in **3b** and **3c** are in the vicinity of 0.4 e. An estimate of the relative capabilities of the O, $C(CN_2)_2$, and tetrachlorocyclopentadienylidene groups for − charge stabilization, in PROPEN, CYANOF, and the tetrachloropentatriafulvalenes, can be obtained from the acidities of the conjugate acids H_2O, $H_2C(CN)_2$, and 1,2,3,4-tetrachlorocyclopentadiene. Although the pK_a of the latter compound is not presently known, the similarities of the pK_a's of water (14) and malononitrile (11.14[42]), and the similarities between the three-ring bond distance in the cyclopropenone and the three fulvenes, suggest that the pK_a of the tetrachlorocyclopentadiene would be in the 11–14 range. Further attempts to induce even larger amounts of charge separation than the *ca.* 40% found in CYANOF and PROPEN should consider CH_2X_2 compounds which are substantially more acidic than malononitrile for use as the $=CX_2$ triafulvene components.

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Supplementary Material Available. Tables IV and VI of the structure factors will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-7093.

(42) K. Bowden and R. Stewart, *Tetrahedron*, **21**, 261 (1965).

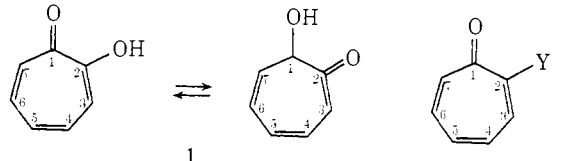
Normal *vs.* Abnormal Nucleophilic Substitutions on Cycloheptatrienones Carrying a Mobile α Substituent. A Rationalization[1,2]

Gino Biggi,[3] Francesco Del Cima,[4] and Francesco Pietra*

Contribution from the Department of Chemistry, University of Pisa, 56100 Pisa, Italy. *Received February 5, 1973*

Abstract: Reactions of 3,5,7-deuterium-labeled 2-Y-cycloheptatrienones with nucleophilic reactants (N) in DMSO solutions are reported. With N = sodium *p*-tolylmercaptide, C(2) substitution is observed. With N = primary or secondary amines, C(7) substitution is observed when Y = quinuclidinio, while C(2) substitution occurs when Y = Cl or OTs. With N = ammonia, C(7) or C(2) substitution is observed for Y = quinuclidinio or F, respectively, whereas with Y = Cl, substitution at C(7) is accompanied by benzenoid rearrangement. With N = *m*-chloroaniline and Y = Cl, C(2) substitution occurs but the reaction course is diverted to C(7) substitution by added triethylamine. Reaction intermediates are detected spectroscopically. These observations are rationalized in terms of three reversibly interconnected pathways and the synthetic utility is exploited.

Shortly after the first laboratory syntheses of tropolone[5] (**1**) and tropone (**2**, Y = H),[6] it was found



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that α substituents on the tropone nucleus, which are stable as anions, can be replaced by a variety of nucleophiles.[7] However, labeling of the seven-membered ring with isopropyl groups[8] revealed a complex behavior. Although the nucleophilic reactant was usually found to take the position vacated by Y (the so-called "normal nucleophilic substitution"), with 4- and 5-isopropyl-2-chlorotropone and ethanolic ammonia, 2-amino-5- and 2-amino-4-isopropyltropone were isolated, respectively, in low yields (the so-called "abnormal nucleophilic substitution");[9] the low yields are due to competing ring contraction of the starting cycloheptatrienone and in many cases, typically with strong bases as reactants, only arene products were observed.[10]

This is quite an interesting situation but one which has received very little clarification after more than 20

(1) (a) "The Reactivity of Pseudoaromatic Compounds. X"; (b) part IX: *Tetrahedron Lett.*, 183 (1973); (c) financial support from Consiglio Nazionale delle Ricerche, Rome.

(2) We thank C. Erkelens, Leiden, for doing deuterium decoupling experiments and Dr. A. J. de Hoog for aid in spectra interpretation.

(3) Postdoctoral Fellow.

(4) Undergraduate.

(5) J. W. Cook, A. R. Gibb, R. A. Raphael, and A. R. Somerville, *Chem. Ind. (London)*, 427 (1950); W. von E. Doering and L. H. Knox, *J. Amer. Chem. Soc.*, **72**, 2305 (1950); T. Nozoe, S. Seto, Y. Kitahara, M. Kunori, and Y. Nakayama, *Proc. Jap. Acad.*, **26**, 38 (1950); *Chem. Abstr.*, **45**, 7098 (1951).

(6) H. J. Dauben and H. J. Ringold, *J. Amer. Chem. Soc.*, **73**, 876 (1951); W. von E. Doering and F. L. Detert, *ibid.*, **73**, 876 (1951); T. Nozoe, Y. Kitahara, T. Ando, and S. Masamune, *Proc. Jap. Acad.*, **27**, 415 (1951); *Chem. Abstr.*, **46**, 7558 (1952).

(7) For a list of such reactions see P. L. Pauson, *Chem. Rev.*, **55**, 9, 56 (1955).

(8) (a) T. Nozoe, *Fortschr. Chem. Org. Naturst.*, **13**, 232 (1956); (b) H. Erdtman and T. Norin, *ibid.*, 24, 206 (1966).

(9) T. Nozoe, S. Seto, and T. Sato, *Proc. Jap. Acad.*, 30, 473 (1954).

(10) G. Biggi, A. J. de Hoog, F. Del Cima, and F. Pietra, *J. Amer. Chem. Soc.*, **95**, 7108 (1973).

Table I. Reactions of Several 2-Y-[3,5,7-$^2H_3$]cyclohepta-2,4,6-trien-1-ones (**3**) with Various Nucleophilic Reactants (N) in Dimethyl Sulfoxide[a]

