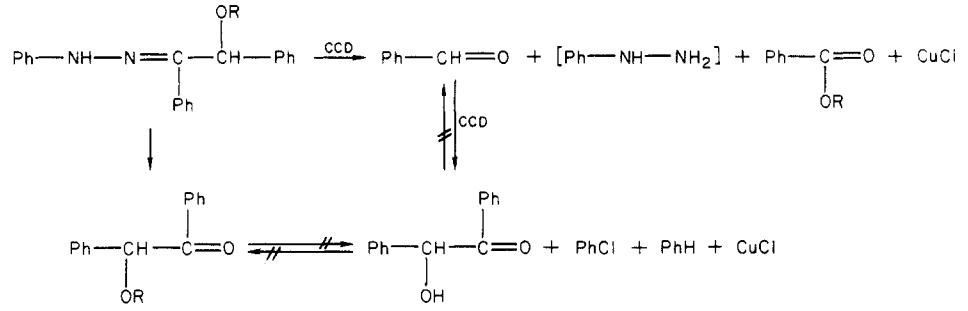
Scheme III



way (TLC, high-performance LC, and IR, ^{1}H NMR, and mass spectra).

Phenylazostilbene. This compound was prepared as previously reported.[2a]

Benzoin Phenylhydrazone Derivatives. These compounds were obtained by reaction between phenylhydrazine and the corresponding carbonyl compounds, according to well-known methodologies.[2b,8] The *syn*-benzoin phenylhydrazone ethyl ether was obtained as previously reported.[2b]

1,4-Additions to Phenylazostilbene. A typical experiment for the 1,4-addition of alcohol to PAS was previously reported in detail.[2b] Anhydrous iron(III)chloride or copper(II) chloride dihydrate (0.035 mmol) was added to an alcoholic solution (25 mL) of PAS (0.35 mmol). The mixture was stirred magnetically at 0–5 °C until the reaction was completed (5–30 min). After evaporation of the alcohol under reduced pressure, the product was poured into ether and washed with saturated aqueous sodium chloride. The ethereal layer was dried with anhydrous magnesium sulfate, and after evaporation it provided the crude AEBP in good purity. Further purification can be obtained by usual methods. However, as reported, these compounds were highly reactive for facile oxygen absorption.[2b,5] For this reason it is convenient to work under a nitrogen atmosphere. The 1,4-addition of water to PAS was carried out in a monophasic 1:1 mixture of tetrahydrofuran and water, using a molecular ratio of 10:2 PAS–CCD. After 4 h under reflux, benzoin phenylhydrazone was obtained. The addition of phenol to PAS was carried out in tetrahydrofuran solution, using a PAS, CCD, and phenol molecular ratio of 1:1:65, respectively. The reaction mixture was kept at room temperature and stirred magnetically. Under these conditions benzoin phenylhydrazone phenyl ether, the 1,4-adduct of phenol to PAS, was detected as the intermediate of the reaction. After 4 h, the usual decomposition products of the benzoin phenylhydrazone derivatives were recovered.

Decomposition of Benzoin Phenylhydrazone Derivatives in the Presence of CCD. After the 1,4-addition to PAS, increasing the CCD amount up to a molecular ratio of 1:1 or 1:3, the benzoin phenylhydrazone derivatives decompose rapidly. The decomposition under reflux is faster than at room temperature and gives the parent carbonyl compounds, benzoin, benzaldehyde, benzoic esters, chlorobenzene, and benzene. As expected, in the case of benzoin phenylhydrazone (derived by 1,4-addition of water to PAS), after 24 h under reflux, in addition to benzaldehyde, benzoic acid, chlorobenzene, and benzene, only benzoin was obtained (60% yields). The reaction of benzoin phenyhydrazone ethyl ether was studied in detail.

