramethylcyclohexanone oxime benzyl ether (IX) was a viscous liquid, δ 1.15 [s, $(\text{CH}_3)_2\text{C}$, 6 H], 1.25 [s, $(\text{CH}_3)_2\text{C}$, 6 H], 1.50 [m, $(\text{CH}_2)_3$, 6 H], 5.01 (s, CH_2O , 2 H), and 7.27 (m, C_6H_5 , 5 H). 2,2,6,6-Tetramethylcyclohexanone oxime di-

phenylmethyl ether (XI) formed light yellow needles, m.p. 53—54 °C, δ 1.06 [s, (CH₃)₂C, 6 H], 1.33 [s, (CH₃)₂C, 6 H], 1.49 [m, (CH₂)₃, 6 H], 6.08 (s, CHO, 1 H), and 7.26 [m, (C₆H₅)₂C, 10 H].

Preparation of (II), the THF Derivative, and of the Diethyl Ether Derivative, of 2,2,6,6-Tetramethylcyclohexanone Oxime.—Under argon, trimethylaluminium (0.55 ml 0.55 mmol) was diluted with tetrahydrofuran (or diethyl ether) (25 ml), both freshly distilled from sodium wire. To the solution was added 1-chloro-1-nitroso-2,2,6,6-tetramethylcyclohexane¹⁷ (1 g, 5 mmol) and the mixture stirred at room temperature until the blue colour of the nitroso-compound had disappeared (3—4 days). The solution was diluted with moist ether and poured onto crushed ice. Dilute hydrochloric acid was added, the organic layer separated, washed several times with water, dried (MgSO₄), and the solvent evaporated. The crude product was purified by preparative g.l.c. (3 m, diam. 10 mm; 20% SE 30 on Chromosorb S, 60 mesh; 120 °C). Compound (II) was a viscous liquid, δ 1.21 [d, (CH₃)₂C, 6 H], 1.29 [s, (CH₃)₂C, 6 H], 1.55 [m, (CH₂)₃, 6 H], 2.0 [m, (CH₂)₂, 4 H], 3.9 (m, CH₂O, 2 H), and 5.72 (t, CHO, 1 H); ν_{\max} . 1 450, 1 380, 1 360, 1 180, 1 070, and 970—910 cm⁻¹. 2,2,6,6-Tetramethylcyclohexanone oxime 1-ethoxyethyl ether was a viscous liquid, δ 1.07 (t, CH₃CH₂O, $J_{\text{AX}_3} = J_{\text{BX}_3} = 7.0$ Hz, 3 H), 1.09 [s, (CH₃)₂C, 6 H], 1.20 (s, CH₃C, 3 H), 1.24 (s, CH₃C, 3 H), 1.25 (d, CH₃CHO, J 5.5 Hz, 3 H), 1.47 [m, (CH₂)₃, 6 H], 3.43 (m, CH₃CH₂O, J_{AX_3} 7.0, J_{AB} 10.0 Hz, 1 H), 3.71 (m, CH₃CH₂O, J_{BX_3} 7.0, J_{AB} 10.0 Hz, 1 H), and 5.03 (q, CH₃CHO, J 5.5 Hz, 1 H).

Preparation of the Oxalate (XIII).—A solution of oxalyl chloride (2.5 g, 20 mol) in ether (10 ml) was added dropwise under nitrogen to a stirred solution of 2,2,6,6-tetramethylcyclohexanone oxime (6.9 g, 40 mmol) and triethylamine (4.0 g, 40 mmol) in ether at 0 °C. After addition was complete, stirring was continued for 1 h at 25 °C. The precipitate was removed by filtration and the solvent evaporated, leaving a solid. Crystallisation from light petroleum gave the oxalate (XIII) (6.5 g, 67%) as needles with m.p. 97—98 °C (decomp), ν_{\max} . 1 610, 1 758, and 1 784 cm⁻¹; δ (60 MHz) 1.18 [s, (CH₃)₂C, 6 H], 1.36 [s, (CH₃)₂C, 6 H], and 1.60 [m, (CH₂)₃, 6 H]. Mass spectra (field desorption through the courtesy of Professor N. M. M. Nibbering, this department) reveal the expected molecular weights.