Carbonyl reactant (**3**), Y	Nuceophilic reactant, N	Products[b,c] **4a**	**4b**
$^+NR_3$[d]	Piperidine[e]		[100%]; δ (C_6D_6) 7.05 (1 H, s), 6.18 (2 H, s)
$^+NR_3$[d]	2-Methylpiperidine		[90%]; δ (CCl_4) 6.7 (1 H, s), 6.4 (2 H, s)
$^+NR_3$[d]	Et_2NH		[85%]; δ (CCl_4) 6.7 (1 H, s), 6.4 (2 H, s)
$^+NR_3$[d]	*n*-$BuNH_2$		[98%]; δ (CCl_4) 6.9 (1 H, s), 6.5 (1 H, s), 6.3 (1 H, s)
$^+NR_3$[d]	$PhNH_2$		[63%]; δ (C_6D_6)[f] 7.32 (1 H, d, J = 0.8 Hz), 6.83,[g] 6.22 (1 H, t, J = 0.8 Hz)
$^+NR_3$[d]	*p*-$CH_3C_6H_4SNa$	[99%]; δ (CCl_4)[f] 7.10 (1 H, d, J = 1.5 Hz), 6.70 (1 H, d, J = 1.5 Hz)	
OTs	Piperidine	[95%]; δ (C_6D_6) 6.5 (2 H, s)	
OTs	*n*-$BuNH_2$	[100%]; δ (CCl_4) 7.1 (2 H, s)	
Cl	Piperidine	[100%]; δ (C_6D_6) 6.5 (2 H, s)	
Cl	2-Methylpiperidine[h]	[100%]; δ (CCl_4), 6.9 (1 H, s), 6.8 (1 H, s)	
Cl	Et_2NH	[100%]; δ (CCl_4) 6.9 (2 H, s)	
Cl	*m*-$ClC_6H_4NH_2$[h]	[41%]; δ (CCl_4)[f] 6.77 (1 H, d, J = 1.2 Hz), 6.47 (1 H, d, J = 1.2 Hz)	
Cl	*m*-$ClC_6H_4NH_2$–Et_3N[h]	[5%]; δ (CCl_4)[f] 6.77 (1 H, d, J = 1.2 Hz), 6.47 (1 H, d, J = 1.2 Hz)	[40%]; δ (CCl_4)[f] 7.33 (1 H, d, J = 0.8 Hz), 6.77 (1 H, d, J = 0.8 Hz), 6.25 (1 H, t, J = 0.8 Hz)
Cl	NH_3		[68%]; δ ($CDCl_3$) 7.2 (1 H, s), 6.9 (1 H, s), 6.7 (1 H, s)
Cl	*p*-$CH_3C_6H_4SNa$	[99%]; δ (CCl_4)[f] 7.10 (1 H, d, J = 1.5 Hz), 6.70 (1 H, d, J = 1.5 Hz)	
F	$PhNH_2$	[99%]; δ (CCl_4)[f] 6.81 (1 H, d, J = 1.2 Hz), 6.58 (1 H, d, J = 1.2 Hz)	
F	*m*-$ClC_6H_4NH_2$	[99%]; δ (CCl_4)[f] 6.77 (1 H, d, J = 1.2 Hz), 6.47 (1 H, d, J = 1.2 Hz)	
F	NH_3	[99%]; δ ($CDCl_3$) 7.2 (1 H, s), 7.1 (1 H, s)	
NC_5H_{10}	NH_3[h]	[20%];[i] δ ($CDCl_3$) 7.2 (1 H, s), 7.1 (1 H, s)	

[a] At room temperature, when not otherwise stated. [b] Yields, within square graphs, are based on starting **3** and, unless otherwise stated, were determined from spectra. [c] Nmr spectral data [δ (solvent), relative to internal TMS] for cycloheptatrienone protons only are listed here, while data for the other protons are reported in the Experimental Section. [d] $^+NR_3$ = quinuclidinium. [e] From ref 12. [f] With deuterium decoupling (to be rigorous these triplets should be really termed pseudo-triplets, the proton concerned being coupled to two nonequivalent "meta" protons. Also, all signals termed as singlets for nondeuterium decoupled spectra should be really termed as pseudo-singlets, because "ortho" coupling with deuterium masks "meta" coupling with proton). [g] Partly obscured by the aniline ring protons (see text for proton and deuterium triple resonance experiments). [h] At 80°. [i] 80% of starting **3** was recovered.

years of active research. Moreover, the predictive power of existing systematization is of limited value. For example, while the reaction of 2-chloro-3,5,7-trideuteriotropone with methylamine was reported to give 40% of substitution at C(2), 23% of substitution at C(7), and 29% of rearrangement to arene (*N*-methyl-2,4,6-trideuteriobenzamide),[11] another closely similar amine, *n*-butylamine, gives quantitative substitution by attack at C(2) on the same substrate (see below).

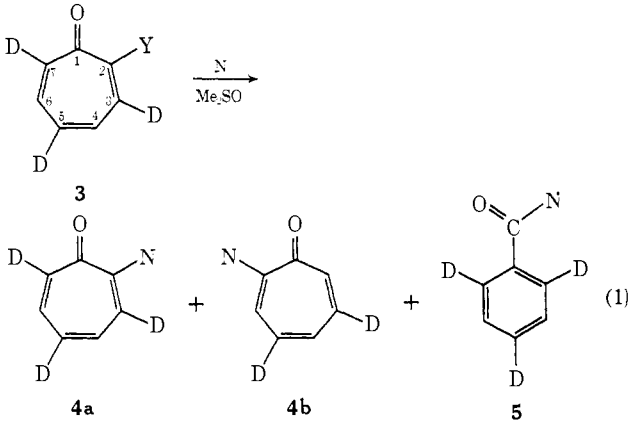
An important advance toward the comprehension of these reactions came from the discovery that the reaction of 2-quinuclidiniotropone (**2**, Y = quinuclidinio) with piperidine proceeds by 100% C(7) substitution.[12] Reaction intermediates were directly detected and a detailed kinetic study of each reaction step led to a satisfactory mechanistic picture for the substitution process.[12] These observations and our previous ideas concerning the mechanism of the "normal" nucleophilic substitution[13] now allowed us to plan a systematic investigation as to which set of structural features and conditions causes the "abnormal" course to prevail over the "normal" course. The results of such a study are reported here, whereas the problem of the competition of substitution with ring contractions to arenes is considered in the accompanying paper.[10]

(11) S. Ito, J. Tsunetsugu, T. Kanno, H. Sugiyama, and H. Takeshita, *Tetrahedron Lett.*, 3659 (1969).
(12) G. Biggi, F. Del Cima, and F. Pietra, *J. Amer. Chem. Soc.*, 94, 4700 (1972).
(13) F. Pietra and F. Del Cima, *J. Chem. Soc. B*, 2224 (1971).

Results and Discussion

Identification of the Reaction Products. The reaction course has been followed, as in a previous case,[12] by labeling the cycloheptatrienone nucleus with deuterium.

In the reactions studied here, in dimethyl sulfoxide three kinds of products have been identified. These are generalized in eq 1 as **4a**, **4b**, and **5** for the products of substitution by attack at the nuclear position bearing the replaceable group Y (normal product), substitution by attack at C(7) (abnormal product), and arene rearrangement, respectively.