Preparation and Decomposition of PAS–CCD Adduct. PAS (100 mg, 0.35 mmol) was dissolved in anhydrous benzene (50 mL) and CCD (6 mg, 0.035 mmol) was added. The mixture was stirred magnetically for 10 days at room temperature under a nitrogen atmosphere. The solid was filtered out and washed twice with 20 mL of anhydrous benzene. This filtration left a product free of residual CCD; mp 140 °C (uncorrected). The IR spectrum (4000–700 cm^{-1}) shows essentially the same features of PAS shifted to higher frequency (from 20 to 50 cm^{-1}). Anal. Calcd: C, 40.77; H, 3.42; N 4.75. Found: C, 40.59; H, 3.31; N, 4.86. This compound was reacted with absolute ethanol and produced benzoin ethyl ether, benzoin, benzaldehyde, ethyl benzoate, chlorobenzene, and benzene, which are the usual products derived from the decomposition of benzoin phenylhydrazone ethyl ether.

Acknowledgment. This work was supported by the financial assistance from the Consiglio Nazionale delle Ricerche (Roma).

Registry No. PAS, 25769-36-2; methanol, 67-56-1; ethanol, 64-17-5; 1-propanol, 71-23-8; 2-propanol, 67-63-0; 1-butanol, 71-36-3; 2-butanol, 78-92-2; phenol, 108-95-2; water, 7732-18-5; *syn*-benzoin phenylhydrazone methyl ether, 70994-05-7; *anti*-benzoin phenylhydrazone methyl ether, 70960-68-8; *syn*-benzoin phenylhydrazone ethyl ether, 70960-69-9; *anti*-benzoin phenylhydrazone ethyl ether, 70960-70-2; *syn*-benzoin phenylhydrazone propyl ether, 70960-71-3; *anti*-benzoin phenylhydrazone propyl ether, 70960-72-4; *syn*-benzoin phenylhydrazone isopropyl ether, 70960-73-5; *anti*-benzoin phenylhydrazone isopropyl ether, 70960-74-6; *syn*-benzoin phenylhydrazone butyl ether, 70960-75-7; *anti*-benzoin phenylhydrazone butyl ether, 70960-76-8; benzoin phenylhydrazone *sec*-butyl ether, 75717-42-9; *syn*-benzoin phenylhydrazone phenyl ether, 75717-43-0; *anti*-benzoin phenylhydrazone phenyl ether, 75717-44-1; *syn*-benzoin phenylhydrazone, 574-08-3; *anti*-benzoin phenylhydrazone, 574-07-2; benzoin, 119-53-9; benzoin ethyl ether, 574-09-4; benzaldehyde, 100-52-7; ethyl benzoate, 93-89-0.

(8) G. Henseke and H. Dalibor, *Chem. Ber.*, 88, 521 (1955).

Disproportionation in a Michael Addition Reaction

Shmaryahu Hoz* and Dov Speizman

Department of Chemistry, Bar-Ilan University, Ramat-Gan, Israel

Ben-Ami Feit,* Geula Djamal, and Uri Melamed

Department of Chemistry, Tel-Aviv University, Tel-Aviv, Israel

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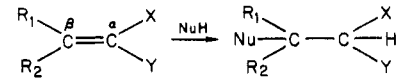
The Michael addition reaction is one of the most synthetically useful reactions.[1] In its normal mode, a nucleophilic attack on the β position of an activated olefin is followed by protonation of the intermediate carbanion to give the neutral adduct (eq 1). An interesting exception



(1)

to this general behavior was reported by Juchnovski et al.[2] The reaction of 1-nitro-1-cyano-2-phenylethylene with amines in ethanol resulted in the bis onium salt of 2,4-dinitro-3-phenylglutaric acid dinitrile instead of the expected normal adduct.[2] The mechanism suggested by Juchnovski involved the formation of the normal adduct

(1) Bergman, E. D.; Ginsburg, D.; Papp, R. *Org. React.* **1959**, *10*, 179.
(2) Demireva, Z. I.; Binev. I. G.; Juchnovski, I. N. *Tetrahedron Lett.* **1976**, 1523.

