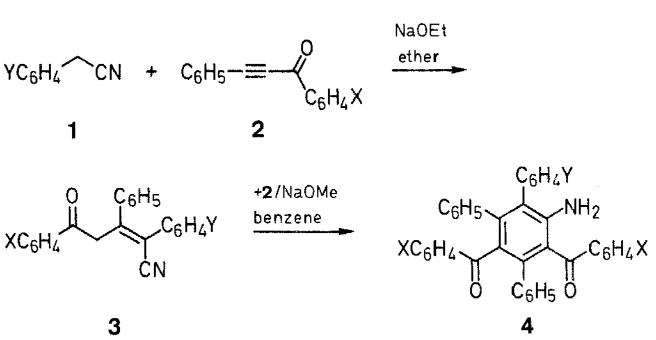
2,4-Diaroyl-3,5,6-triarylanilines from Addition of Benzyl Cyanides to Acetylenic Ketones

Fouli A. Fouli,[a] Ahmed S. A. Youssef,[a] John M. Vernon*[b]

[a] Department of Chemistry, Faculty of Science, Ain Shams University, Abbassia, Cairo, Egypt
[b] Department of Chemistry, University of York, Heslington, York YO1 5DD, GB

Benzyl cyanides **1a–c** react with acetylenic ketones **2a–c** in the presence of sodium alkoxides to afford 1:1 (2,3,5-triaryl-5-oxopent-2-enonitriles **3a–i**) and 1:2 adducts (2,4-diaroyl-3,5,6-triarylanilines **4a–i**).

The structure and *Z*-configuration of the 1:1 adduct **3a** obtained by base-catalysed Michael addition of benzyl cyanide (**1a**) to 1,3-diphenylprop-2-yn-1-one (**2a**) are already established.[1] We have found that **3a** and the analogous compounds **3b–i** are intermediates in a convenient synthesis of 2,4-diaroyl-3,5,6-triarylanilines **4a–i**. Whereas the 1:1 adducts **3a–i** are obtained from the benzyl cyanides **1a–c** and the acetylenic ketones **2a–c** with sodium ethoxide in dry ether, the 1:2 adducts **4a–i** are obtained in a single step, accompanied by lesser amounts of **3a–i**, from **1a–c** and **2a–c** in the presence of sodium methoxide in dry benzene (Scheme A).



1, 2	X, Y	1, 2	X, Y
a	H	c	4-Cl
b	4-OCH$_3$	d	4-NO$_2$

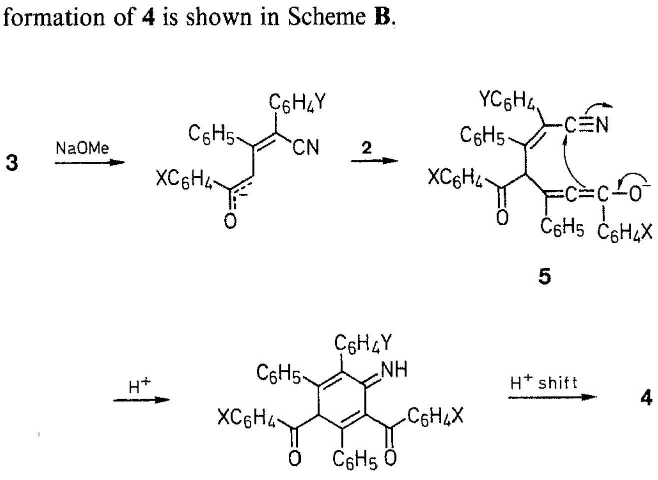
3, 4	X	Y	3, 4	X	Y
a	H	H	f	4-Cl	4-OCH$_3$
b	4-OCH$_3$	H	g	H	4-Cl
c	4-Cl	H	h	4-OCH$_3$	4-Cl
d	H	4-OCH$_3$	i	4-Cl	4-Cl
e	4-OCH$_3$	4-OCH$_3$			

Scheme A

The new 1:1 adducts **3b–i** all show IR absorptions for the conjugated nitrile group (2220 cm^{-1}) and for the aryl ketone (between 1670–1690 cm^{-1}). They all show a ^{1}H-NMR absorption for the COCH$_2$ group (δ = 4.6) (Table 1). In their mass spectra, the corresponding molecular ions are weak or very weak and the base peak is due to the appropriate acylium ion $XC_6H_4CO^+$ in each case.