3 **4a** **4b** **5** (1)

Correspondingly, Table I shows the actual distribution of the products for the reactions of various cyclohepta-

trienones **3** (Y = quinuclidinio, OTs, Cl, F, and piperidino) with several nucleophilic reactants, including ammonia, primary amines, secondary amines, aromatic amines, and sodium *p*-tolylmercaptide in dimethyl sulfoxide. In each case this study has been preceded by that of the corresponding reactions of the undeuterated cycloheptatrienones (**2**), with the relevant data being collected in the Experimental Section.

Except for reactions of *p*-tolylmercaptide, which were able to lead only to **4a**-type products, all other nucleophilic reactants led to both **4a**- and **4b**-type products from the starting cycloheptatrienone **3** (Table I).

For any given (amino) substituent N, the uv absorption spectrum of the **4a**-type product coincides with that for the **4b**-type product, showing typical strong absorptions at *ca.* 350 and 400 nm (Experimental Section). As discussed previously for the case of N = piperidino,[12] substitution at nuclear positions other than C(2) or C(7) of **3** would have given rise to products showing uv spectra markedly different from those actually observed.

Unequivocal decision between substitution at C(2) or C(7) of **3** has been possible in all cases on the basis of the ^{1}H nmr spectra of the substitution products. Except for the cases of N = anilino, *m*-chloroanilino, and *p*-tolylmercapto, structures of the reaction products can easily be assigned on the basis of routine nmr spectra. Thus, for a given substituent N, products of type **4a** show (Table I), in the spectral region δ 6.0–7.5 ppm, either a single absorption, which integrates for two protons, or two absorptions, which integrate for one proton each. These signals can be assigned, in both cases, to C(4) and C(6) protons.

The corresponding products of type **4b** show (Table I), in the above spectral region, either three absorptions, which integrate for one proton each, or two absorptions, which integrate for one and two protons. In both cases, these signals originate from C(2), C(4), and C(6) protons. This assignment is supported by the relative sharpness of these signals, which indicates that no couple of adjacent protons is present on the cycloheptatriene nucleus. Moreover, for any given N group, the signal, or the signals, attributed to the protons at C(4) and C(6) of the **4a**-type product, are lacking from the spectrum of the reaction mixtures where **4b**-type products are formed.

It proved more difficult to assign structures to products **4** in the cases of N = *p*-tolylthio, anilino, and *m*-chloroanilino because of the superimposition of the signals due to the aromatic and cycloheptatrienone protons. These problems were solved by deuterium decoupled ^{1}H nmr spectra of the substitution products. In fact, because with either **4a**- or **4b**-type products all cycloheptatrienone protons, and only those, are adjacent to at least one deuteron, their nmr signals are the only ones which sharpen on deuterium decoupling.

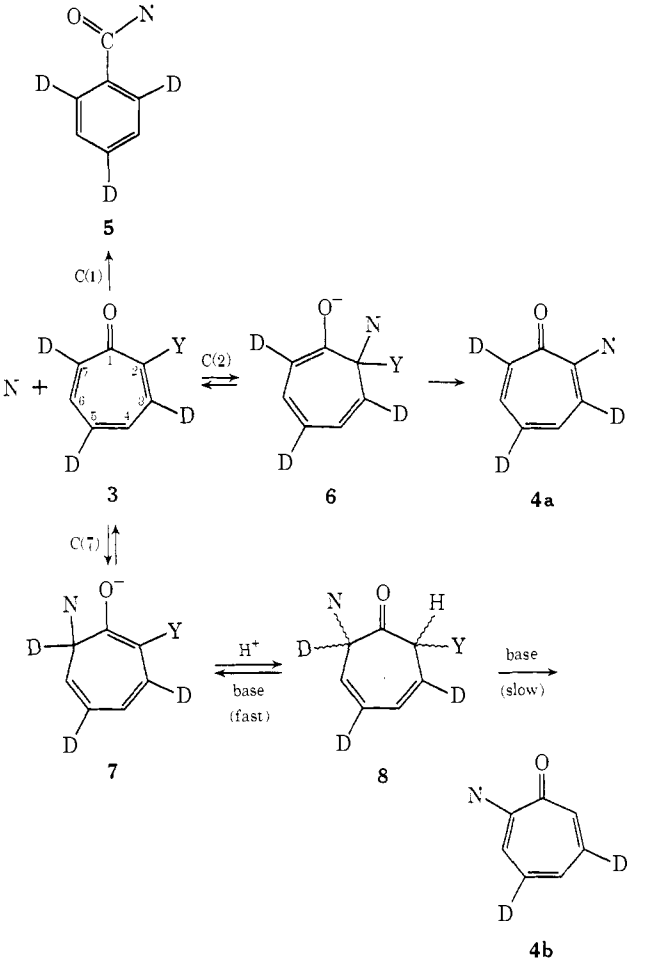
However, this procedure failed to clearly reveal the fine structure of those cycloheptatrienone protons which emerge from the central part of the complex pattern of signals due to the aromatic protons of the N substituent. Rigorous structural assignment in these cases required triple resonance experiments (on deuterium and proton). Thus, with the products of the reactions of *p*-tolylmercaptide with either **3** (Y = quinuclidinio) or **3** (Y = Cl) (Table I), on deuterium decoupling only two ^{1}H nmr signals sharpen, becoming nice doublets which integrate for one proton each. The value of the coupling constants, 1.5 Hz, is reasonable for two "meta" protons at C(4) and C(6) of a **4a**-type product.

Structure of **4b**-type was assigned to the product of the reaction of aniline with **3** (Y = quinuclidinio) on the following basis. Three places (Table I) in the ^{1}H nmr spectrum underwent modification on deuterium decoupling. While the signals at δ 7.32 and 6.22 ppm were doublets and triplets, respectively, that at δ 6.83 ppm was partly obscured by the aniline ring protons. Thus, while decoupling deuterium, the signal at δ 6.22 ppm became a doublet on irradiation at either δ 7.32 or 6.83 ppm. Therefore, the three signals (Table I) at δ 7.32, 6.83, and 6.22 must be attributed to the C(2), C(6), and C(4) of the **4b**-type product.

A similar analysis showed that the reaction of aniline with **3** (Y = F) led to a **4a**-type product. The nmr data for cycloheptatrienone protons are reported in Table I. This is also the case of the reaction of *m*-chloroaniline with **3** (Y = Cl) whereas, with added triethylamine, the **4b**-type product, together with a little **4a**-type product, was mainly obtained. The relevant nmr data are listed in Table I.

