Reactions of Picryl Ethers with Hindered Amines[1]

LEALLYN B. CLAPP, HAREL LACEY, G. G. BECKWITH, R. M. SRIVASTAVA, AND NASEEM MUHAMMAD

Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island 02912

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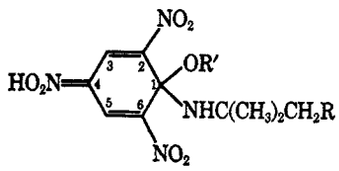
By treating a hindered picryl ether with a hindered amine we have succeeded in forming *neutral* Meisenheimer prototype complexes[2,3] (I) in solution at low temperature and salts of the complexes with 2 mol of the amine. Meisenheimer complexes have recently[4-6] been established as quinoid ionic structures in which the bonding at C-1 is covalent.[7] They are not charge-transfer complexes.

We have found, however, that steric interference of large groups on C-1 with nitro groups at C-2 and C-6 is insufficient to lock the nonbenzenoid ring into a nonplanar structure of sufficient stability to be isolated at room temperature. Even when the ether is picryl mesityl ether and the amine has the tertiary butyl shape the Meisenheimer complex (Ic) forms at −57°, but the deep red color gives way to the bright yellow of a substituted picramide as the solution in tetrahydrofuran warms to ambient temperatures. At the temperature of a Dry Ice bath the red solution of Ic is stable for days, but the neutral complex defies isolation.

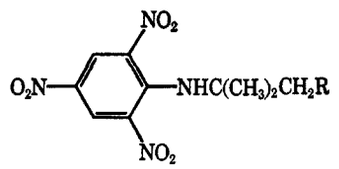
We have verified the findings of Servis[4] with respect to nmr spectra of the Meisenheimer complex Ia. In tetrahydrofuran, a single peak for the two equivalent aromatic protons at C-3 and C-5 (δ 8.40) was observed. In addition, however, the two protons on N at C-4 and O at C-1 in Ia are also clearly distinguishable (NO_2H, δ 11.9, br, and NH, 6.06, br). The peak at δ 11.9 disappears as the color of the solution changes from red to yellow, signalling the change to IIa.

In deuterated dimethyl sulfoxide as solvent, picryl phenyl ether was allowed to react with *t*-butylamine to give equivalent changes in the nmr spectrum at room temperature. When 2 mol of amine was used the low-field peak due to NO_2H was not observed. Instead a broad signal at δ 4.06 (3 H) appeared, which we interpret to be the salt of Ia. In the same solvent the still more hindered picryl mesityl ether gave the same deep red color of the Meisenheimer complex (Ic) and a similar nmr spectrum, and formed the salt of Ic with excess amine.

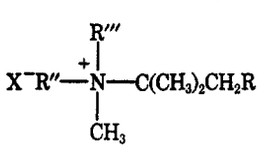
Trinitroanisole, a less hindered ether, gave red solutions of Ib and Id in methanol at low temperatures with the appropriate hindered amine, but picramides formed rapidly even at low temperature. In toluene as solvent, however, the trinitroanisole acted as a methylating agent for the hindered amines, and not even a fleeting red color could be detected. The alkylation does not occur at room temperature, but the insoluble picrate salts III precipitate rapidly from boiling toluene. Alkylation of a tertiary amine, N,N-dimethyl-β-naphthylamine (and others), by trinitroanisole to give the yellow quaternary picrate salt has been observed[8] when the deep red molecular compound of the two components is heated above the melting point of the molecular compound.

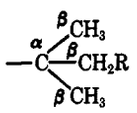


Ia, R = H; R′ = C_6H_5
b, R = H; R′ = CH_3
c, R = H; R′ = $C_6H_2(CH_3)_3$
d, R = OH; R′ = CH_3



IIa, R = H
b, R = OH





the α,β system

IIIa, R = OH; R″ = CH_3; R‴ = CH_3; X = $^-OC_6H_2(NO_2)_3$
b, R = OH; R″ = CH_3; R‴ = CH_3; X = Cl^-
c, R = OH; R″ = H; R‴ = H; X = $^-OC_6H_2(NO_2)_3$
d, R = H; R″ = H; R‴ = CH_3; X = $^-OC_6H_2(NO_2)_3$

The behavior of *t*-butylamine and 2-amino-2-methyl-1-propanol toward alkylation by trinitroanisole was somewhat different, probably a result of solubilities in toluene. With 2 mol (or 5 mol) of trinitroanisole to 1 mol of *t*-butylamine refluxing in toluene dimethylation occurred to an extent of 50% (IIId), and the substituted picramide was formed in 21% yield (IIa). A lower ratio of trinitroanisole to amine gave the same products but no isolable monomethylated product.

On the other hand, with 1.5 mol of trinitroanisole to 1 mol of 2-amino-2-methyl-1-propanol, 19% quaternary trimethylated salt (IIIa) and 21% monomethylated salt (IIIc) were obtained. Excess trinitroanisole increased trimethylation to 36%, but dialkylation was not observed.

