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THE REACTION OF 2,6-DISUBSTITUTED TROPONES WITH HYDRAZINE

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Amination at the C_2 position of tropone with hydrazine is one of the peculiar reactions of the tropone system and is of great importance in the synthesis[1] of 2-aminotropone derivatives from 2-[2], 3-[3], or 4-monosubstituted tropones.[3] It was found, however, that 2,6-disubstituted tropones, such as 2,6-diphenyl- (I), 2-phenyl-6-methyl- (II), and 2-phenyl-6-isopropyltropone (III),[4] although having a vacant position next to the carbonyl group, when treated with hydrazine underwent an abnormal reaction giving products of rearrangement instead of the expected 2-aminotropone derivatives.

When I was refluxed with two equivalents of hydrazine in ethanol for 20 min., a rearranged product (IV), m.p. 175° (decomp.) was obtained in more than 80 % yield. On the other hand, on being treated with hydrazine under the same conditions, II or III did not react and starting material was recovered. If the period of heating with hydrazine was increased to 2 hrs., II or III gave a 10-20 % yield of rearranged products (V), m.p.

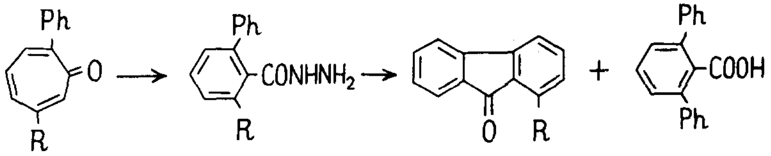
163°, or (VI), m.p. 93°. Physical properties of the products, (IV, V and VI) are shown in Table I. Their UV spectra indicate that IV, V and VI do not possess a tropone nucleus and their IR spectra show the presence of NH_2 and CO groups different from those in 2-aminotropones. From the above and the fact that they all afford an acetonide (see Table 1) with acetone, the products are assumed to be benzhydrazide derivatives.

TABLE I. Properties of the Rearrangement Products.

Product	Formula	λ_{max}^{MeOH} mμ (log ε)	IR(cm^{-1}) in $CHCl_3$		m.p. of acetonide
			CO	NH_2	
IV	$C_{19}H_{16}ON_2$	260 (3.95)	1670	3470 3370	217°
V	$C_{14}H_{14}ON_2$	247 (3.73)	1672	3425 3333	152°
VI*	$C_{16}H_{18}ON_2$	246 (3.66)	1667	3436 3333	163°

* VI is accompanied by a trace of 2-amino-3-isopropyl-7-phenyltropone, m.p. 244°

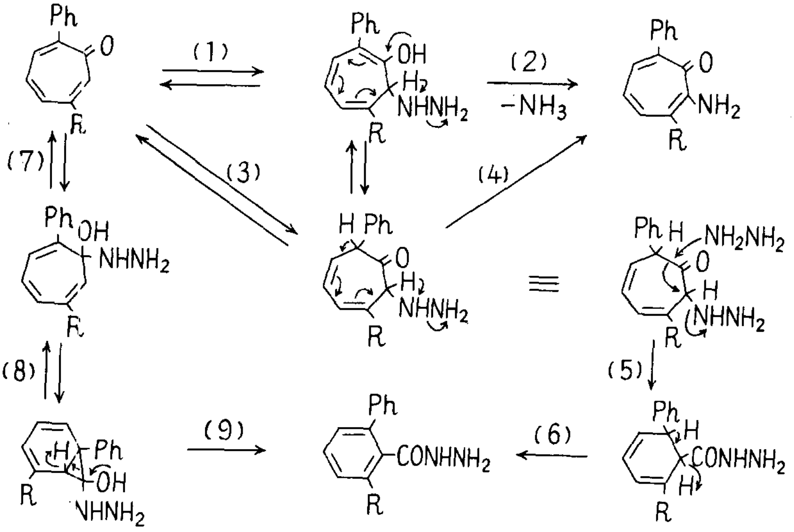
When heated with sulfuric acid-water (1:1) on a boiling water bath, IV afforded 1-phenylfluorenone[5] (VII), m.p. 120-121°, and a carboxylic acid (VIII), m.p. 184°, which, on being heated at about 240° in the presence of copper carbonate, lost carbon dioxide to form m-terphenyl, m.p. 87-88°. Treatment of V or VI with sulfuric acid in the same manner afforded 1-methylfluorenone[6] (IX), m.p. 95-96°, or 1-isopropylfluorenone (X), m.p. 63-65°. These series of experiments prove that IV, V and VI are the corresponding 2,6-disubstituted benzhydrazides.



I. R = Ph IV. R = Ph VII. R = Ph VIII.
II. R = CH_3 V. R = CH_3 IX. R = CH_3
III. R = i-C_3H_7 VI. R = i-C_3H_7 X. R = i-C_3H_7

We explain the difference between the reaction of hydrazine with 2-substituted tropones having a substituent at the C_6 position and those lacking a C_6 substituent, as follows :

It has been proposed previously that amination of tropones with hydrazine proceeds by the steps (1) and (2),[7] or (3) and (4)[8] as depicted in the following scheme. Whereas amination of 2-phenyltropone (R=H) might proceed via the proposed pathway, 2,6-diphenyltropone (R=Ph) would afford an intermediate having four substituents at neighboring positions. These substituents would severely retard the formation of 2-amino-3,7-diphenyltropone in step (2) or (4), because this elimination requires a co-planar arrangement of the four substituents and this would be prevented by their mutual steric hindrance. This steric effect would lead the reaction to other steps, (5) and (6), in which tropones are rearranged to the benzhydrazide derivatives. Otherwise, the starting tropones re-form in the step (1) or (3) and might be subject to attack by hydrazine at the C_1 position as shown in step (7), followed by rearrangement in steps (8) and (9) to give the benzhydrazide derivatives.[9] It is clear from the scheme that hydride abstraction must occur in step (6) or (9), in which hydrazine may play a role as an acceptor. As was pointed out above, there is a great difference in the rate of formation of the products from tropones having a phenyl and those having alkyl groups at C_6 position. This is attributed to the stronger inductive effect of an alkyl group at the C_6 position tending to reject a nucleophilic attack of hydrazine at the C_7 or C_1 position in the step (1), (3) or (7). Since such an inductive effect might play a greater role in step (1) or (3) than in step (7), the reaction is considered more likely to proceed by way of steps (5) and (6) than via the alternative steps (8) and (9).



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