Rationalization of the C(7) *vs.* C(2) Substitution Problem. We show here that the dependence on both structural and environmental factors of the **4a**-, **4b**-, and **5**-type product distribution (Table I) can be rationalized in terms of the framework of the mechanisms in Scheme I, where the mechanisms for both the abnormal (C(7))[12]

Scheme I



and normal substitution (C(2))[13] are sketched. The ring contraction in which C(1) emerges from the seven-membered ring[14] is instead simply indicated by the overall process, while its first step is known to be reversible.[14]

There are other drastic oversimplifications in the mechanistic representation at the scheme, however. In fact, undoubtedly attack at C(7) is preceded, at least when Y is the strongly electron-attracting quinuclidinio group, by faster attack of N at another[12] (or several other, depending on the nature of the attacking base[10]) nuclear position of **3**. However, since in a nonprotonating solvent like dimethyl sulfoxide the resulting side-lying intermediates rapidly revert to **7** *via* **3**,[12] such processes need not be considered here. Also, details of the C(7) pathway are not given here since it is sufficient to the present purpose to realize that the rate-limiting step is the final elimination (Scheme I) (which is known from a previous detailed kinetic study of the reaction of piperidine with 2-quinuclidiniotropone).[12]

If the scheme applies also to the processes studied here, the intimate interconnection of these three pathways demands that any change in the nature of the reagents or the reaction conditions will reflect itself on the whole pattern of reactivity. We anticipate that this is the basic underlying principle governing the behavior of these systems.

Together with this, the other leading idea for the solution of these problems stems from the observation from the scheme that with **6** the group Y is insulated from the conjugate system,[15] whereas with **7** it is bound to the delocalized portion of the molecule. Thus, electron-attracting Y groups are envisaged to favor attack at C(7) (to give intermediates of type **7**) over attack at C(2). If so, the first requirement for the C(7) pathway is met and, if the conditions are favorable for the subsequent steps, **7** changes into **4b**. As a corollary, no special preference for attack at C(7) *vs.* that at C(2) can be expected for substrates **3** carrying electron-releasing Y groups. In the last case it is expected that the C(2) pathway to **4a** will be followed, albeit at low rate, whatever the nature of the attacking nucleophile be.

Ring contraction *via* the C(1) pathway (Scheme I) is considered in more detail in the accompanying paper,[10] where it is shown that it can occur with activated substrates and only when all other substitution or rearrangement processes are rendered difficult. Therefore, **5**-type products are expected only for the slowest reactions of activated substrates.

This picture is fully supported by, and may be further elaborated on the basis of, the data obtained here. Thus, monitoring by uv absorption spectroscopy of the reaction of **3** (Y = quinuclidino) (2×10^{-5} *M*) with 2-methylpiperidine (0.1–0.2 *M*) in DMSO at room temperature revealed the rapid disappearance of **3** and the appearance of a new intermediate species absorbing at *ca.* 350 nm, which then slowly decays into the **4b**-type product. This situation is analogous to that found for the corresponding reaction of piperidine,[12] with the only difference being that the intermediate species is longer living in the case of 2-methylpiperidine. Therefore, a structure of type **7** (Scheme I) seems to be appropriate for this intermediate species and the C(7) pathway accounts for the formation of the abnormal product **4b**.

Also, for the reactions to take the C(7) course to **4b**, it is by no means necessary that the **3** $\rightleftarrows$ **7** equilibrium be strongly displaced toward **7**. This is shown for the reaction of **3** (Y = quinuclidinio) (2×10^{-5} *M*) with aniline (1.5 *M*) in DMSO, where a **4b**-type product is obtained (Table I). Here, the rate of disappearance of **3** (followed by the decrease of the 315-nm uv absorption[12]) equals that of the formation of **4b** (followed by the increase of the 404-nm uv absorption); thus no accumulation of intermediates is involved. It must be then admitted that the C(7) route is followed because the 1,3 elimination step **8** → **4b** is much easier than the C(2) substitution process.

The other cases of the reactions of **3** (Y = quinuclidinio) with primary or secondary (even sterically hindered) amines or of ammonia,[10] where exclusively the C(7) pathway is followed (Table I), serve to generalize the above observations.

Going to a less activated substrate like **3** (Y = Cl), it is observed (Table I) that with both primary and secondary amines, **4a**-type products have been obtained. This fits the above picture because with a mildly electron-attracting Y group such as chlorine, the higher transition state energy for the **3** → **6** rather than the **3** → **7** process is more than compensated for by the ease of the **6** → **4a** process (fast)[13] with respect to the **8** → **4b** one.

Such a compensation could not be envisaged for the strongly activated substrate **3** (Y = quinuclidinio). In fact, on the basis of the mechanisms in Scheme I and our reasoning above, it is expected that with strongly electron-attracting Y groups the energy difference between the transition state for the **3** → **6** and **3** → **7** processes may become very large, favoring the latter. If so, provided that protonating agents are not removed, the C(2) course loses any chance of occurring.

It seems now logical to explain the abnormal course of the reaction of ammonia with **3** (Y = Cl) in terms of the low nucleophilic reactivity of this reagent, thus having the 1,3 elimination step competing effectively with the C(2) route.[16] It is also consistent with our ideas above that with this weakly nucleophilic reagent, a sizable amount of the product *via* the C(1) pathway is observed.

This behavior seems to be peculiar to ammonia, not being shared by other amines of even lower base strength, such as *m*-chloroaniline. In this case the normal course C(2) is followed (Table I). We suggest that this is so because *m*-chloroaniline has more kinetic affinity for carbon than hydrogen, relative to ammonia, which is in accordance with current views; thus the C(2) route is preferred over the C(7) one, which requires attack on deuterium.[17]

(14) W. von E. Doering and D. B. Denney, *J. Amer. Chem. Soc.*, 77, 4619 (1955).

(15) Since along the C(7) route protonation of **7** occurs in a fast step,[12] clearly we have to compare the rate of formation of **7**, and not of **8**, with that of **6**.

(16) In this case also with **3** (10^{-5} *M*) and saturated (*ca.* 1.5 *M*) solution of ammonia in DMSO, no accumulation of intermediates was observed, the rate of disappearance of **3** being identical with that of formation of **4b**. This reinforces our ideas above as to the driving force for the abnormal path C(7).