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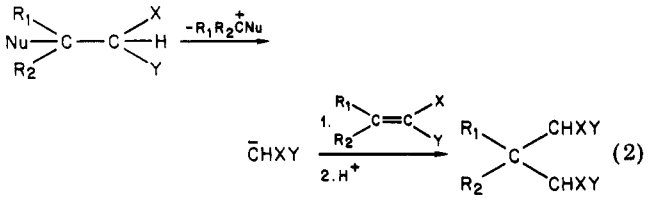
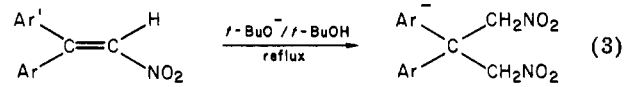
in the first step (eq 1, R_1 = H; R_2 = Ph; X = NO_2; Y = CN) followed by cleavage of the C_α–C_β bond to give the methide carbanion (CHXY) which further adds to the unreacted olefin (eq 2). (A referee has suggested that the



(2)

methide anion is furnished by a nucleophilic attack of a second nucleophile molecule on the adduct. This mechanism, however, is highly unlikely for the cases reported here since (a) carbon β is highly hindered sterically and is thus expected to be inactive in S_N2 processes, and (b) the decomposition of adducts of benzylidenemalononitrile with amines[3] and of 9-dinitromethylene fluorene with alcohols[4] clearly supports the mechanism suggested by Juchnovski et al. In less hindered systems, however, the "nucleophilic-assisted" cleavage of the adduct might prevail.) To the best of our knowledge, this is the only reported example of this variant of the Michael addition reaction.

In the course of our studies of certain aspects of vinyl carbanions[5] and nucleophilic reactivity toward highly activated olefins,[6] we have encountered two additional cases of this uncommon reaction. The first one was observed when 1,1-diaryl-2-nitroethylene (1) was reacted with potassium *tert*-butoxide in *tert*-butyl alcohol to yield the corresponding 1,3-dinitro-2,2-diarylpropane (2) (eq 3).

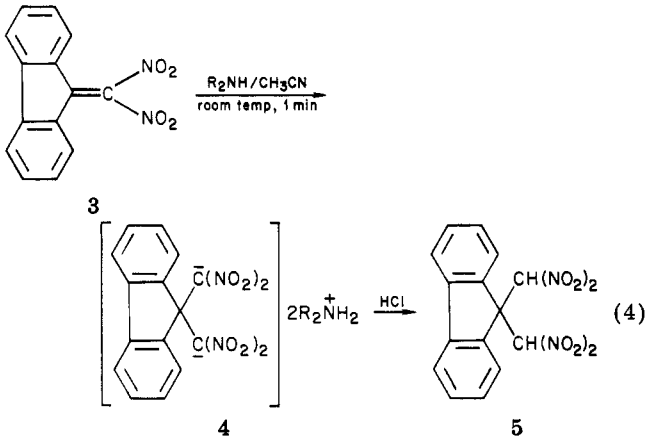


(3)

1a, Ar = Ar′ = Ph
b, Ar = Ph; Ar′ = *p*-CH_3OPh

2a, Ar = Ar′ = Ph
b, Ar = Ph; Ar′ = *p*-CH_3OPh

The second reaction was that of 9-(dinitromethylene)-fluorene (3) with secondary amines (Et_2NH or Bu_2NH) in acetonitrile (eq 4). When the reactants were mixed at



(4)

3 4 5

room temperature, a water-soluble yellow precipitate which was identified as the bis onium salt (4) was formed in less than 1 min. Acidification of this salt gave 9,9-bis(dinitromethyl)fluorene (5) in a high yield.

In order to determine the relative electrophilic reactivity of 1a and 3, we compared their reaction rate constants with CN^- as a nucleophile in Me_2SO. The second-order rate constant for the reaction of 3 is $(3.81 \pm 0.45) \times 10^5$ mol^{-1} s^{-1} [6] and that for the reaction of CN^- with 1a was found to be 0.45 ± 0.02 mol^{-1} s^{-1}. Thus 3 is more reactive than 1a by ca. 6 orders of magnitude. In spite of this very large difference in their reactivity, the two substrates exhibit the same type of behavior in the Michael addition reaction. This observation indicates that the reaction pathway originally reported by Juchnovski et al.[2] is not necessarily limited to a unique single case but rather operates over a large range of olefinic compounds provided that certain conditions are met.