Dimethylation of *t*-butylamine by trinitroanisole (50% yield) is not conspicuously better than the Leuckart method (32%),[9] but the isolation of the product is simple. Unhindered amines such as benzylamine form the substituted picramides so rapidly that alkylation is not a competing reaction even in toluene.

Experimental Section

Melting points are uncorrected. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

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Infrared (ir) spectra were taken using a Perkin-Elmer Model 337 spectrophotometer in Nujol mulls, unless otherwise stated. The nmr spectra were recorded on a Varian A-60A spectrometer using tetramethylsilane as an internal reference. Thin layer chromatography (tlc) was carried out on microscopic slides employing Kieselgel G (Merck) as absorbent. The spots could be detected on the chromatogram from the color of the compounds.

Tetrahydrofuran was refluxed over lithium aluminum hydride and distilled before use. *t*-Butylamine was refluxed over potassium hydroxide and distilled. Dimethyl sulfoxide-d_6 (99.5% deuterated) was obtained from Stohler Isotope Chemicals and used directly.

Trinitroanisole was prepared by nitration of 2,4-dinitroanisole and recrystallized from methanol, mp 67–67.5° (lit.[10] mp 67–68°). Phenyl picryl ether was obtained in 85% yield from picryl chloride and alcoholic sodium phenoxide: mp 157–158° (lit.[11] mp 153°); nmr (DMSO-d_6, 10%) δ 9.26 (s, 2), 7.26 (m, 5).

Picryl Mesityl Ether.—Picryl mesityl ether was prepared by the method just mentioned in 80% yield: mp 154–155°; nmr (DMSO-d_6, 10%) δ 9.13 (s, 2), 6.93 (s, 2), 2.23 (s, 3), 2.06 (s, 6).

Anal. Calcd for $C_{12}H_{13}N_3O_7$: C, 51.87; H, 3.74; N, 12.10. Found: C, 52.12; H, 3.62; N, 12.01.

Neutral Meisenheimer Complex Ia.—Picryl phenyl ether (1 g, 0.0032 mol) in 2.75 ml of tetrahydrofuran (1 *M* sol) at −60° was treated with 0.233 g of *t*-butylamine in 3.18 ml of tetrahydrofuran (1 *M* sol) also at −60°. The nmr spectrum of the mixture was recorded at −57°: δ 11.9 (br, 1, NO_2H), 8.40 (s, 2 at C-3, C-5), 6.96 (m, 5), 6.06 (br, 1, NH), 1.16 (s, 9).

When a second portion of amine solution was added to the picryl phenyl ether solution, the signals δ 11.9 and 6.06 were replaced by 4.06 (br, 3), but the other peaks remained at the same places.

Other Meisenheimer complexes (Ib–d) were formed in like manner at Dry Ice temperatures.

N-β-Hydroxy-*t*-butyl-2,4,6-trinitroaniline (IIb).—A methanol (100 ml) solution of trinitroanisole (5.0 g, 0.021 mol) and 2-amino-2-methyl-1-propanol (1.83 g, 0.021 mol) was kept at room temperature for 30 min. Removal of the methanol gave 6.15 g (90%) of the substituted picramide IIb, mp 95–100°. Two recrystallizations from absolute ethanol gave a yellow compound, mp 106–108.5°, pure by tlc (R_f 0.38 on Kieselgel G; solvent, benzene with 5% methanol). The impure picramide has been made before from picryl chloride and the same amino alcohol[12] but has not been characterized.

Anal. Calcd for $C_{10}H_{12}N_4O_7$: C, 40.00; H, 4.03; N, 18.66. Found: C, 40.59, H, 4.38; N, 17.61, 17.58.

It is not unusual to find low nitrogen content by analysis in compounds that are explosive, and the purity of the picramide IIb was confirmed by the absence of stray peaks in the nmr spectrum: nmr ($CDCl_3$, 5.4%) δ 1.30 (s, 6), 2.11 (unresolved triplet, 1, OH), 3.48 (diffuse doublet, 2, CH_2), 8.41 (br, 1, NH), 8.97 (s, 2). The NH proton moved downfield 5 cps by the addition of a trace of pyridine, whereas the OH signal spread into a broad band between δ 2.83 and 1.97. The methylene doublet changed into a sharp singlet indicating that the coupling between OH and CH_2 protons ceased after pyridine addition.

The ir spectrum of IId showed a broad OH and NH band at 3600–3100 cm^{-1} and the primary alcohol band at 1042 cm^{-1}.

When excess amino alcohol was used in the reaction with trinitroanisole the reaction did not stop at the picramide stage but formed 5,7-dinitro-3,3-dimethylbenzomorpholine by cyclic elimination of the elements of nitrous acid. Stronger bases give higher yields of dinitrobenzomorpholines.[12] The structure of 5,7-dinitro-3,3-dimethylbenzomorpholine has been previously proved[12] but is here substantiated by an nmr spectrum (deuterioacetone, 3.5%): δ 1.52 (s, 6), 3.72 (s, 1, NH), 4.10 (s, 2), 7.77 (d, J = 3 Hz, C-8), 8.63 (d, J = 3 Hz, C-6). The NH proton was unaffected by the addition of pyridine.