(17) It is pertinent at this point to ask what the consequence of kinetic isotope effects may be. It is, in fact, known that the 1,3 elimination step **8** → **4b** for the reaction of piperidine with **3** (Y = quinuclidinio) involves a large primary isotope effect.[12] However, this is

The case of the tosylate **3** (Y = OTs) is akin to that of the chloro derivative because strongly nucleophilic amines lead to reaction along the C(2) route (Table I).

The reaction of ammonia with 2-piperidino[3,5,7-$^2H_3$]tropone (Table I) fulfills all requirements of the above theory. Thus, in spite of the extreme slowness of the reaction, only the C(2) route was observed, as demanded by a nonactivating (amino) group. Neither the product of C(7) substitution nor that of ring contraction was obtained in any detectable amount.

With an anionic nucleophile such as sodium *p*-tolylmercaptide, it is seen that, independently of the substrate nature, only the normal path C(2) is followed.

This process, with **3** (Y = quinuclidinio) 5×10^{-5} *M* and mercaptide 2×10^{-4} *M* in DMSO at room temperature, was monitored by stopped-flow (Durrum) uv absorption spectrometry at 380 nm. An initial absorption was observed which is neither due to the initial reagents nor to the substitution product **4a**. Its intensity was higher for increasing concentrations of mercaptide. However, the rate of this process was much too high for this technique. Then this absorption decayed at a measurable rate into that of **4a**. Therefore, the initial absorption is most reasonably attributed to an intermediate of the **7**-type.[18] That this cannot change into **4b** but is driven off toward **4a** must be attributed to the unavailability of effective protonating agents for the **7** → **8** step.

Extent of this Rationalization. Although full discussion of this section is delayed to a review article,[19] we wish to point out briefly here that we are not aware of any single finding, for processes which conceivably involve reversible attack of N on strongly activated or strongly deactivated substrates of type **3** (Scheme I), which cannot be accounted for in terms of our picture above. Notable is the long known and unexplained observation that 2-methoxytropone typically undergoes substitution at C(2), even by the "peculiar" reagent ammonia.[20] This receives now the same explanation as the last reaction in Table I in view of the similar electronic nature of dialkylamino and alkoxy groups.

It is a consequence of our premises in the preceding paragraph that with mildly activated substrates a lessened selectivity for substitution at C(7) *vs.* C(2) may be observed, so that the very high selectivities observed here for such substrates must be due to a fortuitous combination of factors.

It is also important to realize that our picture is expected to lack validity when the **3** → **6** and **3** → **7** processes in the scheme are irreversible. It is therefore not surprising that substitutions on mildly activated substrates **3** by organomagnesium or organolithium compounds occur exclusively by the C(7) route. Here, in contrast with the reactions of *p*-tolylmercaptide, the intermediate of type **7** cannot revert to **3**, being thus only able to await for aqueous acid work-up, whereby it is transformed into **4b**. It is surprising, however, that also when Y is a dialkylamino group, Grignard reagents lead to "anomalous" products **4b**.[21] We propose that coordination of nitrogen with the metal changes the electronic nature of the dialkylamino group to produce an electron-attracting coordinated Y group.

Synthetic Scope. Functionalization of cycloheptatrienones at the α or α' positions to the carbonyl group is the key step in many synthetic sequences with either simple[20] or quite complex structures.[22] Therefore, we want to illustrate other examples in which the intrinsic aptitude (see preceding paragraph) of mildly activated substrates to undergo facile change of selectivity for substitution at the α or α' positions with small structural or environmental changes is utilized to synthesis. The first case concerns reactions by ammonia. We have seen only cases where this reagent leads to **4b**-type products. However, the mechanisms of Scheme I and our reasoning above predict that if C_2 reactivity is especially enhanced, as is known to occur with Y = F and N = aliphatic amines,[13] the C(2) pathway may effectively compete with the C(7) pathway. Consistent with this expectation is the observation (Table I) that 2-fluorotropone leads to **4a**-type product in practically quantitative yield, the rate of this process (Experimental Section) being much higher than that of the "anomalous" reaction of 2-chlorotropone with ammonia.

The other case concerns reactions by *m*-chloroaniline. We have seen that this amine, in spite of its low strength as a base, lacks the peculiarities of ammonia, the **4a**-type product being obtained with 2-chlorotropone. Also, here the mechanisms in Scheme I suggest the changes to be made in order to drive **3** toward **4b**. This could be achieved if a strong proton base, which lacks nucleophilicity toward carbon but may effect the 1,3 elimination step **8** → **4b**, is made available. A base which may be presumed to meet these requirements is triethylamine and it was rewarding to find (Table I) that the C(2) course of the reaction of 2-chlorotropone with *m*-chloroaniline was nearly entirely changed to the C(7) course on addition of triethylamine. Also, as expected, the reaction rate was higher in the presence of triethylamine (Experimental Section).

One might ask if this interpretation of the change of reaction course on addition of triethylamine is correct or rather if a case of "nucleophilic catalysis with rearrangement"[23] is involved. Although the latter was not expected for a sterically hindered tertiary amine like triethylamine and for chlorine as a replaceable group,[23] we have checked that 2-chlorotropone can be largely recovered, besides a little untractable tar, from a DMSO solution with triethylamine under otherwise identical conditions to those leading to 40% anomalous

partially compensated for by a substantial secondary effect, acting in the same direction, for attack of N at C(2). In fact, by methods already described,[13] we have found that the ratio of the apparent[12] rate coefficients for reactions of **2** (Y = I) and **3** (Y = I) (7×10^{-5} *M*) with piperidine (0.043 *M*) in dried DMSO at 25° is 1.97. These factors are too small to exert sizable influence on the competition between C(2) and C(7) pathways. It is interesting that, in contrast, neither attack at C(7)[12] nor at another nuclear position, which is probably C(6),[10] involves any substantial deuterium isotope effect.

(18) The alternative hypothesis that the initial absorption observed here may be due to a charge-transfer complex formed by the interaction of cycloheptatrienone and mercaptide reagents cannot be rigorously ruled out just because the rate of this process was too high for our technique. However, rates of formation of σ complexes like **8** are expected to be much higher for mercaptide than amine nucleophiles. Moreover, the hypothesis of a σ complex for mercaptide nucleophiles is consistent with the whole picture presented here.

(19) G. Biggi and F. Pietra, manuscript in preparation.

(20) T. Nozoe, "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience, New York, N. Y., 1959.