One of the most crucial conditions for this disproportionation to take place is that the initially formed adduct will undergo a heterolytic cleavage (see eq 2) which furnishes the methidic nucleophile ($^-$CHXY). Thus it is not very likely that an olefin activated by a single cyano group, for example, will follow this path, since, although the acetonitrile anion is capable of participating in the Michael addition reaction,[7] it will probably not be cleaved from the primary adduct under normal conditions. Another necessary requirement is that in cases where the olefinic substrate concentration is not considerably larger than that of the nucleophile, the affinity of the methide anion toward the double bond will exceed that of any other nucleophile present in the solution.

The broad operational range of this reaction is due at least in part to the fact that the same groups which activate the double bond also determine the nucleophilic reactivity of the methidic nucleophile. The effect on the two species, however, is essentially in opposite directions. Strongly electron-withdrawing groups will activate the double bond but will at the same time reduce the activity of the methidic nucleophile. As the rate of the product-determining step is governed by a combination of the activities of the two reactants, a change in the activating group might effectively be canceled out due to these opposing effects, thus enabling various substrates with different activating groups to remain within the domain where this mechanism is operative.

Experimental Section

Starting Materials. 1,1-Diaryl-2-nitroethylene (1a and 1b) and 9-(dinitromethylene)fluorene (3) were synthesized according to published procedures.[8,9]

Reaction of 1-Phenyl-1-(4-methoxyphenyl)-2-nitroethylene (1b) and 1,1-Diphenyl-2-nitroethylene (1a) with Potassium *tert*-butoxide. A 0.5 N solution of *t*-BuO^-K^+ in *t*-BuOH (10 mL, 5×10^{-3} mol) was added to a solution of 1b (1 g, 3.92×10^{-3} mol) in dry *t*-BuOH (80 mL). The mixture was refluxed for 60 min, then cooled, and acidified with an HCl–2-propanol solution. The precipitate formed was separated by filtration and the filtrate evaporated. The residue was extracted with ether, the ethereal extracts were washed with water and dried, and the ether was removed by evaporation. The residue recovered from the ethereal solution was separated by column chromatography over alumina. The products obtained were 4-methoxybenzophenone and 1,3-dinitro-2-phenyl-2-(4-methoxyphenyl)-1-propane (2b): 0.41 g (64%); mp 141 °C (from ethyl alcohol); mass spectrum, *m/e* 316 (M^+); NMR ($CDCl_3$) δ 3.64 (s, 3 H, OCH_3), 5.42 (s, 4 H, CH_2NO_2), 6.5–7.4 (m, 9 H, Ar H). Anal. Calcd for $C_{16}H_{16}N_2O_5$: C, 60.75; H, 5.10; N, 8.86. Found: C, 60.33; H, 5.30; N, 8.66.

(3) Bernasconi, C. F.; Fox, J. P., Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 2810.
(4) Hoz, S.; Perah, S., unpublished results.
(5) Melamed, U.; Feit, B. A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1228, 1232 and references cited therein.
(6) Hoz, S.; Speizman, D., *Tetrahedron Lett.* **1978**, 1775.
(7) Hoz., S.; Albeck, M.; Rappoport, Z. *Synthesis* **1975**, 162.
(8) Charles, G. *Bull. Soc. Chim.* **1963**, 1559.
(9) Gabitov, F. A.; Friedman, A. L., Nikolaeva, A. D. *Zh. Org. Khim.* **1969**, *5*, 2245.

2b was independently prepared by *tert*-buxoxide-catalyzed addition of nitromethane to **1b** in *t*-BuOH, according to a method previously described for other olefins.[10] The product obtained (33%) had mp 140–141 °C (from ethyl alcohol).

Under similar conditions, **1a** (0.88 g, 3.9×10^{-3} mol) gave 1,3-dinitro-2,2-diphenylpropane (**2a**): 0.28 g (51%); mp 198 °C (from ethyl alcohol); mass spectrum, 286 *m/e* (M^+); NMR δ ($CDCl_3$) 5.6 (s, 4 H, CH_2NO_2), 6.8–7.9 (m, 10 H, Ar H). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.78. Found: C, 62.37; H, 5.08; N, 9.64.