Hydrogen Abstractions from (IX) and (XI), the Benzyl and Diphenylmethyl Ethers of 2,2,6,6-Tetramethylcyclohexanone Oxime.—**Warning:** peroxalates must be handled with great care! To a 10% solution of the title compounds in benzene, di-*t*-butyl peroxalate was added at 30 °C, until ca. 10% conversion had taken place (n.m.r.). Solutions were then heated to 70 °C for 10 min, in order to decompose the remaining peroxalate. After cautious removal of the solvent, the resulting oil was analysed by g.l.c. (5 m, diam. 10 mm, 22% SE 30—Chromosorb S, 60 mesh) at 35°. The following products were isolated and yields estimated from n.m.r. spectra with dibenzyl as internal standard: 2-cyano-2,6-dimethylheptane (4%), ν_{\max} . 2 240 (C≡N), δ (250 MHz) 0.86 [d, (CH₃)₂CH, J 6.94 Hz 6 H], 1.19 (m, CH₂, 2 H), 1.32 [s, (CH₃)₂CCN, 6 H], 1.44—1.48 [m, (CH₂)₂, 4 H], and 1.55 [m, CH(CH₃)₂, 1 H], (field desorption) 153 (M^+); 6-cyano-2,6-dimethylhept-1-ene, slightly contaminated with (CH₃)₂=CHCH₂CH₂-C(CH₃)₂CN (total yield 5.7%), ν_{\max} . 893, 3 080 (C=CH₂), and 2 240 (CN) cm⁻¹; δ (250 MHz) 1.34 [s, (CH₂)₂CCN, 6 H],

1.4—1.7 [m, (CH₂)₂, 4 H], 1.72 (s, CH₃C=C, 3 H), 2.05 (t, CH₂C=C, J 10.1 Hz, 2 H), and 4.68 and 4.72 (two s, CH₂=C, 2 H), *m/e* (field desorption) 151 (M^+).

Photolysis of the Oxalate (XIII).—A solution of the title compound (2.5 g) in benzene (or THF) (2 ml) in a wide quartz tube was photolysed in a Rayonet RPR-204 photoreactor, equipped with four RUL 2537 lamps. The tube was shaken occasionally and after 1 h at room temperature the starting material had disappeared (t.l.c., i.r.). The solvent was removed and the crude reaction mixture analysed by g.l.c. as described before. Yields (in THF and benzene) were estimated by means of n.m.r. with dibenzyl as internal standard. Isolated compounds were (II), 5% yield, spectral data as reported before; (IV), 50 (THF) and 60% (C₆H₆) yield; 1,1,5-trimethyl-5-cyanoethyl ether of 2,2,6,6-tetramethylcyclohexanone oxime, pale yellow crystals; ν_{\max} . 2 220, 1 550, 1 470—1 460, 1 380, 1 360, and 980—920 cm⁻¹, δ_{H} (100 MHz) 1.18 (s, CH₃, 6 H), 1.24 (s, CH₃, 6 H), 1.28 (s, CH₃, 6 H), 1.33 (s, CH₃, 6 H), 1.53 (s, CH₂, 12 H), δ_{C} (25.2 MHz) 17.85 (t), 19.7 (t), 25.68 (q), 26.64 (q), 27.29 (q), 31.11 (q), 32.34 (s), 36.61 (s), 38.24 (s), 38.43 (s), 39.78 (t), 41.27 (t), 41.66 (t), 78.97 (s), 124.97 (s), and 164.49 (s) p.p.m.; (V), 25 (THF) and 14% (C₆H₆) yield, i.r. and n.m.r. spectra identical with those of an authentic sample.*

* *Note added in proof:* Formula (V) in Scheme is erroneous; instead of an imine, an amide is formed.

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