(21) P. Akroyd, R. D. Haworth, and P. R. Jefferies, *J. Chem. Soc.* 286 (1954); R. D. Haworth and P. B. Tinker, quoted in ref 7, p 61.

(22) J. Schreiber, W. Leimgruber, M. Pesaro, P. Schudel, and A. Eschenmoser, *Angew. Chem.*, 71, 637 (1959).

(23) G. Biggi, F. Del Cima, and F. Pietra, *J. Chem. Soc., Perkin Trans. 2*, 1424 (1972).

substitution product (Table I) in the presence of *m*-chloroaniline.

With 2-chlorotropone and either *trans*- or *cis*-2,6-dimethylpiperidine, mostly tars were obtained.

We conclude that there is nothing abnormal about C(7) substitution, which is not recognized as the most logical pathway with quite common substrates and reagents.

Experimental Section

Product yields are based on starting **3**. Melting points were taken on a Kofler hot-stage apparatus without correction. Nmr measurements were made with Hitachi Perkin-Elmer R10, Varian S 60T, or Jeol SP 100 (equipped with deuterium decoupling device) spectrometers using 5–20% (w/v) solutions with TMS as internal standard. Uv spectra were taken with a Unicam SP 800 spectrophotometer. Dimethyl sulfoxide was distilled from calcium hydride under N_2. Amines were freshly distilled from potassium hydroxide pellets or K–Na alloy, as appropriate, under N_2.

Reactions of 2-(1-Azoniabicyclo[2.2.2]oct-1-yl)cyclohepta-2,4,6-trien-1-one Iodide[24] (2, Y = Quinuclidinio) or of 2-(1-Azoniabicyclo-[2.2.2]oct-1-yl)[3,5,7-$^2H_3$]cyclohepta-2,4,6-trien-1-one Iodide[24] (3, Y = Quinuclidinio). **(a) With 2-Methylpiperidine.** A solution of **2** (Y = quinuclidinio) (0.1 g, 0.3 mmol) in dried DMSO (10 ml) was added to the equimolar amount of dried 2-methylpiperidine in the same solvent (3 ml). After 1 week, 2-(α-methylpiperidino)tropone was detected (uv) in 96% yield. The mixture was then poured into water and ether extracted to give a dark oil which was instilled as a yellow-brown oil (which failed to crystallize) on a cold finger (bath temp 50–60° (0.1–0.2 mm)) (80% yield): δ (Varian, $CDCl_3$) 7.2–6.5 (complex pattern, 5 H), 4.4 br (1 H), 3.3 br (2 H), 1.8 br (6 H), 1.1 (3 H, d, J = 7.0 Hz); λ_{max} (EtOH 95%) 360 and 410 nm (log ε 3.91 and 3.87); picrate (from 95% ethanol), mp 164–165° (*Anal.* Calcd for $C_{19}H_{20}N_4O_8$: C, 52.8; H, 4.7; N, 13.0. Found: C, 53.0; H, 4.6; N, 13.0.). The corresponding reaction of **3** (Y = quinuclidinio) was carried out under identical conditions, the yield (uv) of **4b** (Y = α-methylpiperidino) being 90%. Here the dark oil obtained as above was twice chromatographed on a 1.5-mm thick silica gel layer and activated at 110° for 1 hr, with a solvent mixture of 9:1 benzene–95% ethanol, with the prominent yellow band being collected. Extraction gave a yellow oil, the uv spectrum of which was identical with that for the corresponding undeuterated material above: δ (Hitachi Perkin-Elmer, CCl_4)[25] 4.3 br (1 H), 3.2 br (2 H), 1.7 br (6 H), 1.2 (3 H, d, J = 7.0 Hz).

(b) With Diethylamine. Reaction conditions and procedures to recover reaction products (chromatographic eluent 8:2 benzene–95% ethanol) were as above for 2-methylpiperidine. 2-Diethylaminotropone (**2**, Y = diethylamino) (99 and 80% spectroscopic (uv) and recovered yields, respectively) was collected as a yellow-brown oil: δ (Varian, C_6D_6) 7–6 (complex pattern, 5 H), 3.2 (4 H, q, J = 7.0 Hz), 0.9 (6 H, t, J = 7.0 Hz); λ_{max} (EtOH 96%) 354 and 415 nm (log ε 3.94 and 3.83); picrate (from 95% ethanol), mp 163–165° (*Anal.* Calcd for $C_{17}H_{18}N_4O_8$: C, 50.2; H, 4.5; N, 13.8. Found: C, 49.9; H, 4.4; N, 13.7). 2-Diethylamino-[4,6-$^2H_2$]tropone (**4b**, N = diethylamino) was a yellow-brown oil, uv spectrum (yield *85%*) identical with that for 2-diethylaminotropone; δ (Hitachi Perkin-Elmer, CCl_4)[25] 3.5 (4 H, q, J = 7.0 Hz), 1.2 (6 H, t, J = 7.0 Hz).

(c) With *n*-Butylamine. Reaction conditions and product recovery as in (a) above. 2-*n*-Butylaminotropone (**2**, Y = butylamino) was collected as a yellow semisolid oil (98 and 75% spectroscopic (uv) and isolated yields, respectively); δ (Varian, CCl_4) 7.7–6.2 (complex pattern, 6 H), four absorptions at 3.4, 3.3, 3.2, 3.1 (2 H), 1.6 br (4 H), 1.0 (3 H, d, J = 6.0 Hz); on shaking with D_2O a signal at *ca.* 7.2 ppm, corresponding to one proton, disappeared while the four signals at δ 3.4–3.1 became a nice triplet at δ 3.2 (3 H, t, J = 6.0 Hz); λ_{max} (EtOH 95%) 337 and 406 nm (log ε 3.95 and 3.93); picrate (from 95% ethanol), mp 110–112° or 88–90° (with identical analysis and uv spectrum) (*Anal.* Calcd for $C_{17}H_{18}N_4O_8$: C, 50.2; H, 4.5; N, 13.8. Found: C, 50.2; H, 4.4; N, 13.8.). 2-*n*-Butylamino[4,6-$^2H_2$]tropone (**4b**, N = *n*-butylamino), yellow oil, uv spectrum (98% yield) identical with that for 2-*n*-butylaminotropone; δ (Hitachi Perkin-Elmer, CCl_4)[25] from 7.2 upwards identical with that for 2-*n*-butylaminotropone.