Reaction of a Secondary Amine with 9-(Dinitromethylene)fluorene (3). Diethylamine or di-*n*-butylamine (1.4×10^{-3} mol) was added to a solution of **3** (0.16 g, 0.6×10^{-3} mol) in acetonitrile (3 mL) at room temperature. The mixture was stirred for 0.5 min, during which time all the olefin dissolved, and the bis onium salt **4** precipitated: NMR (Me_2SO-d_6) of the diethylammonium salt δ 1.42 (t, 12 H), 3.21 (q, 8 H), 6.1 (s, 4 H), 7.5–8.2 (m, 8 H); mass spectrum, *m/e* 374 ($M^+ - 2Et_2NH$). The salt rapidly decomposed on standing. The reaction mixture was extracted with ether and aqueous NaOH. Fluorenone (0.03 g, 56%) was recovered from the ethereal extract. The aqueous solution was acidified and extracted with ether. The crude product recovered from the ethereal solution was crystallized to give 9,9-bis(dinitromethyl)fluorene (**5**): 0.10 g (90%); mp 156–157 °C (from chloroform); mass spectrum, *m/e* 374; NMR (CD_3CN) δ 7.6–7.1 (m, 8 H, Ar), 7.75 (s, 2 H, $CH(NO_2)_2$). Anal. Calcd for $C_{15}H_{10}N_4O_8$: C, 48.1; H, 2.7; N, 14.9. Found: C, 48.22; H, 2.7; N, 14.77.

Kinetic Measurements. Kinetic rate measurements of the reaction of **1a** with CN^- were carried out in Me_2SO (refluxed over CaH_2 and vacuum distilled),[11] using a 2400 Gilford spectrophotometer. The consumption of the olefinic starting material was monitored at 330 nm. The reaction was conducted under pseudo-first-order conditions (with respect to **1a**). Cyanide ion concentration ranged from 5×10^{-4} to 5×10^{-3} M. Substrate concentrations were ca. 10^{-5} M. The spectrophotometer was interfaced directly to a PDP 11/40 minicomputer for data aquisition and analysis. Correlation coefficients were better than 0.999 (eight determinations).

Registry No. **1a**, 5670-69-9; **1b**, 75700-13-9; **2a**, 75700-14-0; **2b**, 75700-15-1; 3, 25945-85-1; 4 bis(diethylamine) salt, 75700-17-3; 5, 75700-16-2; 4-methoxybenzophenone, 611-94-9.

(10) Schechter, H.; Ley, D. E.; Zeldin, L. *J. Am. Chem. Soc.* **1952**, *74*, 3664.

(11) Riddick, J. A.; Bunger, W. B. "Organic Solvents"; Wiley and Sons: New York, 1970, p 46.

Trifluoromethylated Steroidal C-17 Spirofuranones

Giorgio Ortar* and Enrico Morera

Centro di Studio per la Chimica del Farmaco del CNR, Istituto di Chimica Farmaceutica dell' Università, 00185 Roma, Italy

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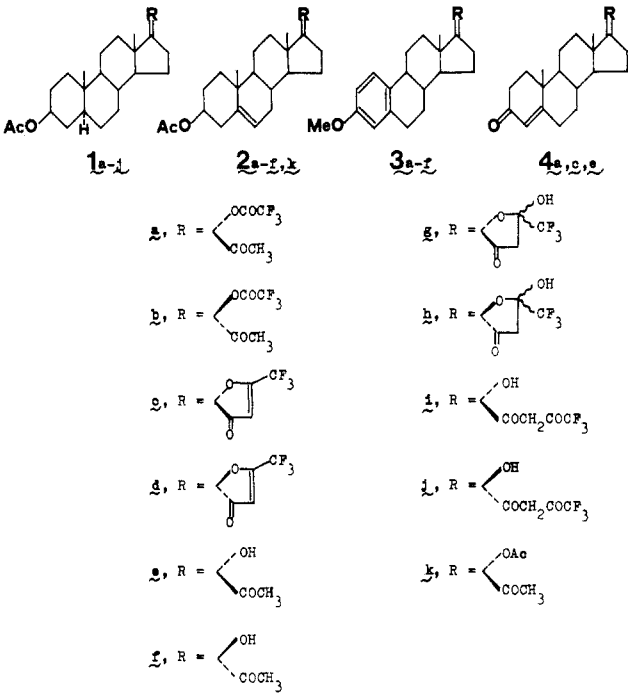
The development of new, relatively inexpensive methods for the introduction of a trifluoromethyl group into the steroid system is of considerable interest from both synthetic and pharmaceutical standpoints.[1]