Chemical and spectroscopic evidence supports the structures of the highly substituted aniline derivatives **4a–i** (Table 2). Their IR spectra show no absorption for a nitrile group, but instead two absorptions characteristic of a primary amine (between 3360–3500 cm^{-1}), as well as absorption in the carbonyl region (1630–1670 cm^{-1}). Their mass spectra show strong peaks for the corresponding molecular ions, as well as for fragment ions $[M-XC_6H_4]^+$ and $XC_6H_4CO^+$. They are further characterized by diazotisation and coupling with alkaline 2-naphthol, and by acetylation of **4f** to give the corresponding acetanilide derivative.

Our expectation that the 1:2 adducts **4** are formed via further reaction of the 1:1 adducts **3** with the acetylenic ketones **2** was confirmed when **4f** was obtained from **3f** and **2c** in the presence of sodium methoxide. A mechanism suggested to account for the formation of **4** is shown in Scheme **B**.



Scheme B

Table 1. 2,3,5-Triaryl-5-oxopent-2-enonitriles 3 Prepared

Product	Yield[a] (%)	mp[b] (°C)	Molecular Formula[c] or Lit. mp (°C)	UV (C$_2$H$_5$OH) λ_{max} (nm) (log ε)	^{1}H-NMR (CDCl$_3$/TMS) δ OCH$_3$ (s)	CH$_2$ (s)	aromatic (m)
3a	20	138–139	138–139[1]	–			
3b	27	119–120	$C_{24}H_{19}NO_2$ (353.4)	280 (4.47), 221 (4.39)	3.85	4.58	6.9–8.0
3c	45	111–112	$C_{23}H_{16}ClNO$ (357.8)	280 (4.10), 253 (4.42), 226 (4.26)	–	4.60	7.1–8.1
3d	12	121–122	$C_{24}H_{19}NO_2$ (353.4)	296 (4.00), 238 (4.44)	3.74	4.60	6.6–8.0
3e	11	128–129	$C_{25}H_{21}NO_3$ (383.4)	280 (4.36), 230 (4.39)	3.74	4.65	6.6–8.0
3f	11	112–113	$C_{24}H_{18}ClNO_2$ (387.9)	298 (4.30), 254 (4.69)	3.74, 3.79	4.56	6.6–8.0
3g	45	111–112	$C_{23}H_{16}ClNO$ (357.8)	280 (4.24), 236 (4.57)	–	4.60	6.8–8.1
3h	11	145–146	$C_{24}H_{18}ClNO_2$ (387.9)	280 (4.48), 222 (4.42)	3.90	4.60	6.9–8.2
3i	11	139–140	$C_{23}H_{15}Cl_2NO$ (392.3)	274 (4.27), 252 (4.59), 228 (4.46)	–	4.57	7.0–8.0

[a] After recrystallization.
[b] Uncorrected.
[c] Satisfactory microanalyses obtained: C ±0.3, H ±0.3, N ±0.2.

Table 2. 2,4-Diaroyl-3,5,6-triarylanilines **4** Prepared

Product	Yield[a] (%)	mp[b] (°C)	Molecular Formula[c]	UV (C_2H_5OH) λ_{max} (nm) (log ε)	^{1}H-NMR ($CDCl_3$/TMS) δ OCH$_3$ (s)	NH$_2$ (br)	aromatic (m)	MS[d] m/z (%)
4a	27	197.5–198.5	$C_{38}H_{27}NO_2$ (529.6)	350 (3.30), 298 (3.78), 232 (4.59)	–	4.46	6.7–7.6	529 (100), 452 (31), 105 (100), 77 (82)
4b	23	204–205	$C_{40}H_{31}NO_4$ (589.7)	300 (3.41), 294 (4.51), 268 (4.41), 257 (4.35), 223 (4.70)	3.71 3.76	4.25	6.5–7.7	589 (100), 482 (12), 454 (10)
4c	34	240–241	$C_{38}H_{25}Cl_2NO_2$ (598.5)	354 (3.94), 258 (4.81), 250 (4.81), 234 (4.83)	–	4.52	6.6–7.7	601 (7), 599 (40), 597 (60), 460 (7), 458 (22), 141 (34), 139 (100), 113 (9), 111 (28)
4d	42	187–188	$C_{39}H_{29}NO_3$ (559.6)	356 (3.67), 296 (4.11), 236 (4.86)	3.67	4.37	6.6–7.8	559 (95), 482 (30), 105 (100), 77 (32)
4e	11	209–210	$C_{41}H_{33}NO_6$ (619.7)	356 (3.55), 290 (4.75), 270 (4.67), 224 (4.93)	3.68 3.71	4.28	6.5–7.8	619 (100), 135 (35)
4f	41	217–218	$C_{38}H_{27}Cl_2NO_3$ (628.5)	360 (4.08), 260 (4.86), 235 (3.94)	3.75	4.55	6.5–7.7	631 (12), 629 (60), 627 (85), 518 (7), 516 (20), 141 (34), 139 (100), 113 (7), 111 (21)
4g	34	212–213	$C_{38}H_{26}ClNO_2$ (564.1)	346 (3.91), 294 (4.43), 231 (5.17)	–	4.20	6.7–7.8	565 (23), 563 (68), 488 (7), 486 (21), 105 (75), 77 (100)
4h	41	236–237	$C_{40}H_{30}ClNO_4$ (624.1)	358 (3.54), 294 (4.57), 270 (4.51), 255 (4.45), 224 (4.78)	3.75	4.20	6.5–7.8	625 (7), 623 (20), 518 (7), 516 (21), 135 (100), 107 (13), 77 (27)
4i	51	229–230	$C_{38}H_{24}Cl_3NO_2$ (633.0)	356 (3.49), 256 (4.79), 232 (5.00)	–	4.48	6.8–7.5	637 (3), 635 (24), 633 (100), 631 (91), 524 (2), 522 (14), 520 (22), 141 (35), 139 (100), 113 (12), 111 (36)