(d) With Aniline. Reaction conditions and product recovery as in (a) above. 2-Anilinotropone (**2**, Y = anilino) was collected as a yellow-brown oil (75 and 35% spectroscopic (uv) and recovered yields, respectively); δ (Varian, C_6D_6) 9 br (1 H), 7.5–6.2 (complex pattern, 10 H); the signal at 9 ppm disappears on shaking with D_2O; λ_{max} (EtOH 95%) 347 and 404 nm (log ε 4.02 and 4.63); picrate (from 95% ethanol), mp 142–143° (*Anal.* Calcd for $C_{19}H_{14}N_4O_8$: C, 53.5; H, 3.3; N, 13.1. Found: C, 52.8; H, 3.1; N, 13.6). 2-Anilino[4,6-$^2H_2$]tropone (**4b**, N = anilino) was a yellow-brown oil, uv spectrum identical with that for 2-anilinotropone (63% yield); δ (Jeol, C_6D_6)[25] 9 br (1 H, which disappeared on shaking with D_2O), 7.2–6.7 complex pattern due to aniline ring protons (see text).

(e) With Sodium *p*-Tolylmercaptide. Since 2-*p*-tolylmercaptotropone is known,[26] the reaction was carried out with the deuterated cycloheptatrienone only; 0.1 g (0.29 mmol) of the latter, dissolved in dried DMSO, 8 ml, was added at room temperature to the equimolar amount of sodium *p*-tolylmercaptide dissolved in the same solvent, 2 ml. The mixture, after 2 days at room temperature, showed the uv absorption spectrum of the expected product (see below) in 98% yield. The mixture was then poured into water and ether extracted, and the ethereal layer dried over $MgSO_4$ and then evaporated to leave 2-*p*-tolylmercapto[3,5,7-$^2H_3$]tropone (**4a**, Y = *p*-tolylmercapto), mp 138–139° (from methanol), in 70% yield; δ (Jeol, CCl_4)[25] 7.35 (4 H, AA'BB' system), 2.45 (3 H, s); λ_{max} (EtOH 95%) broad absorptions from 300 to 400 nm with peaks at 326, 344, and 370 nm (log ε 3.87, 3.98, and 4.01).

Reactions of Tropolone Tosylate[11] (2, Y = OTs) or of [3,5,7-$^2H_3$]-Tropolone Tosylate[11] (3, Y = OTs). **(a) With Piperidine.** To a solution of **2** (Y = OTs) (0.15 g, 0.54 mmol) in dried DMSO (10 ml) dried piperidine (0.15 ml, 1.4 mmol) was added. The uv spectrum of the reaction mixture after a few minutes showed the formation of 2-piperidinotropone[13] in a practically quantitative yield. The reaction of **3** (Y = OTs) was carried out under identical conditions. The reaction mixture was poured into water and ether extracted, and the ether layer dried and evaporated to leave a brown liquid which was sublimed to give yellow-orange crystals, mp 56–57° (75% yield), of 2-piperidino[3,5,7-$^2H_3$]tropone.[13]

(b) With *n*-Butylamine. The reaction of **3** (Y = OTs) was carried out under the conditions used above for the corresponding reaction of piperidine. Monitoring by uv showed the rapid formation, in practically quantitative yield, of 2-*n*-butylamino-[3,5,7-$^2H_3$]tropone.

Reactions of 2-Chlorotropone[13] (2, Y = Cl) or of 2-Chloro[3,5,7-$^2H_3$]tropone[13] (3, Y = Cl). **(a) With Diethylamine.** A solution of dried diethylamine (0.7 ml, 6.8 mmol) in 1 ml of dried DMSO was added to a solution of **3** (Y = Cl) (0.126 g, 0.9 mmol) in 2 ml of the same solvent. The mixture, after 1 day at room temperature, showed a uv absorption spectrum identical with that for 2-diethylaminotropone (above) in practically quantitative yield. Work-up as above for the corresponding reaction of **3** (Y = quinuclidinio) gave 2-diethylamino[3,5,7-$^2H_3$]tropone as a yellow-brown oil (65% yield).

(b) With Piperidine. The reaction was carried out as above for diethylamine. The spectroscopic (uv) and recovered yields of 2-piperidino[3,5,7-$^2H_3$]tropone were 100 and 60%, respectively.

(c) With 2-Methylpiperidine. To a solution of **3** (Y = Cl) (0.1 g, 0.7 mmol) in dried DMSO (1.7 ml), dried 2-methylpiperidine (0.3 ml, 2.55 mmol) was added. The mixture was sealed in a glass ampoule and heated at 80° for 24 hr. The 350–450-nm region of the uv absorption spectrum was identical with that of 2-(α-methylpiperidino)tropone formed in practically quantitative yield. The mixture was then worked up as for the corresponding reaction of **3** (Y = quinuclidinio) to give 2-(α-methylpiperidino)tropone as a yellow-brown oil (70% yield).

(d) With *m*-Chloroaniline. To a solution of **2** (Y = Cl) (0.13 g, 0.93 mmol) in dried DMSO (1 ml), dried *m*-chloroaniline (0.5 ml, 4.8 mmol) was added. The mixture was flushed with dry N_2, sealed in a glass ampoule, and heated at 80° for 2 days. The uv absorption spectrum showed the formation of 2-(*m*-chloroanilino)-tropone (**2**, N = *m*-chloroanilino), see below, in *ca.* 50% yield. The mixture was then poured into water and ether extracted. The ethereal layer was dried and then evaporated *in vacuo*, and the

(24) F. Pietra, G. Biggi, and F. Del Cima, *J. Chem. Soc. C*, 3626 (1971).

(25) ^1H nmr spectral data for the cycloheptatrienone moiety are reported in Table I.

(26) T. Nozoe, M. Sato, and K. Matsui, *Sci. Rep. Res. Inst., Tohoku Univ.*, **I37**, 211 (1953).

resulting liquid mixture was chromatographed on a silica gel column (eluent 9:1 cyclohexane–95% ethanol). The yellow eluate was evaporated to leave a brown oil which was chromatographed on a 1.5-mm thick silica gel layer (activated at 110° for 1 hr), solvent mixture 8:1.2:0.8 benzene–cyclohexane–95% ethanol, to give a yellow band at R_f 0.4 which gave crystals (0.06 g, 30% yield), mp 93–94°. Recrystallization from *n*-hexane raised the mp to 97–98° (*Anal.* Calcd for $C_{13}H_{10}ClNO$: C, 67.5; H, 4.3; N, 6.1. Found: C, 67.3; H, 4.3; N, 6.2): δ (Varian, CCl_4) 8.8 br (*ca.* 1 H, the signal was extremely broad so that it could not be accurately integrated), 7.4–6.5 (complex pattern, 9 H); λ_{max} (EtOH 95%) 345 and 401 nm (log ε 4.07 and 4.21). The corresponding reaction of **3** (Y = Cl) was carried out under identical conditions, the spectroscopic yield of a product showing a uv spectrum identical with that of 2-(*m*-chloroanilino)tropone being *ca.* 41%; δ (Jeol, CCl_4)[25] 9.1 br (*ca.* 1 H, see above for integration) and a complex pattern superimposed to the signals due to the cycloheptatrienone protons (Table I). Gas chromatographic analysis (column 1 × 2 mm of 1% neopentyl glycol succinate on silanized Chromosorb W 80–100 mesh; temp, 215°; N_2 45 ml/min) of the other extracts from the reaction mixture revealed the presence of benzoyl-*m*-chloroanilide, whose amount was not accurately evaluated.