In this context we describe here a simple, yet effective preparation of potentially useful 5′-(trifluoromethyl)spiro[steroid-17,2′(3′*H*)-furan]-3′-ones, the fluorinated analogues of a class of bioactive C-17 spirosteroids.[2]

(1) J. Fried and N. A. Abraham in "Organic Reactions in Steroid Chemistry", J. Fried and J. A. Edwards, Eds., Van Nostrand-Reinhold Co., 1972, Vol. 1, Chapter 8; G. H. Rasmusson, A. Chen, and G. E. Arth, *J. Org. Chem.*, **38**, 3670 (1973), and references therein; G. H. Rasmusson, R. D. Brown, and G. E. Arth, *J. Org. Chem.*, **40**, 672 (1975).

Chart I



The requisite substrates **1a,b**, **2a,b**, **3a,b**, and **4a** were all, except for **4a**,[3] readily prepared from the corresponding alcohols **1e,f**, **2e,f**, and **3e,f** with trifluoroacetic anhydride–pyridine at room temperature.

Treatment of **1a,b**–**4a** with a catalytic amount of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in refluxing benzene (Dean–Stark apparatus) afforded the spiro derivatives **1c,d**, **2c,d**, **3c,d**, and **4c** in 78–90% yields. The only isolable byproducts were the original alcohols **1e,f**–**4e** (see Chart I for structures).

The structure of all the C-17 spirofuranones followed from their analytical and spectral data.

Thus, both elemental analyses and mass spectra were consistent with the assumed composition. The IR spectra exhibited a band at 1705–1720 cm^{-1} characteristic of similar five-membered α,β-unsaturated ketones.[4] The ^1H NMR spectra showed a singlet[5] near δ 5.9 for one vinylic proton.

The above reaction conditions were found to be the most suitable ones to drive to completion the desired condensations and minimize hydrolytic cleavage of the labile trifluoroacetoxy group.

Substitution of potassium *tert*-butoxide for DBU gave, in the case of **1a**, the intermediate aldol-type product **1g** (vide infra) as the major component (62% yield) but no trace of **1c**.

Acidic catalysts proved to be completely inefficient since **1a**, when azeotropically refluxed in benzene in the presence of *p*-toluenesulfonic acid for 48 h, was recovered practically unchanged.

In contrast to the smooth conversion of **1a,b**–**4a**, the less electrophilic[6] 17-acetoxy derivative **2k** failed to undergo

(2) B. Patelli and R. Schiaky, French Patent, 1 384 204, Jan 4 (1965); *Chem. Abstr.*, **62**, 14789 (1965); G. Anner, German Offen., 2 109 154, Sept 23 (1971); *Chem. Abstr.*, **76**, 4078 (1972); A. A. Akhrem, F. A. Lakhvich, and V. A. Khripach, *Zh. Obshch. Khim.*, **45**, 2572 (1975); *Chem. Abstr.*, **84**, 90400 (1976); P. K Gupta, J. G. Ll. Jones, and E. Caspi, *J. Org. Chem.*, **40**, 1420 (1975); A. V. Kamernitskii, I. G. Reshetova, K. Yu. Chernyuk, *Isv. Akad. Nauk SSSR, Ser. Khim.*, **1**, 184 (1978); *Chem. Abstr.*, **89**, 43945 (1978).

(3) B. R. Samant and F. Swet, *J. Org. Chem.*, **42**, 1981 (1977).

(4) P. Margaretha, *Tetrahedron Lett.*, 4891 (1971); C. Venturello and R. D' Aloisio, *Synthesis*, 754 (1977).

(5) C-4′ H could be occasionally observed by careful sweep-width expansion as a partially resolved quartet with $J_{H,F} = 0.7$ Hz.

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