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TROPENYLATION, DETROPENYLATION AND SCHIFF BASE FORMATION IN THE REACTION OF 3,4,5-TRIMETHOXYANILINE WITH TROPENYLIUM ION

Josuke TSUNETSUGU, Masaru SATO, and Seiji EBINE*
Department of Chemistry, Faculty of Science and Engineering
Saitama University, Urawa, Saitama 338

Tropenylation of 3,4,5-trimethoxyaniline (II) with tropenylium ion (I), generated by action of acid on 7-ethoxy-1,3,5-cycloheptatriene, gave C-tropenyl derivative (III) and its Schiff base (VI). Further reaction of (III) with (I) gave not only tropenylation products (IV) and (XI) but also detropenylation product (II). Detropenylation has proved to take place in the presence of acid.

Tropenylation of various aliphatic amines gave 7-tropenylamines[1) and that of various aromatic amines gave N- and/or C-tropenylanilines.[2). 7-Tropenylamines were reported to give the corresponding tropenylidenimmonium salts[3,4) when treated with tropenylium fluoroborate. Rearrangements of tropenylium ion (I) to benzaldehyde and benzene by the reaction with oxidizing reagents, such as selenium dioxide, chromium trioxide and hydrogen peroxide, are also known.[1,5)

We wish to report tropenylation of 3,4,5-trimethoxyaniline (II) accompanying a novel type of oxidative rearrangement of (I) to benzaldehyde[6) (in a form of Schiff base) and detropenylation encountered in further reaction of tropenylanilines with (I). (II) was allowed to react with 1.2 molar amount of (I), generated from 7-ethoxy-1,3,5-cycloheptatriene and a minute amount of concentrated hydrochloric acid, in ethanol under nitrogen atmosphere. The reaction mixture was neutralized and the solvent was removed under a reduced pressure at low temperature. The residue was extracted with dichloromethane and chromatographed to separate the products listed in Table I. The reaction is delicately dependent on temperature. Schiff base (VI); yellow needles, mp 127-127.5°C; IR(KBr), 1627 cm^{-1}; PMR(60 MHz, $CDCl_3$), δ 3.49(1H,t,J=5.0

Table I. Tropenylation of 3,4,5-trimethoxyaniline (II)

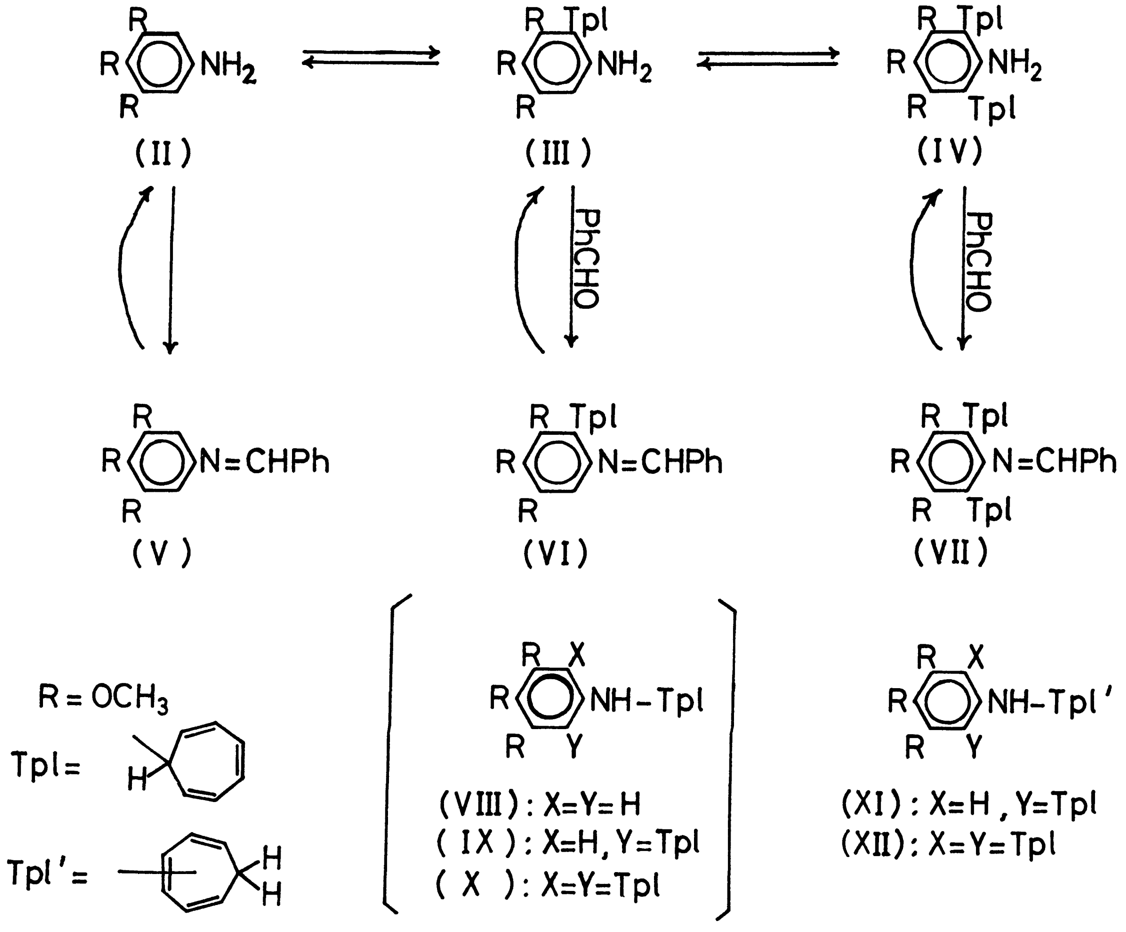
Reaction temp. (°C)	Reaction time (hr)	Yield (%)			
		III	IV	VI	Recovery
40	2.0	77.9	-	7.2	14.7
45	2.0	83.7	-	11.3	-
50	1.5	72.5	-	10.3	-
78	2.0	33.8	9.6	3.3	43.2