The picramide IIa[13] was made in a similar manner: mp 94–95°; 95%; nmr ($CDCl_3$) δ 1.56 (s, 9), 3.33 (br, 1, NH), 8.53 (s, 2).

Trimethyl-β-hydroxy-*t*-butylammonium Picrate (IIIa) and Hydrochloride (IIIb).—Trinitroanisole (5 g, 0.021 mol) in 16 ml of dry toluene was brought to reflux, and 1.4 g (0.015 mol) of 2-amino-2-methyl-1-propanol in 10 ml of toluene was added dropwise in 20 min and then refluxed 0.5 hr more. Removal of the solvent gave a brown viscous oil. The oil was dissolved in a minimum of methanol and triturated with ether to give 1.1 g (19%) of crude trimethyl-β-hydroxy-*t*-butylammonium picrate, mp 225–228° dec. Recrystallization from methanol–ether and then methanol gave a pure sample, mp 245–246° dec. The picrate is slightly soluble in water. Tlc (R_f 0.43 on Kieselgel G; solvent, 1-propanol–chloroform–water 2:1:0.2) gave a single spot.

With an excess of trinitroanisole and slow addition of the amino alcohol, the yield of the picrate was raised to 36%: nmr (deuterioacetone, 5%) δ 1.53 (t, 6, $J_{^{14}NH\beta}$ = 2 Hz), 3.33 [s, 9, $N(CH_3)_3$], 3.93 (t, 2, $J_{^{14}NH\beta}$ = 2 Hz), 8.63 (s, 2 aromatic). At δ 2.95 a broad peak, possibly due to the OH signal, became sharp after addition of pyridine.

The picrate was converted into trimethyl-β-hydroxy-*t*-butylammonium chloride by treatment with hydrochloric acid. Two recrystallizations from methanol–ethyl acetate and one from ethanol gave a white product: mp 242–245° dec; nmr (methanol-d_4) δ 1.45 (t, 6, $J_{^{14}NH\beta}$ = 2 Hz), 3.20 (s, 9) 3.81 (t, 2, $J_{^{14}NH\beta}$ = 2 Hz).

Anal. Calcd for $C_7H_{18}NOCl$: C, 50.14; H, 10.82; N, 8.35. Found: C, 50.21; H, 10.78; N, 8.16.

Methyl-β-hydroxy-*t*-butylammonium Picrate (IIIc).—The mother liquor from the preparation of the trimethylated derivative of 2-methyl-2-amino-1-propanol (previous paragraph) was concentrated and triturated with chloroform. On standing (with refrigeration) 1.1 g (21%) of the monoalkylated derivative was obtained as the picrate. Repeated recrystallization gave the analytical sample: mp 174–176°; nmr (deuterioacetone, 10%) δ 1.47 (s, 6), 2.86 (s, 3, N–CH_3), 3.76 (s, 2, CH_2), 8.71 (s, 2, aromatic). The remaining three protons appeared in two broad diffuse curves at 7.26–8.6 (1 H) and 4.0–5.2 (1 < H < 2) but were brought together in a nicely rounded peak of the correct integrated area centered at δ 6.06 by the addition of pyridine. The R_f value of 0.46 was observed for the compound when the previously mentioned tlc system was used.

Anal. Calcd for $C_{11}H_{16}N_4O_8$: C, 39.74; H, 4.86; N, 16.87. Found: C, 39.56; H, 5.04; N, 17.02.

N,N-Dimethyl-*t*-butylammonium Picrate (IIId).—In the manner just described 4.08 g (0.02 mol) of trinitroanisole and 0.73 g (0.01 mol) of *t*-butylamine gave 2.27 g (50%) (after recrystallization from methanol) of N,N-dimethyl-*t*-butylammonium picrate, mp 278–280° dec. The analytical sample was sublimed at 150° (0.06 mm): nmr (DMSO-d_6, 10%) δ 1.33 (s, 9), 2.76 (s, 6, NCH_3), 3.03 (s, 1, NH), 8.60 (s, 2).

Anal. Calcd for $C_{12}H_{18}N_4O_7$: C, 43.63; H, 5.45; N, 16.96. Found: C, 44.11; H, 5.33; N, 17.17.

From the toluene solution, a 21% yield of N-*t*-butyl-2,4,6-trinitroanisole (IIa) was recovered. The yield of IIId was not changed when 0.05 mol of trinitroanisole was used in a similar experiment.

Registry No.—Picryl mesityl ether, 17691-66-6; 5,7-dinitro-3,3-dimethylbenzomorpholine, 17691-69-9; Ia, 17691-67-7; IIb, 17691-68-8; IIIa, 17691-70-2; IIIb, 17691-71-3; IIIc, 17691-72-4; IIId, 17691-73-5.

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1-Methyl-4-phenyl-2(1H)-quinazolinone

HANS OTT AND MAX DENZER

Sandoz Pharmaceuticals, Hanover, New Jersey 07936

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In the course of investigations in the quinazoline field we discovered an interesting series of reactions leading to 1-methyl-4-phenyl-2(1H)-quinazolinone (**4**),