(d′) With *m*-Chloroaniline plus Triethylamine. An N_2 flushed solution made of **3** (Y = Cl) (0.10 g, 0.71 mmol), dried *m*-chloroaniline (0.2 ml, 1.92 mmol), and dried triethylamine (0.3 ml, 2.2 mmol) in 0.5 ml of dried DMSO was sealed into a glass ampoule and heated at 80° for 24 hr. The long wavelength region of the absorption uv spectrum of the reaction mixture was identical with that for either **2** or **3** (N = *m*-chloroanilino) formed in 45% yield. The reaction mixture was worked up as in the two cases above in (**d**), with, however, 9.8:0.2 benzene–95% ethanol as chromatographic eluent. The central part of the yellow band at R_f 0.35 gave crystals (0.037 g, 21% yield), mp 93–94°, after sublimation *in vacuo;* δ (Jeol, CCl_4)[25] as above in (**d**).

(e) With Ammonia. 2-Aminotropone was prepared by standard procedures;[27] mp 102–104° (lit.[27] 102–104°). In the case of deuterated materials, a solution of **3** (Y = Cl) (0.28 g, 2.0 mmol) in dried DMSO (3 ml) was added to a 1.7 *M* solution of dried ammonia in the same solvent (2.5 mol) at room temperature. After 2 days the uv spectrum showed absorptions attributable to a compound having the structure of 2-aminotropone (68% yield). The mixture was then poured into water and ether extracted. The ethereal layer was dried and evaporated to leave a brown oil which was thoroughly sublimed *in vacuo* on a cold finger to give a crystalline powder: mp 85–90°; δ (Jeol, $CDCl_3$) 6.3 br (2 H, which disappeared on shaking with D_2O), 7.4 (0.6 H, s), 7.2 (0.7 H, s), 6.9 (0.7 H, s), 6.7 (0.7 H, s). On repeated fractional sublimation of this powder the melting point sharpened and the signal at δ 7.4 ([2,4,6-$^2H_3$]benzamide) became much more pronounced that those at δ 7.2, 6.9, and 6.7. The fractions enriched in the last three signals were recrystallized from benzene and then from acetonitrile to give 2-amino[4,6-$^2H_2$]tropone, mp 102–104°; δ (Jeol, $CDCl_3$)[25] 6.3 br.

(f) With *p*-Tolylmercaptide. The reaction with **3** (Y = Cl) was carried out, and the product (spectroscopic uv, yield 95%), mp 137–139°, was isolated (60% yield) as described for the corresponding reaction of **3** (Y = quinuclidinio). Both the uv and the ^{1}H-nmr spectrum were identical with those above for **4a** (Y = *p*-tolylmercapto).

Reactions of 2-Fluorotropone[13] (2, Y = F) or of 2-Fluoro[3,5,7-$^2H_3$]tropone[13] (3, Y = F). (a) With Ammonia. The reaction was carried out as described above for the corresponding reaction of **3** (Y = Cl). The uv absorption spectrum of the reaction mixture after 1 hr corresponds to quantitative formation of 2-aminctropone. The mixture was then poured into water and ether extracted. The ethereal layer was dried over $MgSO_4$, filtered, and evaporated to leave a brown oil. This was sublimed to give yellow crystals; mp 102–104° (50% yield) of 2-amino[3,5,7-$^2H_3$]tropone; δ (Jeol, $CDCl_3$)[25] 6.3 br.

(b) With Aniline. A solution of **3** (X = F) (0.066 g, 0.61 mmol) and dried aniline (0.3 ml, 3.3 mmol) in 0.5 ml of dried DMSO was left at room temperature for 36 hr. The uv spectrum corresponded to formation of 2-anilinotropone in quantitative yield. The mixture was then worked up as in the corresponding reaction with **3** (Y = quinuclidinio) to give yellow crystals, mp 30–41°, of 2-anilino[3,5,7-$^2H_3$]tropone (67% yield); δ (Jeol, CCl_4)[25] 9 br (1 H, which disappeared on shaking with D_2O), 7.3–6.7 complex pattern due to the aniline ring protons.

(c) With *m*-Chloroanilino. The reaction was carried out as above (b) and worked up as in the case of the corresponding reaction of **3** (Y = Cl). 2-(*m*-Chloroanilino)[3,5,7-$^2H_3$]tropone was observed in quantitative yield (uv) and isolated in 65% yield.

Reaction of 2-Piperidino[3,5,7-$^2H_3$]tropone[13] (3, Y = Piperidino) with Ammonia. A solution of **3** (Y = piperidino) (0.09 g, 0.48 mmol) in dried DMSO was added to 3 ml of a 1.7 *M* solution of dried ammonia in the same solvent. The mixture was sealed under N_2 into a glass ampoule and heated at 80° for 6 days. The uv absorption spectrum of the reaction mixture showed a substantial amount of the starting piperidinotropone to be still present. The mixture was then ether extracted. The ethereal layer was dried and evaporated to leave a brown oil which was chromatographed on a 1.5-mm thick silica gel layer to give two major yellow bands. That at R_f 0.6 corresponded to unreacted **3** (Y = piperidino) (77% yield), while that at R_f 0.3 gave, after sublimation, yellow crystals, mp 102–104°, of 2-amino[3,5,7-$^2H_3$]tropone (20% yield). ^{1}H nmr spectra proved the absence of benzamide, which has the same R_f value as 2-aminotropone, under the above chromatographic conditions.

(27) W. von E. Doering and L. Knox, *J. Amer. Chem. Soc.*, 73, 828 (1951); 74, 5863 (1952).