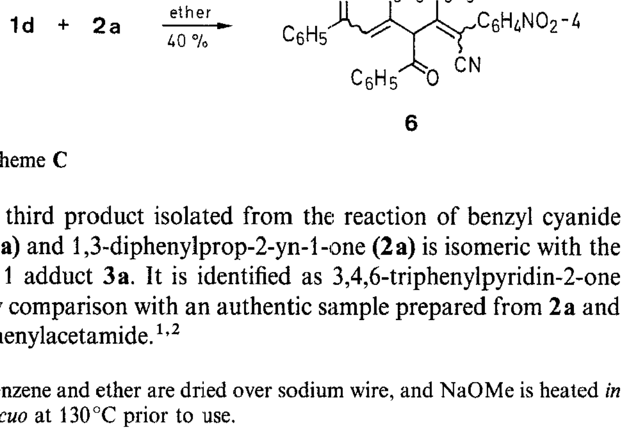
[a] After recrystallization.

[b] Uncorrected.

[c] Satisfactory microanalyses obtained: C ±0.3, H ±0.3, N ±0.2.

[d] By electron impact at 70 eV.

Interestingly, 4-nitrobenzyl cyanide (**1d**) behaves differently from **1a–c** and affords with **2a** in the presence of sodium ethoxide in ether the open-chain 1 : 2 adduct **6** (Scheme C). The conjugate base of **6** is additionally stabilized by the nitro group, which may account for the usual cyclisation shown in structure **5** not occurring in this case.



Scheme C

A third product isolated from the reaction of benzyl cyanide (**1a**) and 1,3-diphenylprop-2-yn-1-one (**2a**) is isomeric with the 1 : 1 adduct **3a**. It is identified as 3,4,6-triphenylpyridin-2-one by comparison with an authentic sample prepared from **2a** and phenylacetamide.[1,2]

Benzene and ether are dried over sodium wire, and NaOMe is heated *in vacuo* at 130 °C prior to use.

Phenylacetylene is treated with ethylmagnesium bromide in dry ether and then with benzaldehyde, *p*-anisaldehyde, and *p*-chlorobenzaldehyde, to give 1-aryl-3-phenylprop-2-yn-1-ols, which are oxidized to the corresponding acetylenic ketones **2a–c**, respectively, with chromic acid.[3]

Reaction of Benzyl Cyanides 1a–d with Acetylenic Ketones 2a–c; General Procedures:

Method A: The benzyl cyanide **1** (5 mmol) and acetylenic ketone **2** (5 mmol) are added successively to a stirred suspension of NaOEt (5 mmol) in dry benzene (15 mL). An exothermic reaction occurs, accompanied by the formation of a dark red colour. The mixture is heated at 100 °C under reflux for 10 min, then cooled and filtered. The cake of red solid is further washed with dil. HCl until the red colour is discharged, and then extracted with ether. After drying ($MgSO_4$), the 2,3,5-triaryl-5-oxopent-2-enonitriles **3a–i** are obtained by evaporation of the ether and recrystallization of the residue from petroleum ether (80–100 °C) [except **3a** from cyclohexane and **3i** from petroleum ether (80–100 °C)/benzene].