Precision; ±1°C

Hz,H-7'), 6.46(1H,s,H-6) and 8.40(1H,s,methine proton). C-Tropenyl derivative (III); a brown oil; IR(KBr), 3475 and 3375 cm^{-1}; PMR(CDCl$_3$), δ 3.43(1H,t,J=5.0 Hz,H-7') and 6.13(1H,s,H-6); (diacetate, mp 113-114°C). C,C-Ditropenyl derivative (IV); colorless needles, mp 136.0-136.5°C. Interestingly, at the higher temperatures the better recoveries of (II) were obtained. To clearify the reaction sequence to form (VI), (III) was further tropenylated with one molar amount of (I) and the various products were obtained according to the reaction conditions (Table II). C-Tropenyl derivative (III'); a brown oil, a 2 to 5 mixture of 3'- and 2'- (or 2'- and 3'-) tropenyl isomers8) of (III). C,N-Ditropenyl derivative (XI); a brown oil, a 2 to 5 mixture of 1'- and 2' or 3'-tropenyl isomers about N-tropenyl group of (IX); IR(KBr),

Table II. Tropenylation of 3,4,5-trimethoxy-2-(7'-tropenyl)aniline (III)

Reaction temp. (°C)	Reaction time (hr)	Solvent	HCl	Yield (%)				
				II	III	III'	IV	XI
25	30	EtOH	+	-	52.0	-	36.5	-
50	1.5	EtOH	+	4.6	27.6	-	40.0	9.3
85-90	1.5	EtOH	-	-	64.7	-	8.1	-
160-170	1.5	-	-	-	-	70	-	-



(II) (III) (IV)

(V) (VI) (VII)