The benzene mother liquor is further worked up by pouring into water, acidifying with dil. HCl, shaking, and extracting with ether. The combined benzene ether extract is washed, dried ($MgSO_4$), and evaporated *in vacuo*. The residue solidifies on standing or on trituration with MeOH, affording the 2,4-diaroyl-3,5,6-triarylanilines, which are recrystallized from aqueous EtOH (**4a, f**), EtOH (**4d, e**), benzene (4 h), petroleum ether (80–100 °C) (**4i**), or petroleum ether (80–100 °C)/benzene (**4b, c, g**).

Method B: The benzyl cyanide **1** (5 mmol) and acetylenic ketone **2** (5 mmol) are added successively to a stirred suspension of NaOEt (5 mmol) in dry ether (50 mL). The mixture is stirred for 2 days, then poured onto water, and acidified with dil. HCl. The ether layer is separated, washed with aqueous $NaHCO_3$, then with water, dried ($MgSO_4$), and the ether evaporated. Crystallization of the residue from petroleum ether (80–100 °C) affords the 1 : 1 adducts **3a–i** identical with those prepared by Method A. Acidification of the $NaHCO_3$ washings gives, in some cases, smaller amounts of the corresponding benzoic acid resulting from hydrolysis of **2a–c**.

3,4,6-Triphenyl-1H-pyridin-2-one: This is obtained as a by-product from the reaction of **1a** with **2a** from the same fraction of crude product which contains **4a**, by chromatography on activated alumina; yield: 20%, mp 301–302 °C (EtOH), not depressed on admixture with an authentic sample (Lit.[4] mp 300–301 °C).

Qualitative Test for Substituted Anilines **4**: Compound **4** is diazotized by treatment with dil. HCl and aqueous $NaNO_2$ at 0 °C and then coupled with an excess of alkaline 2-naphthol to give red or brown precipitate of azo dyes.

Derivatization of **4**; *Acetylation of* **4f**: Compound **4f** is acetylated by heating with acetic anhydride to give the corresponding acetanilide derivative; mp 160–161 °C (petroleum ether, 80–100 °C).

$C_{41}H_{29}Cl_2NO_4$	calc.	C 73.43	H 4.36	N 2.09
(670.6)	found	73.74	4.59	2.18

IR (nujol): ν = 3400 br (NH), 1725, 1680, 1640 cm^{-1} (C=O).

^{1}H-NMR(CDCl$_3$/TMS): δ = 1.68 (s, 3H, CH$_3$); 3.78 (s, 3H, OCH$_3$); 6.65–7.65 (m, 23 H$_{arom}$).

MS: *m/z* (%) = 673, 671, 679 (M$^+$, 4, 26, 36); 629, 627 (17, 25); 532, 530 (M – ClC$_6$H$_4$CO, 12, 36); *516 (11)*; *141, 139* (*p*-ClC$_6$H$_4$CO$^+$, *31, 100)*; 113, 111 (*p*-ClC$_6$H$_4$$^+$, 8, 25).

Preparation of **4f** *from* **3f**: The 1:1 adduct **3f** (97 mg, 2.5 mmol, obtained from **1b** and **2c**) and **2c** (60 mg, 2.5 mmol) are allowed to react in the presence of NaOMe (13 mg, 2.5 mmol) in dry benzene (25 mL). After 2 days, the mixture is worked up as given above for Method A. The crude product is chromatographed on activated alumina, *using petroleum ether (40–60 °C)/ether (1: 1) as eluent; mp 218 °C*, identical with the sample obtained in one step.

4-Benzoyl-2-*p*-nitrophenyl-7-oxo-3,5,7-triphenylhepta-2,5-dienonitrile (6):

From the reaction of 4-nitrobenzyl cyanide (**1d**) and 1,3-diphenylprop-2-yn-1-one (**2a**) by method B, the crude product obtained after evaporation of ether is an oil, which crystallizes on trituration with MeOH. The solid is recrystallized from petroleum ether (80–100 °C)/benzene to give **6**; yield: 40%; mp 196–197 °C.

$C_{38}H_{26}N_2O_4$	calc.	C 79.42	H 4.56	N 4.87
(574.6)	found	79.42	4.96	4.60

IR (nujol): ν = 2200 (C≡N), 1665, 1690 cm^{-1} (C=O).

^{1}H-NMR (CDCl$_3$/TMS): δ = 6.21, 6.28 (2s, 1H each, =CH); 6.8–8.0 (m, 24 H$_{arom}$).

MS: *m/z* (%) = 574 (M$^+$, 20); 497 (M – C$_6$H$_5$, 12); 469 (M – C$_6$H$_5$CO, 16); 105 (C$_6$H$_5$CO$^+$, 100); 77 (C$_6$H$_5$$^+$, 57).

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