R = OCH$_3$

Tpl=

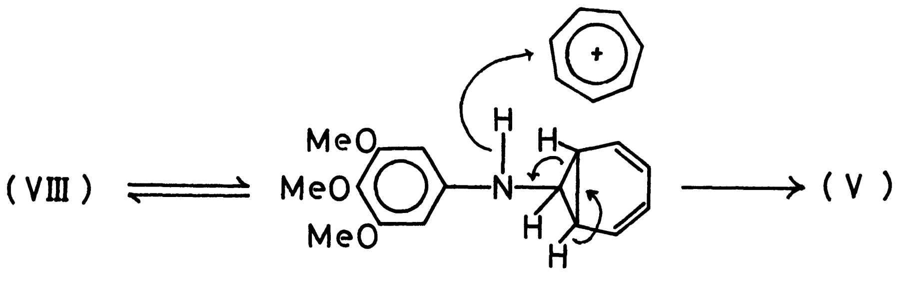
Tpl'=

(VIII): X=Y=H
(IX): X=H,Y=Tpl
(X): X=Y=Tpl

(XI): X=H ,Y=Tpl
(XII): X=Y=Tpl

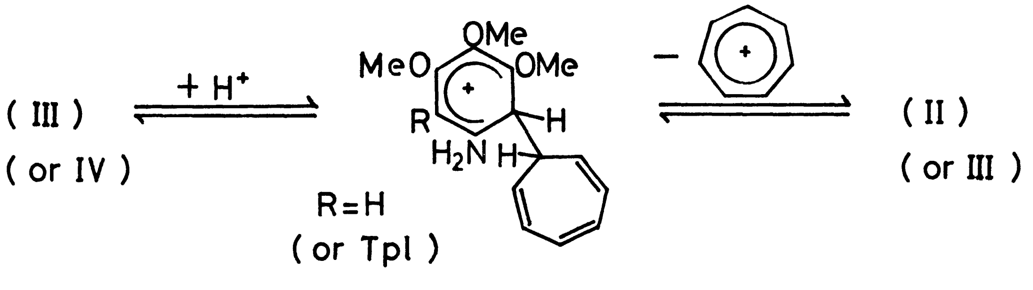
3375 cm^{-1}; PMR(CDCl$_3$), δ 1.94(q,J=8.0 Hz,H-2' or H-3'), 2.33(d, J=7.0 Hz,H-1') and 5.61(1H,s,H-6). The better recoveries of (III) were again observed at the higher temperatures. No (VI) was formed on tropenylation of (III) under various experimental conditions. The reaction of the Schiff base (V), synthesized by another route, with one molar amount of (I) at 60°C for 1.5 hr in acidic ethanol solution yielded (VI, 4.9 %), (VII, 0.8 %), colorless needles, mp 169-170°C, and (III, 62.0 %). Thus the formation of (VI) by tropenylation of (II) could be considered as follows: (II) reacts with (I) to give (III) and (V), and then (III) condenses with benzaldehyde, liberated by hydrolysis of (V),[9] to give (VI).[10,11] (IV) was also allowed to react with one molar amount of (I) at 50°C for 1.5 hr under acidic condition, resulting (III,7.5 %), C,C,N-tritropenyl derivative (XII,28.5 %), a brown oil, a 1 to 2 mixture of 1'- and 2' or 3'-tropenyl isomers of C,C,N-tritropenyl derivative (X), and recovery of (IV,57.7 %). Even the reaction with 1.5 molar amount of (I) gave no detectable amount of (VI), showing that (IV) cannot be a precursor of (VII).

Tropenylation of aromatic amines is considered to proceed via N-tropenyl derivatives which then rearrange to C-tropenyl ones.[2a] We therefore deduce that, on tropenylation of (II), the first-formed N-tropenyl intermediate (VIII)[10] rearranges to (III) and at the same time (VIII) transforms to (V) via the norcaradiene form(VIII')[12] by hydride abstraction with (I). On tropenylation of (III) and (IV), however, N-tropenyl intermediates (IX) and (X) do not rearrange to the corresponding Schiff bases (VI) and (VII) respectively, because (IX) and (X) have steric hindrance due to one and two C-tropenyl groups which prevent (I) from approaching to the reaction center.



(VIII')

Finally, detropenylation of (III) and (IV) would be a cation exchange reaction between a proton and (I), since (IV) was found to be easily detropenylated to (II,48.5 %) and a mixture of 1'- and 2'- or 3'-tropenyl isomers of (III,16.1 %) in hot acidic ethanol. Such type of detropenylation has never been observed on aromatic nuclei.[13]



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9. Schiff base (V) was easily hydrolyzed to give a quantitative amount of aniline (II) and benzaldehyde under the similar reaction conditions without 7-ethoxy-1,3,5-cycloheptatriene.
10. An attempt to capture the key intermediate N-tropenyl derivative (VIII) resulted to afford only (III,71 %) on treatment of (II) with 7-ethoxy-1,3,5-cycloheptatriene in pyridine-ethanol at 60°C for 1.5 hr.
11. Based on the fact that aniline is easily tropenylated while N,N-dimethylaniline having no amino-hydrogen is not directly tropenylated,[2a)] direct tropenylation of (V) to (VI) seems to be less probable although δ 6.54 (s) for aromatic 2- and 6-protons suggests a higher electron density.
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